Foresight Marine Panel

Marine Biotechnology Group

A STUDY INTO THE PROSPECTS FOR MARINE BIOTECHNOLOGY DEVELOPMENT IN THE UNITED KINGDOM

VOLUME 1 - STRATEGY

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ABBREVIATIONS

AIMS	Australian Institute for Marine Science
BBSRC	Biotechnology and Biological Sciences Research Council
CCAP	The Culture Collection of Algae and Protozoa
DEFRA	Department for Environment, Food and Rural Affairs
DFES	Department for Education and Skills
DTI	Department of Trade and Industry
ECF	Enterprise Capital Fund
ECMB	European Centre for Marine Biotechnology, Dunstaffnage
EIS	Enterprise Investment Scheme
EPSRC	Engineering and Physical Sciences Research Council
ESF	European Science Foundation
EU	European Union
FP6	The EU's Framework Programme 6, of Research and Technology Development
GVA	Gross Value Added
HEFCE	Higher Education Funding Council of England
HEI	Higher Education Institution
HEIF	Higher Education Innovation Fund
HIE	Highlands & Islands Enterprise
IACMST	Inter-Agency Committee on Marine Science and Technology
IP	Intellectual property
ITI	Intermediary Technology Institute
KTN, KTP	Knowledge Transfer Networks and Partnerships
LEC	SE Local Enterprise Company
M&FMB	NERC Marine and Freshwater Microbial Biodiversity programme
MBA	Marine Biological Association of the UK

MBG	Fore*sight* Marine Panel - Marine Biotechnology Group
MDIS	Medical Devices in Scotland
MRC	Medical Research Council
MSTP	the proposed Plymouth Marine Science and Technology Park
NERC	Natural Environment Research Council
NESTA	National Endowment for Science, Technology and the Arts
NGO	Non-Governmental Organisation
NHS	National Health Service
NNFCC	National Non-Food Crops Centre
OST	Office of Science and Technology, DTI
PML	Plymouth Marine Laboratory
PMSP	Plymouth Marine Sciences Partnership
PSRE	Public Sector Research Establishment
R&D	Research & Development
RCUK	Research Councils UK
RDA	Regional Development Agency
RSE	Royal Society of Edinburgh
RVCF	Regional Venture Capital Fund
SAMS	Scottish Association for Marine Science
SBRI	Small Business Research Initiative
SBS	DTI's Small Business Service
SE	Scottish Enterprise
SEERAD	Scottish Executive Environment and Rural Affairs Department
SME	Small and medium-sized enterprise
SRIF	Science Research Infrastructure Fund

EXECUTIVE SUMMARY

Marine biotechnology in the UK has huge potential for innovative, sustainable development. Marine biotechnology is unlike other areas of biotechnology in that it is defined in terms of its source material, rather than the market it serves. It is best described as the use of marine organisms, at the whole, cell, or molecular level, to provide solutions, thereby benefiting society.

With a global market valued at $2.4 billion in 2002, and a predicted growth rate exceeding 10% per annum over the next three years, there is no doubting that marine biotechnology represents one of the most exciting emerging technology sectors. Marine biotechnology will contribute to nearly every industry sector, from healthcare to bioremediation and from cosmetics to nutraceuticals. The time to invest in the underpinning science, knowledge networks, and public understanding of this major biotechnology field has now arrived.

The UK is well placed to maximise the potential afforded by marine biotechnology due to its maritime heritage with an extensive coastline and easy access to diverse marine habitats. The foundations for a thriving community are in place through a number of geographically dispersed centres of excellence, scientific endeavour in a number of key areas, and a small, but growing, company base.

This report highlights some key areas that would allow this novel sector to mature and flourish:

- A more co-ordinated approach between the research base, entrepreneurial enterprise and the large pharma, biochemical and food multinational companies.
- The integrated use of Research Council funding and the new initiatives offered by Government to promote and encourage innovation.
- Training of researchers and public appreciation of the innovation, sustainability, legal framework[1] of marine biotechnology.

The key issues facing the UK marine biotechnology sector are:

- Developing stable financial investment.
- Creating productive communication between the marine biotechnology community and the private and public sectors.
- Delivering to the industrial sector development leads that are needed and for which they are willing to pay.
- Educating and training the people to make this possible.
- Promoting, marketing and positioning the marine biotechnology sector in a distinctive way.

Through analysis of marine biotechnology prospects in the UK, five areas of activity are identified, with a key recommendation for action attributed to each one:

Maintaining and developing the R&D base: The Foresight Marine Panel - Marine Biotechnology Group will consider further, in collaboration with a network of researchers

[1] Owen, D., 2004. A Study into the Legal Framework for Marine Biotechnology Development in the United Kingdom, Report commissioned by the Foresight Marine Panel - Marine Biotechnology Group, sponsored by Defra. ISBN 0 906940 43 5

and companies already established in the sector, the strengthening of one or more centres of excellence in discussion with appropriate bodies (e.g. RCUK - Research Councils UK, DTI and regional development and enterprise agencies).

Sustaining networks: By building on existing funded networking activities by the research councils, such as the NERC M&FMB (Marine & Freshwater Microbial Biodiversity) programme, and using new initiatives, for example a Knowledge Transfer Network under the DTI's Technology Programme, to develop a pan-UK approach to marine biotechnology.

Commercialisation and funding: The FMP-Marine Biotechnology Group will develop a register of interested venture capitalists, and garner support from biotechnology trade associations (e.g. the BIA), to develop a portfolio of funding opportunities, with the help of the DTI.

These three objectives are underpinned by:

Scientific Understanding of Marine Biotechnology and Marketing: New initiatives in public understanding of science will be harnessed to develop readily accessible information that fulfils promotion, PR and marketing objectives.

Stimulate training and education: Working with the Funding Councils and Research Councils, the FMP-Marine Biotechnology Group will seek to identify opportunities for modular cross-institution courses in marine biotechnology, including specialist technical skills training.

By adopting these key recommendations identified in this Marine Biotechnology Prospects Study a focussed strategy for novel and innovative marine biotechnological development in the UK will be realised. "We want the UK to be a key knowledge hub in the global economy, with a reputation not only for world-class scientific and technological discovery but also for turning that knowledge into new and profitable products and services."

The Rt Hon Tony Blair, Prime Minister

The Innovation Report (DTI – December 2003) [2]

Examples of marine biotechnology applications:

- The potential for marine natural products as pharmaceuticals was first developed in the 1950s which led to two marine-derived pharmaceuticals that are still in use today. Ara-C is an anti-cancer drug (used against acute myelocytic leukemia and non-Hodgkin's lymphoma) and Ara-A used as an antiviral drug for treating herpes. Both these drugs were derived from natural compounds found in sponges off the coast of Florida. Sponges have provided over 30% of the 5,000 + chemical compounds derived from marine organisms to date.
- More recently, Vent™ DNA polymerase has been isolated from microorganisms living around deep-sea hydrothermal vents. Polymerase Chain Reaction (PCR) is used to amplify very small amounts of DNA or RNA, and forms the basic process

[2] DTI Innovation Report "Competing in the global economy: the innovation challenge" DTI. December 2003 URN 03/1607. Further information available at www.innovation.gov.uk.

behind the gene mapping for the Human Genome Project. PCR requires enzymes that are stable at high temperature, precisely the conditions that the Vent™ DNA microorganism has become adapted to.

- Nutraceuticals, or nutritional supplements, is a major growth area for the large pharma companies. Marine microalgae are known to produce high levels of the fatty acids, docosahexenoic acid (DHA) and arachidonic acid (ARA), both of which are found at high level in breast milk. Because these polyunsaturated fatty acids (PUFAs) have been linked to brain grey matter development, they are regarded as an important nutritional supplement, especially for infants. One such product, developed by Martek Biosciences in the USA, is a market leader.

1. INTRODUCTION

1.1 This Study

This work was commissioned by the UK Fore*sight* Marine Panel's Marine Biotechnology Group (MBG). It includes information gathered to profile the sector, within UK and in an international context, to provide an overview of market opportunities and to explore strategic options (see **Volume 2** for fuller information). This volume analyses these in a strategic context and includes responses to the interim outcomes from people active in research and commercial development (see **Chapter 5** and **Annex E**). Given the resources available to fund this project, the report cannot be exhaustive. However, the approaches and material collected during the work should form a very useful starting-point for more detailed work during application of a co-ordinated strategy which would allow the UK's marine biosciences and biotechnology community to rise to the challenges presented in the short term and move ahead of other countries in the medium-term.

This study was based on information gathered by BioBridge Ltd during the course of this project from desk research, material to-hand, contacts, and as a result of the workshop/brainstorm on 8 March 2004, a project meeting on 18 May and a project workshop on 7 September 2004. The information has been generated by BioBridge Ltd except where it is directly attributed.

1.2 A Definition of Marine Biotechnology

An early question is a definition of marine biotechnology, which is currently origin-defined in a way that may give the impression that it can only take place in or near the sea, or be applied to oceanic activities. Other biotechnology is defined in terms of the end-market applications – food biotech, healthcare biotech, agribiotechnology for example, which tends to make utility to these sectors less of a question. For this project, we chose as our definition of marine biotechnology the following:

"Marine biotechnology is the use of marine organisms, at the whole, cell, or molecular level, to provide solutions, thereby benefiting society."

The sector has also been defined[3] in a way that focuses more on the end-uses, as:

"biotechnology with marine organisms, feeding into aquaculture, marine animal and fish health, marine natural products (including medicines), biofilms, bioremediation, marine ecology and bio-oceanography and other marine products (e.g. enzymes)"

[3] *UK Marine Industries World Export Market Potential* October 2000, Douglas-Westwood Associates for the Fore*sight* Marine Panel

In this report, the term ‘marine biotechnology’ is taken to include aspects of marine biology and other marine sciences necessary for the exploitation of living marine resources, but excluding fisheries and conventional aquaculture. For the purposes of the project we have removed vertebrates from the scope. We have also excluded genetically-modified animals, though including in the work some consideration of the use of genetically-improved micro-organisms and processes involving these, as a potential way forward for the constructive use of marine resources.

1.3 Vision and Goals

Explicitly stated goals are important for the focus of all players in the sector and are a cornerstone of co-ordinated action. In the case of UK marine biotechnology, developing a mission statement is rather complex, due to the variety of technology streams constituting the output of research and the range of potential end-markets.

Examples might include:

- To be the fastest-growing sector of biotechnology in the UK in terms of project funding and trained researchers
- To be Number 1 in Europe for productive marine biotechnology research by 2010
- To be Number 1 in Europe for exploitation of marine outputs, using marine biotechnology
- To make ECMB (European Centre for Marine Biotechnology) and Plymouth MSTP (Marine Science and Technology Park) the pre-eminent places in Europe for national and international, multi-disciplinary research, and effective technology transfer
- To put UK marine biotechnology on the same level as conventional biotechnology, as a source of new products and processes for other industrial sectors, within 5 years
- By the year 2010, to establish three centres of excellence in marine biotechnology, in Scotland, North of England and South of England
- Of the additional £80 million allocated to the Research Councils in the 2004 spending review, marine biotechnology will aim to secure £4-5 million
- Of the average 5.8% annual growth rate in science funding from 2004 to 2008[4], marine biotechnology should aim to utilise 15-20%
- By 2010, Marine Biotechnology R&D will have contributed 20 new products and spun out 10 new companies in the UK.

Marine bioscience activities should be seen as strategic in a broader context than programmes for monitoring biodiversity that ultimately serve large-scale policies for sustainable management of the seas. Marine biotechnology can contribute to economic development at regional and national level. The costs of establishing marine biotechnology as a productive component of wealth creation do not seem insurmountably high, based on the costs of some of the development instruments

[4] *Science & innovation investment framework* 2004-2014 July 2004 HM Treasury, DTI, DfES, page 8

reviewed in **Annex D** and given that the instruments are largely in place that will assist both scientific and economic development.

2. PROSPECTS FOR MARINE BIOTECHNOLOGY

2.1 Commercial Prospects – Potential Market Size

Marine biotechnology can contribute to marine and non-marine sectors. The overall contribution of marine-related activities to the UK's economy in 1999-2000 has been estimated at £39 billion[5], largely in sectors such as engineering and leisure boating. On a national scale, important marine sectors include fish farming and processing, marine environmental activities and oil/gas extraction. The potential markets for marine biotechnology in these sectors have not been quantified.

An estimate for the eventual contribution of UK marine biotechnology activities to global trade has been provided by a recent report for the Fore*sight* Marine Panel[6]. This estimate of £2.0-2.6 billion is subject to two important *caveats*, that there must be development of added-value products and sufficient financial support to achieve exploitation. The report believes that, in the short-term, the market might evolve from £0.5 billion in 1999 to £1.5 billion by 2004, but does not go in any detail into which sectors might be the most productive and the potential UK contribution to this has not been quantified.[7]

A recent report[8] estimated the 2002 market for marine biotechnology products and processes at $2.4 billion[9], 1/3 in the USA and 2/3 elsewhere, and projected growth of about 6% p.a. 1999-2007, accelerating to 9% p.a. in the 02-07 period.

TABLE 1: PRODUCTS FROM MARINE BIOTECHNOLOGY - ESTIMATES OF WORLD MARKETS[10]

REGION	YEAR AND MARKET £ MILLIONS					AVERAGE Annual Increase
	1999	2000	2001	2002	2007	
USA	310	350	405	450	570	4.7%
REST OF WORLD	745	795	855	920	1250	6.4%
TOTAL	1055	1145	1260	1370	1820	5.9%

This overall estimate includes existing products from marine sources produced using new technologies as well as products such as novel bioadhesives, novel bioactives, for which the risks of failure are quite high.

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5 A New Analysis of Marine-Related Activities in the UK Economy with Supporting Science and Technology August 2002, David Pugh & Leonard Skinner for IACMST

6 *UK Marine Industries World Export Market Potential*, D Westwood for the Fore*sight* Marine Panel 2000, ISBN 1-902536-38-X p7

7 UK Marine Industries World Export Market Potential October 2000, Douglas-Westwood Associates for the Foresight Marine Panel

8 Biomaterials from Marine Sources, Business Communications Company Inc Report No. RC-184R, February 2003

9 £1.4 billion at $1.78 = £1.00 (2004 rates), which is used for all subsequent data

10 Source: Business Communications Company 2003

Nevertheless, we believe that the UK's marine biotechnology has a tremendous potential to contribute to the UK, in export terms, as part of the UK's excellent science base and as a driver for regional and national economic development. The overview of market opportunities (here and **Volume 2**) demonstrated that if even a fraction of possibilities for new molecules from the sea could be successfully addressed, there were sufficiently promising markets to make the effort worthwhile to develop and commercialise these marine outputs.

The table below is not intended to indicate the eventual sales of products and raw materials of marine origin, but it demonstrates that there are substantial and significant markets where the characteristics of known products of marine biotechnology can make some contribution to new products.

TABLE 2: POTENTIALLY ACCESSIBLE MARKET SECTORS FOR UK MARINE BIOTECHNOLOGY

Sectors	Value per Annum (circa)
cosmetics skin care, sun care, hair care	£47 billion
raw materials chondroitin, glucosamine, chitosan	£1.34 billion
pharmaceuticals pain-killers, anti-cancer, anti-inflammatories, anti-infectives	£22.5 billion
medical devices/biomaterials hydrogels, colloids, cytotoxins	£0.6 - £1.0 billion
Tissue engineering	£0.6 - £1.0 billion
diagnostics enzymes, biochemicals, chemicals	£1.0 billion
Agrochemicals	£17 billion
industrial and specialty enzymes	£2.0 billion
environmental monitoring and remediation, bioengineering and bioprocess	not estimated

Notes: $1.78 = £1.00; estimate for marine materials as components of tissue engineered products given as 5% of total estimate; data relates to various years in period 2000-2003; industrial enzymes est Diversa Corp

2.2 Potential Applications

The range of sectors and potential applications is very wide – the list below in Table 2 is not exhaustive. In addition there is the potential for exploitation of techniques, instrumentation, equipment, engineered products and IT systems that have been developed to assist marine bioscience R&D in other areas. The potential markets for the products of marine biotechnology are expanded upon later in this Chapter. This underlines the need for either strategic focus or the development of a structure (such as a network or platform) that will allow productive discussions between these diverse elements of industry and the academic and institutional research efforts that feed into them, to make best use of the UK's expertise.

TABLE 3: SECTORS IN WHICH MARINE BIOTECHNOLOGY CAN MAKE A CONTRIBUTION

SECTOR	POTENTIAL CONTRIBUTIONS
FOODS	• new colorants, anti-oxidants, texturing agents, preservatives • enzymes for food processing • edible coatings for foods • functional foods for general healthy lifestyles
NUTRACEUTICALS	• specific targets – e.g. heart, joints, osteoporosis • calcium products and other trace elements • anti-oxidants, astaxanthin, carotenoids • marine organisms as probiotics
MEDICINE	• pain management products • anti-inflammatory agents • anti-infectives • growth factors • hormones • anti-viral agents • anti-cancer agents
HEALTHCARE	• biomaterials, including biopolymers and bioceramics • novel adhesives • biocompatible anti-adhesion coatings for vascular devices • anti-fouling agents for implants and catheters • components of medical devices • encapsulating drug delivery systems
COSMETICS	• collagens • anti-oxidants and sunscreens • revitalisers and anti-ageing products
RESEARCH TOOLS	• reagents including enzymes • bioactive molecules for growth media • new tools for discovery and testing • libraries of organisms and extracts • model organisms for safety and toxicity tests • marker genes and gene products for molecular biology research
PROCESSING TECHNOLOGIES	• extremophile management • improved bioreactor technology • improved purification methods and reagents
NEW ENERGY SOURCES	• light-capture • microbial batteries • energy-rich oils • hydrogen-producers
AGRICULTURAL	• seed coatings • pesticides, such as toxin from nereid worms or insecticide from sponges • additives, proteins and oils as animal feed ingredients • probiotic organisms in aquaculture • new vaccines and disease control in aquaculture

TABLE 3: CONT

SECTOR	POTENTIAL CONTRIBUTIONS
INDUSTRIAL	• novel adhesives • foams for oil industry and other surfactants • non-polluting metal extraction • anti-fouling materials • polymers for general use, thickeners and coatings for textiles and paper • new enzymes for chemical, food, household and other industries • ceramic materials • organisms and wastes as feedstock for biotech and chemical processes • nanotechnological developments
FOOD SAFETY	• diagnostics for toxins in seafood • materials for preserving and decontaminating foods and feeds
ENVIRONMENT ENHANCEMENT	• pollutant and toxin detection and removal by biocatalysis or digestion • desalination • metal removal and retrieval from soils, water and mining • marine phage viricides for use in microbial films

It has been possible to identify certain nearer-term targets for UK's marine biotechnology, partly from the recent activities of the Technology Translator within the NERC's M&FMB programme and partly from our broad approach to end-user markets. Realistic early candidates are applications of biofilm knowledge in anti-fouling, applications of marine viruses and new enzymes for biocatalysis. Applying the UK's excellent expertise in marine microbes is also a realistic opportunity, including screening marine actinomycetes for new bioactives. In the longer-term, investigating the potential for marine bioactives in treatment of cell dysfunctions is attractive, since it extends beyond the current preoccupation with cancer to other important therapeutic sectors such as acute and chronic inflammatory diseases, auto-immune diseases and regulating the normal turnover of cells, which would be helpful in supporting skin, intestine and other tissues as they age.

The following section reviews the following sectors and some opportunities within them:

- marine products as raw materials
- food, including health foods and nutraceuticals
- cosmetics
- pharmaceuticals
- medical devices and biomaterials
- regenerative medicine
- diagnostics
- research tools
- agriculture
- industrial uses

- environmental management
- bioengineering

2.3 Marine raw materials

Marine products are well-established in many sectors of industrial activity, mainly food, healthcare and agriculture. The three primary groups of product are seaweeds and their constituents, chitin and chitosans from crustacean shells, and vitamins, colorants and lipids from microalgae.

Seaweeds are a source of three very important hydrocolloids used across many of the market sectors that are included in this report – agar, alginates and carrageenan. Agar (agar agar), which contains agarose and agaropectin, is produced by processing of the Rhodophyacean seaweeds *Gelidium sesquipedale*, *Gracilaria* spp. and *Pterocladia*. Alginates, composed of polyguluronate and polymannuronate, are produced by *Laminaria* spp., *Ascophyllum* and *Durvillea*.

Production of high-performance hydrocolloids could be an opportunity for UK companies. NovaMatrix[11], the Norway-based new division of FMC BioPolymers, sells pure sodium alginate at £30/gram, and freeze-dried sterile sodium alginate for pharmaceutical formulations at £190/gram. These alginates are also used in bead encapsulation processes for cells, for research, drug delivery and tissue engineering.

Chitin and chitosans are widely used in healthcare (especially for wound-healing), food, food packaging, healthfoods, flocculation of impurities in liquids, and as antifungals and soil conditioners in agriculture. The higher-volume low-value uses are in agriculture, higher-value in medical devices, and high-volume, high-value in health and food supplements. Because chitosans can be sprayed onto surfaces, they are also used as edible moisture-retaining coatings for fruit, foods and meat, as a means of removing egg yolk from processed egg white, and have been investigated as carcass surface antimicrobial sprays in abattoirs.

In healthcare, high-value uses are obtainable. NovaMatrix produces ultrapure chitosan for intranasal drug delivery and other medical uses from crustacean exoskeleton; sold at £22/gram. The price of glucosamine, an acetylated derivative of chitosan produced from crustacean shells, has risen sharply during 2004 from about £2/Kg to £10/Kg, as a result of US anti-dumping action against shrimp shells from India and an EU ban on Chinese seafood imports. Companies such as Glucomed of Norway are now planning to introduce pharmaceutical-grade glucosamine. Chondroitin is also a health supplement, recommended for skin and joints, which can come from a marine source eg sea cucumbers. Sales of chondroitin, glucosamine and chitosan based products in US alone were £140 million in 1996, rising to £1.35 billion in 2000 as a result of their heavy promotion as nutritional supplements.

The most attractive products from microalgae are surfactants, PUFAs and beta-carotenoids. The current market for surfactants is >4 x 10^6 tonnes pa. Surfactants from microalgal sources are produced not by the algae themselves but by their

[11] see www.novamatrix.biz

symbiotic micro-organisms, giving rise to the possibility that surfactants can be produced in bioreactors, either by the micro-organisms if culturable or by gene cluster transfer into a conventional fermentation organism. Development work is still required to make the manufacturing process competitive in price with petroleum-based surfactants. SAMS is a UK leader in surfactants from marine sources. Polyunsaturated fatty acids (PUFAs) and pigments have a combined global market of more than several £ billions per year – astaxanthins are worth approx. £115 million per year. These are attractive targets for marine-resource companies and Aquapharm is focusing on a new method of producing astaxanthin.

Marine invertebrates are of interest for their unusual peptides, and one focus is management of pain using derivatives of cone snail neurotoxins. Ziconotide is under development and clinical use by a number of companies under licence from Neurex, a subsidiary of the Irish company élan.

2.4 Food, food additives, healthfoods, nutraceuticals, nutritional supplements

Marine products are already well-established in the food sector, particularly gelling and forming agents derived from seaweeds, including agar, alginates and carrageenan. The rise in sales of reduced fat, reduced sugar, reduced calorie and health-image foods opens an added-value opportunity in conventional foods and food additives for the products of marine biotechnology and sustainable production methods of natural marine organisms. Bread baked with fish oil is palatable as long as the oils have been encapsulated, but since fish-origin PUFAs come from marine microbes in the fish diets, such as thraustochytrids, then there should be the potential for using algal oils or fatty acids instead.

There is clearly potential for soya flours to be replaced by marine-origin flours, high in protein and essential fatty acids, provided that controlled and safe production of microalgal biomass and equivalent oxidation stability can be achieved. Marine-origin protein biomass may also provide an alternative to meat. New colorants, anti-oxidants, preservatives and novel flavours from marine sources are possibilities.

Other current trends in food and eating include more snacking and grazing, more convenience foods, organic foods, healthy and vitamin-enriched food for the elderly, added value presentations and character merchandising.

In UK, breakfast cereals and in particular cereal bars are seen as high-growth areas, together estimated at £3.14 billion in 2001 rising to £4.59 billion by 2006, 9% of the total estimated £51 billion market. There should be some potential for use of marine organisms and their extracts as ‘healthy lifestyle’ and ‘natural’ ingredients for such foods. These developments seem likelier to be higher-valued, and to move towards functional food and nutraceutical sectors.

Functional foods form one of the most exciting ‘clusters’ in the food sector, including probiotic products, sports drinks and foods, cholesterol-reducing foods and drinks such as fortified milks, fortified fruit drinks and plant-extract preparations. Vitamin and mineral supplements, which are regarded more as ‘health’ products than functional or nutraceutical, include products containing ω-3 fatty acids, enzymes, fibre-enriched products and concentrated plant and animal-source products, including algae and fish oils. One successful export from Ireland is calcined seaweed, which is sold by Marigot as an aid in prevention and treatment of osteoporosis. The overall UK market for diet food in 2000 was £5.39 billion, projected to rise to almost £7 billion by 2006[12].

TABLE 4: MARKET SECTORS FOOD UK, RELEVANT TO PRODUCTS OF MARINE BIOTECHNOLOGY[13]

CATEGORY	YEAR & SALES IN £ BILLION (10^9)					COMMENTS
	1997	2001	2002	2005 EST.	2006 EST.	
FISH AND FISH PRODUCTS	1.95	2.26	2.33	2.48	2.57	marine products easiest to establish in processed fish sector – as feed additives or as novel foods
BREADS, CAKES, CEREALS	7.71	8.96	9.33	9.97	10.18	marine products as humectants, protein and oil ingredients, whole organisms
DAIRY, EGGS, OILS, FATS	8.03	9.89	9.14	9.66	9.76	marine organisms as probiotics, sources of EFAs

The single most interesting development in conventional foods is the rise of the functional drink, especially that built on dairy produce and/or probiotic organisms. The major players in this sector are the French company Danone, whose Actimel® sold £285 million world-wide in 2002, from group total sales of £8.1 billion, a good result considering that 90% of the company's turnover in the Asian markets comes from bottled water, and the Japanese company Yakult, 86% of whose £1.0 billion sales come from foods and drinks[14] and whose main Yakult® probiotic drink sells over 600,000 bottles a day in Europe[15].

It seems quite realistic to explore the use of UK marine algae and other organisms and marine extracts as ingredients of such functional foods and drinks. In addition, algae are already available as health foods, including *Dunaliella* and *Spirulina* as sources of antioxidant carotenoids. The US company Martek sells algal fatty acids/oils in baby food formulae. We believe that similar UK-manufactured products from the sea should be able to capitalise on an image of 'organic' and 'natural'.

There may be a rôle for marine-sourced foods and food ingredients in the sectors of fat-reduced and calorie-reduced foods. There is tremendous growth in this market, driven by the realisation that western populations are becoming more obese and developing disorders such as heart disease, arthritis and Type II Diabetes at an earlier age and with greater frequency. Use of marine-origin ingredients can capitalise on existing uses in health and nutritional supplements,

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12 *Diet and Fat-free foods market assessment 2001*, ed. S Taylor, Key Note (2001), ISBN 1-86111-379-9

13 Source: *The UK Industry Food Market Review*, ed. D Fenn, Key Note Ltd (2002), ISBN 1-84168-394-9

14 *Global Nutraceuticals*, Datamonitor August 2003, Report No 0199-0759

15 *Europe Nutraceuticals*, Datamonitor 2002

of which the commonest are glucosamine from crustacean-shell chitosan, extract of green-lipped mussels from New Zealand and carotenoids such as astaxanthin from microalgal culture.

Astaxanthin is also being marketed as an anti-inflammatory and anti-oxidant, potentially protective against retinal deterioration, diseases caused by inflammation-mediated vascular problems such as heart attacks, providing general support of the immune system and protecting against cancer, all effects apparently observed *in vitro* and in laboratory animals. Mera Pharmaceuticals and Cyanotech of Hawaii are two of the largest producers of microalgal astaxanthin from *Haematococcus*, a freshwater alga, taking advantage of Hawaii's sunshine and warmth to grow the algae in photobioreactors. Microalgal astaxanthin, in pure form for health supplement use, is priced at more than £56,000 per kilogram at retail. It is easy to see why this market could be attractive for UK marine produce.

2.5 Cosmetics

Seaweeds already provide many ingredients used in cosmetics formulation. In terms of new product development, the growing interest in cosmetic-based skin protectants and repairing agents and concerns about the impact of sunshine on skin cancers mean that companies active in these sectors are looking for new functional ingredients. The sun care sector has the fastest growth (+7.8% compared with +4.8% overall).

TABLE 5: MARKETS FOR COSMETICS[16]

CATEGORY	2003 SALES IN £ BILLION (10^9)						
	TOTAL	US	JAPAN	FRANCE	GERMANY	UK	ITALY
ALL COSMETICS	113	25	12	6.8	6.5	5.7	4.8
OF WHICH:		-	-	-	-	-	-
HAIR CARE	23						
SKIN CARE	22						
COLOUR COSMETICS	16						
FRAGRANCES	12						
BATH & SHOWER	11.5						
ORAL HYGIENE	11						
MEN'S GROOMING	9.6						
DEODORANTS	5.3						
SUN CARE	2.4						
BABY CARE	2.0						
DEPILATORIES	1.7						

Marine-origin sodium alginates and chitosans can be used as micro-encapsulators for active ingredients and, in the case of chitosan, provide some stabilising and anti-oxidant activities that are of interest in new-wave cosmeceuticals. The prospects are also very interesting, in the context of this project, for bioactives as cosmetic and cosmeceutical ingredients. In addition to novel bioactives from

16 Source: The Hellenic Centre for Investment, see www.elke.gr

marine invertebrates and their associated microbes, there are anti-oxidants and other compounds from seaweeds including fucoidans and carrageenan.

Examples of successfully-commercialised products which would bear analysis by any UK initiative in this area include

- a liposome-based product from the US company AGI Dermatics, containing a photolyase from the blue-green alga *Anacystis nidulans*
- pseudopterosin, the anti-inflammatory extracted from the sea-fan *Pseudopterogorgia elisabethae*, the active ingredient in Estée Lauder skin lotions, which has generated more than $2 million royalties for the University of California
- the St Malo, France, company Laboratoires Codif's algal extracts from microalgae and from seaweeds, including Dermochlorella®, an extract of *Chlorella vulgaris*, which is claimed to be a skin restorative and Phycosaccharides® from *Laminaria digitata*, a skin penetrant used to treat acne and ageing skin.

2.6 Pharmaceuticals

In 1999, 20 of the best-selling non-protein human medicines were natural products or natural product-derived (synthetic or semi-synthetic analogues). Combined sales of these products exceeded £9 billion[17]. According to the authors of the report on Antarctic bioprospecting[18], annual sales derived from traditional knowledge using genetic resources are £1.7 billion for the cosmetics and personal care industry, £11 billion for the botanical medicine sector and £42 billion for the pharmaceutical industry. More than 60 percent of the cancer drugs approved by the US Food and Drug Administration are of natural origin or are modelled on natural products.

The human pharmaceutical products market is enormous, which is what makes it appear so attractive. The Top 20 companies sold over £160 billion-worth of products in 2001[19]. The single largest sector of medicines is antibacterials, estimated at £14 billion, projected to grow to £18 billion by 2010[20]. The market for non-antibiotic prescription medicines is dominated by three sectors – depression, hypertension and cancer. The world market for antidepressants is estimated at £9.5 billion in 2002, with five products each contributing more than £0.6 billion in sales[21]. The anti-cancer sector, estimated at £8.5 billion, includes several products that are, in fact, 'blockbusters' – Taxol® is one such, with sales of more than £0.6 billion a year. In the cancer sector, almost half of the products are cytotoxic agents, the class into which almost all anti-cancer marine bioactives fall. The value of the active ingredients used in all medicines is estimated at £28 billion, 15-16% of the total price of the product.

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[17] A Harvey, *Drug Discovery Today*, Vol 5 No 7 July 2000

[18] The International Regime for Bioprospecting, Existing Policies and Emerging Issues for Antarctica UNU/IAS Report August 2003

[19] see http://www.abpi.org.uk/statistics

[20] figure extracted from Quorex web-site www.quorex.com

[21] *Antidepressants world prescription drug markets*, Theta Report #1234 December 2003, PJB Publications

Accordingly these would seem a naturally-attractive target for marine biotechnology and, indeed, there has been a drive to develop bioactives from marine sources since the adenine arabinosides A and C (Ara-A and Ara-C) were isolated from *Cryptotethya crypta*, a Caribbean sponge, in the 1960s and discovered to be potent antiviral and anticancer agents, respectively.

There are other sectors of the pharmaceutical and biopharmaceutical markets that could also be targets for marine-derived products and might prove to be less problematic than anti-cancer agents:

TABLE 6: ESTIMATES FOR SOME MEDICAL SECTORS

CONDITION	MARKET	COMMENTS
Sepsis	£3 billion worth of healthcare costs per annum in the US alone[22]	products that can more effectively disarm the organisms causing this, or reduce and reverse the effects of endotoxic shock and multiple organ failure, will be very attractive
Neuropathic pain	in US alone, £240m in 2002 to £450m by 2007 and £700m by 2012)[23]	ziconotide, derived from the cone shell venom, is already being developed
NSAID market	world-wide of about £5.5 billion	anti-inflammatories and mild-to-moderate pain
Urinary incontinence	£600m, 5-8%, of a total £11b market	projection for drug-related management is >£6 billion by 2008; marine-origin products could be active in both these sectors, as bioactives with neuromuscular effect or as biomaterials for implantable devices
Gout	over £1.1 billion each year	Lytone Enterprise, a Taiwanese company launching a product made from deep-sea fish peptides

On the research front, and underlying the pathogenesis of several important groups of human and animal diseases, are two fundamental cellular and cell-cell signalling processes – apoptosis and angiogenesis. Molecules that control these processes have tremendous potential in the management of cancers, chronic inflammatory diseases, and our responses to body damage and acute infections (see **Tables 7 and 8**). It is clear already that many bioactives obtained from marine invertebrates and/or symbiotic or free-living microbes have a strong effect on cells and, doubtless, they will also have effects on apoptosis and angiogenesis. There is also potential for exploitation of signalling molecules in control of bacterial diseases, particularly quorum or consensus molecules, which regulate the interaction between micro-organisms in monospecific populations and in the communities that make up biofilms and other assemblages. This is an area of activity in which the UK is especially expert, partly as a result of the NERC's Marine Biofouling Thematic Programme MBTP.

22 see www.theratase.com web-site

23 *Neuropathic Pain*, EP Publications, WWMR Inc, www.WWMR.com

TABLE 7: ESTIMATE OF WORLD MARKET FOR APOPTOSIS-RELATED PRODUCTS, 1999-2005[24]

PRODUCT TYPE	SALES (£ MILLIONS)	
	1999	2005
Diagnostics and laboratory research materials	6	11
Cancer	0	200
CNS and neurodegenerative	0	45
Cardiovascular	0	45
Total	6	301

TABLE 8: MARKET ESTIMATES FOR ANGIOGENESIS MODULATORS[25]

SECTOR	YEAR AND ESTIMATED SALES IN £ MILLION				
	2003	2004	2005	2006	2007
Total of which:	56	65	320	690	1670
anti-cancer (AI)	-	-	70	170	450
dermatology (AI)	-	-	56	135	365
cardiovascular disease (AS)	-	-	56	110	280
diseases of back of the eye (AI)	-	-	35	67	225
arthritis (immune and damage) (AI)	-	-	28	100	210
advanced wound care (AS)	56	65	80	105	140

notes: AI = angiogenesis inhibitors, AS = angiogenesis stimulators

One challenge facing marine biologists and chemists is that too many novel compounds can be isolated from marine invertebrates, marine symbionts and free-living micro-organisms. Producing a list of all those mentioned in the literature would be a monumental task and is beyond the scope of this project, though a partial list is given in **Volume 2**. It is, however, a suitable target for a web database, especially if information on sources, activities, commercial developers, development stages and holders of Intellectual Property Rights is included. There are disparate databases available but nothing that truly co-ordinates all information.

More importantly, investigating all these molecules is impossible. Finally, a successful bioactive is one that reaches the patient, not one that has exciting new activity *in vitro*. These challenges are drivers for new developments in isolation, identification, characterisation and biological screening techniques. Biological screening in particular moves away from the chemist's arena of the structure-activity relationship as a predictor of therapeutic potential to actual testing against

[24] *Apoptosis: New Growth Opportunities*, Business Communications Co Inc July 2000

[25] Theta Report *Angiogenesis Inhibitors & Stimulators* PJB Publications 2002

targets in a high throughput screen. This also drives cross-discipline developments on novel sensors that can be incorporated into autonomous underwater vehicles (AUVs) and other sampling equipment.

2.7 Medical devices and biomaterials

The medical device market is the most definable of those that use biomaterials and is worth >£20 billion. Device sales in Europe are estimated at approximately £7 billion, about a third of these sales coming from biomaterials-dependent devices; this proportion probably holds true in US as well. The majority of these are based on biocompatible synthetic polymers but there is an established sector of natural biomaterials (see **Table 9**). Those hydrocolloids and materials of marine origin include chitosans and chitins from crustacean exoskeletons, alginates and other seaweed hydrocolloids and coral-origin bone replacers. There is some additional potential for marine-origin collagens and gelatins to replace mammalian material, as a result of concerns over disease transmissions and improvements in economy of waste-processing.

TABLE 9: NATURAL BIOMATERIALS – FORECASTS FOR USE[26]

SECTOR	GLOBAL ESTIMATES £ MILLION
Hyaluronic acid & collagen (cosmetic use)	170 – USA only
Hyaluronic acid for viscosupplementation (use in joints, eyes)	85 – world, growth 40% pa
Collagen injectable and other device uses (cosmetic and woundcare)	225 – world
Gelatin (cosmetic, device component)	900 – world
Hydrocolloids and hydrogels (woundcare)	450 – growth 8% pa US, 12% pa EU

Biomaterials for wound-care and general surgical use, and devices for cardiovascular and orthopaedic use are the sectors of interest for products from marine biotechnology. Drug delivery can also provide a market for marine-derived ingredients as carriers and formulation components. An added area of opportunity might come from increased understanding of cell-to-cell signalling, to aid integration of devices by the patient.

26 *Biomaterials Strategy for Scotland*, BioBridge 2003 for SE Edinburgh & Lothian

TABLE 10: BROAD ESTIMATES FOR MEDICAL DEVICE END-USE SECTORS OF INTEREST, GLOBAL DATA[27]

SECTOR	ESTIMATED ANNUAL SALES £ MILLION					
	1999	2000	2001	2002	2003	GROWTH RATE
Devices	16,300	18,250	21,250	22,250	24,700	8-14%
Medical coatings[28]		5,600	6,000	7,500	10,000	
Drug delivery	3,000	3,500	4,000	5,000	6,000	>16%
Tissue engineering[29]	10	11	12	16	20	>16%
Approx. total	20,000	27,000	31,000	35,000	41,000	

One important and growing sector of medical devices is cardiovascular stents, tubes that can replace blood vessels in the heart, main blood vessel trunks or peripheral blood system when they have been narrowed by disease. The US sales for conventional stents of £2.3 billion (2001) are projected to rise to £2.5 billion if drug-eluting and other controlled-cytotoxicity stents are successful, and will also enlarge the £0.9 billion for other angioplasty products used in peripheral blood vessels. Marine-origin bioactives and biomaterials may certainly have a role to play in coating devices and implants with a biocompatible and lubricated surface and in cutting down unwanted cellular reactions.

In the orthopaedic area, there is research activity to produce usable scaffolds from ordered combinations of chitosan fibres, which can be turned into woven, knitted or non-woven fabrics, and bone-like minerals such as coral-derived hydroxyapatite[30]. Chitosan-based materials are already used as sutures and wound dressings. The potential here seems, however, to be rather low compared with other applications such as wound-healing, largely because of current reliance on metals for orthopaedic devices and the slow uptake of bone replacers containing bioactives such as bone growth factors. This will change in the next 5 years, so that any marine-origin bioactive that is likely to have a cell- or healing-stimulating effect should be screened for its osteogenic or chondrogenic activity.

In drug delivery (see **Table 11**), rapidly-growing product sectors include inhalable therapies, gene therapy delivery using polymeric carriers (of which chitosan is one) and mucoadhesive products (mouth, gastrointestinal tract, anogenital). Delivery systems in which marine-derived materials could be used as carriers include quick-dissolve tablets and no-water tablets; mucosal bioadhesives; hydrocolloid osmotic devices; lipid-encapsulation technologies; nasal and pulmonary delivery of microparticles.

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27 PJB New Developments in Biomaterials 2000

28 *Advanced Polymers for Medical Applications* Kalorama Information KLI 513 899 2002, ISBN 1-56241-781-9

29 virtually all bioartificial skin products

30 Japanese and European work described in Baran Et, Tuzlakoglu K *et al.*, *Multichannel mould processing of 3D structures from microporous coralline hydroxyapatite granules …* J Mater. Sci.: Mater. Med. 15 (2004) 161-165

TABLE 11: MARKET BREAKDOWN FOR DRUG DELIVERY SYSTEMS – US ONLY[31]

SECTOR	MARKET SIZE £ BILLION			GROWTH RATE
	1990	2000	2005	2000-05
Oral administration (prolonged release, delayed release, mucoadhesive)	1.4	12	19	8.6%
Parenteral (injectables, targeted therapies, liposomes)	3	7	11	9.5%
Inhalation products	1.6	4.2	6.4	9.0%
Transdermal & implantable	0.08	0.8	1.5	13.3%
Total	6	24	29	9.1%

2.8 Cell therapy, tissue engineering, regenerative medicine

Marine biotechnology and marine biological research could make a strong contribution to these areas of frontier medicine, through marine-origin materials (see **Table 12**) – bioactives, adhesives, anti-adhesives, biocompatible colloids, nanostructures, porous materials – as well as increasing our knowledge about how cells and substrates interact and how cell-cell signalling can be affected. Beneficial discoveries in this area might include molecules that alter the ability of cancer cells to coalesce and multiply, or metastasise.

Targets for marine biotechnology might be cell-activating and cell-maintaining agents or biocompatible cell carriers that help to localise cell implants, thus providing opportunities for marine-derived actives as well as biomaterials.

TABLE 12: POTENTIAL ROLES FOR MARINE-DERIVED PRODUCTS IN TISSUE ENGINEERING

POTENTIAL ROLES FOR MARINE-DERIVED PRODUCTS
protectants for cells (oils, chitins, polysaccharides)
scaffolds for cells (chitins, diatoms)
stem-cell differentiator (bioactives)

Because of differences in definition and what is included, estimates of the future global tissue regeneration market vary from £1.2 billion through £2.6 billion[32], even to £45 billion, the latter including wound healing and chronic non-healing ulcers as well as products replacing existing devices for soft and hard tissue repair.

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[31] Drug Delivery Systems, Freedonia Reports 2001

[32] *New Development in Biomaterials*, a Clinica report, PJB Publications 2000

TABLE 13: MARKET BREAKDOWN FOR POTENTIAL TISSUE ENGINEERED TARGETS[33]

PRODUCT SECTOR	MARKET SIZE (£ BILLION)	YEAR
Venous stasis ulcers	**1.6**	2002
Pressure ulcers	**1.1**	2002
Diabetic foot ulcers	**0.8**	2002
Other soft tissue/surgical	**2.1**	
of which acute wounds	1.1	
anti-adhesions	0.6	
Heart valves	**0.6**	2008
	0.4	2000
of which:		
tissue valves	0.15	
pericardial-flap valves	0.06	
mechanical valves	0.2	
Cardiovascular stents	**1.2**	2001
	1.7	?
Of which:		
small-diameter	0.2	
Regeneration of bone, cartilage, tendon, ligaments	**8.5**	

One activity that could enhance opportunities for marine biotechnologists and researchers of marine-origin materials in the UK would be to interact with the increasing numbers of centres for regenerative medicine and tissue engineering in Europe, to explore opportunities for co-developments.

2.9 Diagnostics

The global *in vitro* diagnostics market was estimated to reach £13 billion by 2003[34], and revenues of European biotechnology-based diagnostics companies reached about € 1 billion in 2002[35].

[33] *Biomaterials Strategy for Scotland*, BioBridge 2003 for SE Edinburgh & Lothian
[34] New Trends in Viral Diagnostics, Clinica, 2001
[35] Surviving Uncertainty: The Pan European Mediscience Review 2002, Deloitte & Touche 2002

TABLE 14: ESTIMATES OF SALES OF *IN VITRO* DIAGNOSTICS BY TECHNOLOGY TYPE, 1999-2004[36]

TEST TECHNOLOGY/PURPOSE	SALES IN £ BILLION	
	1998	2004
Immunochemistry	4	4.9
Blood glucose detection	1.5	2.2
Microbiology & nucleic acid tests	1	1.5
Chemistry	1.75	1.5
Haematology & flow cytometry	1.0	1.3
Coagulopathies	0.4	0.45
Blood gases, electrolytes	0.3	0.45
Urinalyses	0.3	0.4
Others	0.4	0.6
total	10.6	13.4

Recent industry estimates put the global market for diagnostic enzymes at £70 million. Marine-origin products already established in this sector include the fluorescent phycoerythrin from seaweeds and alkaline phosphatase from shrimp, both also used as laboratory research reagents. As more research reveals the ways in which specific marine-origin bioactives work, or materials interact with cells and surfaces, other potential uses in diagnostics may well emerge.

2.10 Research tools

Marine Organism Culture Collections can generate substantial income through fees and royalties from the supply of samples and subsequent development of bioactives or materials. The American Type Culture Collection raised over £8.1 million in fees in 2001[37]. CSIRO's Microalgae Research Centre (CMARC) in Australia has over 750 strains, mainly marine, which are supplied for research, teaching, commercial assessment and as aquaculture larval feeds, at approx. A$100 for 20ml[38]. The UK has 19 collections, several of which are relevant to marine biotechnology. Most are supported by the NERC (CCAP-Marine at SAMS, for example) and BBSRC (Newcastle's NICMB and the overall co-ordinating body the UKNCC, UK National Culture Collection) and charge a small amount for access (£25-30, occasionally £50) to other academic or commercial customers. If the promotion and marketing of the UK's marine collections were co-ordinated, additional income could be generated to maintain the collections and fund improved methods of curating, propagating and storing the accessions. CCAP and NCIMB have recently begun a collaboration to make better use of their resources.

[36] D P Kelly in Medical Device Manufacturing and Technology, World Market Research Centre September 2000 p40

[37] Marine Science Review, Report of Visit to Maryland & Virginia, New Park Management June 2001, chapter 4

[38] contact microalgae@marine.csiro.au

Some marine sources for research reagents are well-known: the value of alkaline phosphatase isolated from frozen shrimp melt-water is approximately €110,000 for Novozymes, for example, and the catalogue price for 1000U is approx £50. Phycoerythrin, pre-conjugated with streptavidin, sells for approx. £110/100ml or £280/mg dry-form, and phycocyanin is also available. These seaweed-origin fluorophores are often used unconjugated as the fluorescent vital dye in cell sorting and are generally obtained outside the UK. There might be some potential for import substitution here.

The market for general-purpose biotechnology reagents has been estimated at over £0.7 billion by 2002[39], as shown below.

TABLE 15: SALES ESTIMATES FOR BIOTECHNOLOGY REAGENTS[40]

SECTOR	SALES ESTIMATES £ MILLION	
	2000	2002
DNA sequencing reagents	150	215
General purpose biotechnology reagents & materials	120	160
Electrophoresis reagents	100	150
Tissue culture reagents & materials	70	90
Liquid chromatography reagents	65	80

Extremophile and marine organisms have generated three of the most widely-known of modern bioreagents:

- Taq polymerase, a vital ingredient of the Polymerase Chain Reaction, from *Thermus aquaticus*, a hot-springs organism
- aequorin, the blue bioluminescent indicator of calcium flux, from the north-east Pacific coldwater jellyfish *Aequoria victoria*
- Green Fluorescent Protein, also from *Aequoria*, which converts aequorin to green light.

Following on the heels of Taq polymerase are Vent and Deep Vent polymerases, derived by New England Biolabs from the deep-sea hot vent relative, *Thermus thermophilus*. Laboratory reagent companies supply this in the UK at about £200 per 1000 units. Sales of PCR enzymes are estimated at up to £60 million annually world-wide, and the market for extremophilic enzymes is projected to grow 15-20% per year[41].

Other marine bioactives are in use as laboratory tools; manoalide and staurosporine from the US company AG Scientific Inc at £200 and £160 per mg for synthetic analogues, and natural bryostatin I from GPC Biotech Munich and LC

39 Theta Reports 767, *Biotech Research Reagents*, May 1998. Theta Publications Inc (part of PJB Publishing Ltd)

40 ibid.

41 quoted in The International Regime for Bioprospecting, Existing Policies and Emerging Issues for Antarctica UNU/IAS Report August 2003

Laboratories at £2,200 per mg[42] are examples. A recent discovery, too soon to have a price-tag, is that 6-bromoindirubin-3'-oxime, a constituent from Tyrian Purple, a dye found in a Mediterranean relative of the cone snail, inhibits glycogen synthase kinase-3 in vertebrate cells and stabilises and allows differentiation of human embryos and stem cells, thus simplifying their handling in the laboratory.

There are broader benefits from undertaking fundamental marine bio[techno]logical research, including an increased understanding of how cells interact and signal to each other in complex communities, how cells and biomaterials bind to inorganic surfaces, and how micro-organisms keep each other under control. The understanding of cell-to-cell signalling is one area in which there is considerable research strength in the UK.

2.11 Agriculture

Chitin and chitosans have been used widely in agriculture as soil conditioners, anti-fungal materials and components of seed coatings. Work at Washington State University is capitalising on the abundance of crab-shell chitin to produce fungicidal chitosan for control of potato blight, and lobster-shell waste has been put to practical use in production of organic potatoes on Prince Edward Island Canada for McCains Potatoes, after drying, grinding and extraction of astaxanthin[43].

More recently, marine biotechnology is yielding bioactives of interest. AIMS has isolated more than 30 potential herbicides since the late 1990s, in collaboration with the Nufarm company, and the AIMS spin-out ToxiTech has succeeded in growing one source, a marine fungus, on large-enough scale to yield enough material for initial trials. The US company AgriQuest is developing biopesticides from marine and other natural sources.

The global crop protection market consists of products applied to plants to kill or repel pests, including fungal diseases and insects, and to control weeds. In 2000, the world market was approx £17 billion, projected to rise to £23 billion by 2010[44].

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[42] Blaue Biotechnologie: Stand und Perspektiven der marinen Naturstoffe, Technologiestiftung Schleswig-Holstein, June 2003 pp 25-26

[43] B Burles *pers. comm.* 2004

[44] *The Global Crop Protection Industry in 2010*, Agrow Reports DS221, PJB Publications 2001

TABLE 16: SALES OF CROP PROTECTION PRODUCTS WORLD-WIDE 2000[45]

<table>
<tr><th rowspan="2">CROP-PROTECTION PRODUCT TYPE</th><th colspan="3">EST. REGIONAL SALES 2000, £ BILLION</th></tr>
<tr><th>EUROPE</th><th>USA</th><th>JAPAN</th></tr>
<tr><td>FUNGICIDE</td><td>1.5</td><td>0.5</td><td>0.4</td></tr>
<tr><td>POST-EMERGENCE HERBICIDES</td><td rowspan="2">1.6</td><td>2.2</td><td rowspan="2">0.5</td></tr>
<tr><td>PRE-EMERGENCE HERBICIDES</td><td>0.9</td></tr>
<tr><td>INSECTICIDES</td><td>0.7</td><td>1.2</td><td>0.6</td></tr>
<tr><td>COMBINED INSECTICIDE-FUNGICIDE</td><td>-</td><td>-</td><td>0.2</td></tr>
<tr><td>GROWTH REGULATORS, OTHERS</td><td>0.2</td><td>0.2</td><td>0.25</td></tr>
<tr><td>TOTAL</td><td>4.4</td><td>5.0</td><td>1.9</td></tr>
</table>

Animal feeds, aquaculture feeds and pet food are three markets where marine-origin ingredients provide nutritional benefits and profitable markets. There is increasing pressure against the use of antibiotics and other pharmaceutical-type products in farm animals, so that such ‘natural’ extracts are attractive. A fermentation product from a terrestrial *Aspergillus oryzae* strain is used in animal feeds to produce stimulation of the animal’s normal flora and fauna and increased performance and better feed use. **β**-glucans from yeasts are also reported to produce immunostimulant effects. This suggests the possibility that extracts of marine organisms might also have a positive impact.

The total sales of pet foods are astonishingly high, about £9.5 billion in the USA, £7.2 billion in the UK and £1.5 billion in France. Alginates and carrageenan are used as fillers and humectants. One avenue to explore is algal-based foods for pets, with high carotenoids, PUFAs and other components.

There is also a considerable market for microalgae as fresh food for organisms in aquaculture, including larval fish and crustacea, as well as filter-feeders such as clams, oysters and abalone, with at least 50 species or strains being in use or of potential value. The most important components of microalgae for nutrition are polyunsaturated fatty acids, sugars, vitamins, and sterols. There is also interest in chitin derivatives such as chitosans and glycosaminoglycans, which have health benefits for young fish and invertebrates, and some evidence that intact marine microbes are immunosupportive for salmon.

Given the current concerns about using fish in the feeds of farmed salmon and other species, as well as unfavourable comparisons between the texture of wild-caught and farmed fish, it would be worth investigating use of microalgal oils in fish diets.

Mixtures of marine and aquatic microbes are being widely used as probiotics, aids to healthy production in fish and shellfish farming and improvers of water quality in growing ponds. The probiotic effect is thought to be achieved by a combination of digestion of waste materials in the water (heterotrophic action), competitive exclusion of pathogens, production of enzymes that help fish and crustacean digestion, and release of nutrients from other aquatic organisms.

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[45] ibid.

The use of astaxanthin as an antioxidant in nutraceuticals has been mentioned; it is also an important additive for feeds for salmon and trout, crustacea and laying poultry, where a pink or orange coloration has an organoleptic benefit to the consumer.

2.12 Industrial uses and enzymes

There are existing processes using marine materials where use of enzymes of marine origin might be expected to improve economic efficiency; an example is the conversion of chitin into chitosan, which currently has an overall production efficiency of only 3%. There are also problems with management of wastes from fish processing and fish farming. Wastes are high in recoverable protein, collagens, oils, fatty acids, calcium and chitin but current processing systems add too much cost.

We believe there is potential in management of fish and shell-fish wastes for appropriate-scale biotechnology approaches that, without needing high-volume ultra-clean and consistent input, can still produce pure, high-quality, toxin-free outputs, ideally in separated streams. Mixed composting, adding wastes from other sources as balancers, could produce energy on-site as well as yielding a reusable residue, again in appropriate-scale and economically-effective systems. Intuitively, marine-origin enzymes should be better able to handle marine-origin wastes than enzymes from terrestrial sources.

Higher-technology development of marine microbes might be forthcoming as a result of a £20 million collaboration between Dow Corning and Genencor, aimed at understanding and using the physiology and biochemistry of marine plankton that utilise silicon. The companies hope to commercialise biologically-mediated silicone products for the life sciences, personal care, cleaning and fabric care markets, in the short-term, then move on to applications in diagnostics, biosensors, electronics and controlled delivery of active ingredients. The materials may also be used in developing new biochip-based devices with acute recognition and superior signal transduction capability. The ability of marine micro-organisms to build protein lattices for deposition of silica and other inorganic material in a nanostructured way holds out potential for bioproduction of silicon chips and other nano-structures.

In general terms, novel enzymes from marine sources may enter a market estimated at £2 billion; nevertheless, more than 90% of industrial enzymes are accounted for by fewer than 30 enzymes.[46] Specialised niche applications seem indicated, rather than a blockbuster enzyme.

2.13 Environmental management, remediation and energy

The global sensor technology market, both for environmental sensors and new forms of monitoring and exploration, is estimated at £2.8 billion per annum and is growing at 5 per cent per annum[47]. Marine organisms or molecules might find a place here, because of their reactivities. The UK company Remedios, a spin-out

[46] see http://www.diversa.com/markprod/mark/induappl.asp

[47] Marine Foresight Panel Ireland 2003

from the University of Aberdeen, has commercialised a novel eukaryotic biosensor based on a marine microbe, in which pollution concentrations can be measured by the degree of suppression of its bioluminescence. Remedios also uses other biosensor organisms that are representative of the bacterial strains found in the environment as well as those involved in bioremediation.

It is estimated that about 3.5 billion gallons (1.2 x 10^{10} litres) of oil are extracted at sea or are in transit across the oceans each day, and spillage is estimated at over 120 million gallons per year. Marine-origin biodegradable dispersants or *in situ* bioremediation by surface spray of oil-degrading microbes or enzymes would be welcome. Chitin is a chelator and powdered chitins have the ability to act as sequestrators of metal ions; dried microalgae such as *Chlorella* are powerful adsorbents of organic fluids. Other pollutants can be handled by marine micro-organisms: transferring mammalian or avian metallothionein genes to *Synechococcus* and *Chlamydomonas* produces genetically enhanced microalgae that are better at extracting and sequestering heavy metal pollutants from seawater. Research with a modified *Delinococcus radiodurans* has shown an ability to degrade organopollutants in radioactive surroundings.

There would be an exciting potential for genetically-enhancing marine organisms so that they are more capable of metabolising and detoxifying pollutants in sea water arising from human activities, particularly in concert with closed bioremediation bioreactors or process conduits.

A significant source of ecological pollution is ship ballast water. Problems caused by exotic organisms are well-known and there are, as yet, no really effective ways of dealing with this. Forcing ships to flush their ballast-holds while out in open water may help the final dock to avoid contamination, but the action simply shifts the load elsewhere rather than removing it altogether. It seems viable to explore whether a combination of ‘probiotic’ non-exotic organisms, marine viruses and suitable neutralisers might not eliminate stowaways in ship ballast water.

CO_2-neutral and renewable energy sources are of increasing importance due to climate change and the increasing global CO_2 concentrations in the atmosphere. One of these alternative energy sources is hydrogen, which can be used to generate electricity and heat in a fuel cell at a high efficiency. USA and Japan have invested in biological hydrogen production using photosynthetic bacteria and algae. The Dutch have established a significant national effort in this field, co-ordinated from the Food and Bioprocess Group in Wageningen University[48].

2.14 Bioengineering and new production techniques

Countries in the tropics and sub-tropics, such as Greece, Spain, Brazil, Australia or the American states of Florida and Hawai'i are able to use sunshine and exterior bioreactors for batch or continuous culture of microalgae in a way not yet possible in the UK. Here, effort can be directed into developing novel bioreactors for extremophilic microbes, creating optimised culture media and conditions of pressure, heat, cold, saltiness or electromagnetic radiation. Alternatively, and perhaps more cheaply, a focus on techniques for identifying genes of interest

[48] see http://www.biohydrogen.nl for information

without necessarily culturing or even identifying the producing organism, cloning and expressing reliably in reactor-adapted conventional organisms will be beneficial.

Similarly, due to the UK's cold and temperate waters, it is unlikely that we will emulate culturing of sponges for extraction of bioactives that is possible in Mediterranean and Adriatic waters; however, the University of Wageningen is culturing sponge primmorphs, clusters of cells that form small colonies, in closed reactors, which is a technology that can also be assessed in the UK.

3. MARINE BIOTECHNOLOGY IN THE UK

We identified a total of 21 companies involved in marine biotechnology or related fields and 49 Higher Education Institutions (HEIs) and other organisations, listed in **Tables 20-24** at the end of this Volume.

3.1 Companies

We have identified 21 companies that appear to have some connection with use or exploitation of marine resources. This is by no means a maximum, since there are undoubtedly more companies in the UK who use ingredients of marine origin as a basis for cosmetics, healthfoods, medical devices, foods and medicines.

Of the companies, 13 (over 60%) are Scottish, 7 are English and one (Carapacics) has its head office in Northern Ireland although it also has a site in Ayrshire – this has therefore been counted as a Northern Irish company. One service company (SEAS) based at SAMS (Scottish Association for Marine Science) has now merged with SAMS Research Services Limited, and one company is registered at Companies House but we have no other information about its activities. Two companies, Coastal & Marine Biotechnologies and Integrin also sell diagnostic and monitoring kits for environmental quality or toxins in shellfish, so are double counted in the table below.

TABLE 17: TYPES OF COMMERCIAL ACTIVITY IN MARINE BIOTECHNOLOGY IN UK

COMMERCIAL AREA	NUMBER
Developing or producing **bioactives**	9
Service companies, consultancies	4
Producing **ingredients** eg agar, colloids for cosmetics, food, research use	2
Developing or producing **biomaterials**	2
Environmental applications	5
Unknown	1

Most of the directly-involved businesses are based on culture collections, providing samples, extracts, bioactives, screening or storage services – only one of these (Aquapharm Bio-Discovery Ltd)) is also developing its own products; three are involved in monitoring of the environment or toxins in shellfish; one is developing medical materials from prawn wastes; another company is the commercial arm of a marine research laboratory but is also working on exploitation of raw materials from marine algae. Not all companies can be said to use primary marine biotechnology; some are using marine-origin microbes as an element of a wider collection for screening bioactives, others are using marine-origin molecules for diagnostic and monitoring purposes, or have service activities aimed at marine biotechnology. At least two have not so far started trading and one has been acquired by a US company since we began the work. Marine engineering companies are not included.

3.2 Academia and Research Institutions

Of the HEIs and organisations, 33 are in England, 10 are in Scotland, 4 are in Wales and 2 are in Northern Ireland (excluding the Centre for Innovation in Biotechnology, which is a joint-venture between the two Northern Ireland HEIs, and the Department of Agriculture and Rural Development for Northern Ireland, which is almost exclusively fisheries-oriented). Full lists are given in **Tables 21-24**.

TABLE 18: UK'S STRENGTHS IN MARINE BIOTECHNOLOGY RESEARCH

ACTIVITY	UK BASE	COMMENTS
Marine viruses	Plymouth	novel enzymes and bioremediation
Actinomycetes	Newcastle	novel bioactives; some industrial collaboration
Oceanic marine science	Southampton	environmental management, deep extremophiles
Estuarine and coastal shelf marine sciences	Plymouth	new organisms, halophiles and others
Biofouling	St Andrews Heriot-Watt UG Millport	medical devices, marine engineering, boatbuilding, ballast-water management
Cell signalling	MBA Plymouth	human and animal disease processes and prevention
Cell cultures	SAMS, Newcastle	screening, new bioactives, biochemical models
Marine algae, plankton	Plymouth	environmental management, food safety
Bio-surfactants	SAMS	chemical and household industry
Bioreactors	Heriot-Watt	bioprocess for novel organisms
Bioactives	Aberdeen	screening for medical applications
Mariculture	Stirling	food, feed, research models, GM for
Chemistry	Plymouth	adaptation of biosynthesis to on-shore conditions
Genomics	St Andrews Stirling Plymouth SFA	disease and breed improvement, environmental monitoring

3.3 Current Initiatives in the UK

The most relevant sources for an examination of strategies for economic development are the studies examining the development of marine sciences in Scotland[49] and the potential for development of a science and technology cluster based on Plymouth[50]. In addition, NERC's M&FMB (Marine & Freshwater Microbial Biodiversity) programme provides a panorama of people and institutions

[49] *Marine Science in Scotland. A strategy for developing its potential* Draft Report February 2004, for Highlands & Islands Enterprise and Scottish Enterprise - unpublished

[50] Feasibility Study for the development of a marine science and technology (MST) cluster in Plymouth Final Report April 2003, GHK & BMT, for the City of Plymouth

currently working in areas of marine bioscience that might give rise to development activities.[51]

NERC's Marine & Freshwater Microbial Biodiversity (M&FMB) Programme

We identified a very strong dynamism resulting from the early support of the UK's Biotechnology and Biological Science Research Council (BBSRC) of marine sciences, and the consistent support from the Natural Environment Research Council (NERC), for infrastructure such as research vessels, facilities and culture collection maintenance, but also for important integrative programmes including the Marine Biofouling and the more recent and ongoing Marine & Freshwater Microbial Biodiversity (M&FMB) programme, to which much reference is made in the text. The Technology Transfer activities of this programme are beginning to generate significant interest amongst the new companies seeking to commercialise marine-derived products and processes.

Marine Science in Scotland

This study was carried out during late 2003 and early 2004 and aims to establish a strategy for developing and exploiting marine science in Scotland. Marine biotechnology is one of the topics addressed and it is seen as a "*seedbed for novel industrial developments*".[52] The study also includes a report addressing the possibility of creating an integrated marine science campus, to include research, applied sciences, commercial development and recreational aspects. The major proposal is to set up a Scottish Marine Science Alliance, representing academic, commercial and voluntary interests in the sector. The Alliance would therefore include members from SE (Scottish Enterprise), HIE (Highlands & Islands Enterprise), the Scottish Executive, SAMS, the RSE (Royal Society of Edinburgh), HEIs in Scotland, appropriate companies and a charity or NGO (Non-Governmental Organisation), to be funded by HIE and SE and staffed by a small secretariat. The role of the Alliance would be to establish the priorities for action within an overall strategy and delineate the implementation plan. Should this proposal be accepted, it would make sense for any initiative for marine biotechnology in the UK to take account of the Scottish Marine Science Alliance and ensure that appropriate integration takes place.

European Centre for Marine Biotechnology

The European Centre for Marine Biotechnology (ECMB), sited at SAMS, Dunstaffnage, Oban, was conceived in 2000 and opened in 2004 as the first business incubator in the UK for marine start-ups. Its strategic function is to create a marine-oriented cluster of research, application and new business, with a stated aim of translating investigative and applied research ideas into products and processes for a variety of markets.

The national Culture Collection of Algae and Protozoa (CCAP) now occupies part of the new ECMB building, and the first new business occupant of the building will be Aquapharm Bio-Discovery Ltd. Occupants of the ECMB will have access to

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[51] see http://www.nerc.ac.uk/funding/thematics/mfmb/

[52] Report by Professor I N McCave, incorporated into the report *Marine Science in Scotland*

SAMS's laboratory equipment, scientific expertise in marine organisms, biotechnology & molecular genetics, aquaria, algal culture systems and research vessels, as well as its human resources – over 100 marine-dedicated scientists and the NERC National Centre for Scientific Diving. They will also use shared facilities such as a library, conference suite and refreshment areas, with the aim of enhancing networking between business and research.

One of ECMB's goals is to become part of a network with similar activities across Europe and beyond; another is to establish trans-national development projects.

Marine Science and Technology Cluster in Plymouth

The City of Plymouth report confirms the strength of the region's education, training and academic research almost across the board of general marine-related areas of expertise.[53] Marine biotechnology itself is characterised as "*well-positioned, possibly requiring further development*" for biomolecular sciences, plankton science, marine chemistry and ecotoxicology, with the remaining 21 areas, including bioscience and physical science/engineering areas, characterised as "*less well positioned*".

The report identifies £20.9 million research revenues in Plymouth in 2002-2003, with £10.5 million (approx 50%) coming from the activities of **Plymouth Marine Laboratory** (PML) and the **Marine Biology Association** (MBA). Together with the Sir Alistair Hardy Foundation for Oceanographic Science, the University of Plymouth and the National Marine Aquarium, these have formed the Plymouth Marine Science Partnership (PMSP). However, set against the strengths in these institutions is "*a very weak exploitation record and an almost complete absence of local marine services*".[54]

Our view is that, in terms of fitting marine biotechnology activity into local marine businesses, development of new anti-fouling products, ballast-water clean-up and spin-offs of marine research in IT-linked sensing and navigation would be the most appropriate plan, since the most obvious local cluster is in boat design, boat-building, boat maintenance and marine electronics, mainly for pleasure craft (the latter a business of nearly £2.5 billion for the UK economy). The development of marine materials and molecules as aids in the oil and gas extraction and processing sectors would also be a realistic target, in view of the importance of these sectors globally.[55]

The outcome of this report is the strong recommendation that a Marine Science and Technology Park (MSTP) would answer most of the strategic goals for science and economic development and overcome many if not all of the challenges and barriers, although the report does not discuss whether the biological marine sciences and marine engineering and technology might have different needs and routes to fulfilment. The University of Southampton's focus on research and

[53] Feasibility Study for the development of a marine science and technology (MST) cluster in Plymouth Final Report April 2003, GHK & BMT, for the City of Plymouth page 23

[54] *Feasibility Study for the development of a marine science and technology (MST) cluster in Plymouth* Final Report April 2003, GHK & BMT, for the City of Plymouth page 40, and see Annex A for core competence mapping of PML and MBA

[55] see Table 3.4 of the *Feasibility Study*, page 26

applications in deep-sea marine engineering and technologies are complementary to Plymouth's shelf and coastal expertise and one attraction of the proposed Plymouth MSTP would be the potential for productive linkage with Southampton.

3.4 Location of activities in the UK/clusters

TABLE 19: LOCATION OF RESEARCH AND COMMERCIAL ACTIVITIES

	ENGLAND	NORTHERN IRELAND	SCOTLAND	WALES
HEI, institute	33	2	10	4
Company	7	1	13	0

Regionalism is very evident. Scotland leads in the establishment of companies based on marine bioscience or servicing this sector. There is some reason for this – 63% of the UK's seas are in Scotland's area (though not under its direct control) and seas-based economy has been important in Scotland, especially for the Highlands & Islands region. The Scottish economic development agencies - Scottish Enterprise and Highlands & Islands Enterprise and the associated Local Enterprise Companies - are sensitised to marine opportunities in a way that most of the rest of the UK is not. There is some evidence of support for development of marine sciences in the South West, building on the Plymouth Marine Sciences Partnership of Marine Biological Association Plymouth, Plymouth Marine Laboratory, the University of Plymouth and the Sir Alister Hardy Foundation for Ocean Science. Regionality is not seen as critical to the development of viable businesses based on marine biotechnology or its outputs, though it may be important for raw material extraction and marine engineering *per se.*

DTI's guide to cluster development[56] is useful in pointing to models for networked activity (Scottish Food and Drink, for example) and structural development (Enterprise Hubs) as well as providing insights into the necessary factors for successful community-building.[57] Support for clusters is mainly at regional and local level.

Clusters are a positive initiative and are of especial benefit to SMEs growing in a sector.[58] Through interactions with a cluster, HEIs get a clearer knowledge of what target industry sectors need, and companies can find research and applied technologies to address those needs.[59] This has implications for research-driven marine activities that have applications in more than one industrial sector.

In terms of 'clusters' of marine bioscience and biotechnology research activities, there are what can be described as developing clusters in Scotland (e.g.

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[56] *A Practical Guide to Cluster Development: A Report to the Department of Trade and Industry and the English RDAs* December 2003 Ecotec Research & Consulting for DTI

[57] see Annex E of the Guide, which provides a 'quick reference guide' in table form

[58] Competitiveness: cluster-based policies 2002 The Cluster Competitiveness Group SA, Cerdanolya, Barcelona Spain

[59] Enhancing the Productivity of the British Economy: Cluster lessons and others September 2001 Paul Miller Trends Business Research

Aberdeen, Edinburgh, and at an early stage, Dunstaffnage[60]) and Plymouth[61] and Newcastle. Other centres of research activity include Glasgow, Essex and St Andrews. There is no formalised structure for networking and interaction between these and other sites with marine activity at institutional level; however, in Plymouth there is the Plymouth Marine Sciences Partnership, which forms a research and commercial support cluster, and across the UK there is collaboration between individual academics and departments in the NERC-funded M&FMB programme.

For marine biotechnology, important issues include how to make a marine biotechnology cluster work at national level and how to engage businesses who want to adopt best practice and learn more about new technology and science. A fairly comprehensive review of clusters in the UK could be useful in identifying regional end-user clusters that could be targets for marine biotechnology and its outputs, including regional strengths in biopharmaceuticals, chemicals, environmental industries, food, marine technology and classical pharmaceuticals.[62]

3.5 The context for Science and Innovation Strategies in the UK

Central Government

The UK Government responded in late 2003 to the Trade and Industry Committee's report on UK Biotechnology[63] with commitments relevant to marine biotechnology. These include increases in the budgets of MRC (Medical Research Council) and BBSRC (Biotechnology and Biological Sciences Research Council) of 57% and 62% respectively for 2005-2006 compared with 2000-2001, with investment in cross-council research on stem cells and genomics, both areas to which marine biotechnology can contribute (cell-to-cell signalling and genome analysis techniques, as well as data on conserved genetic information). The Science **Spending Review** of March 2004 formally recognised the need to spend more on R&D.

The most detailed exposition of the UK Government's intentions with regard to the support of science, development and innovation is to be found in the **Science & Innovation Investment Framework** document issued in July 2004.[64] It codifies the Science Spending Review and begins with the bold but true statement that **"*Harnessing innovation in Britain is key to improving the country's future wealth creation prospects*"**. The main challenge for marine biotechnology is to work out how to take advantage of this explicit statement of policy and genuinely move forward, scientifically and in economic development terms.

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[60] *Assessment of Marine Science activities and Capability in Scotland (Abridged Version)* October 2001, Scientific Generics Ltd for Highlands & Islands Enterprise and Scottish Enterprise

[61] Feasibility Study for the development of a marine science and technology (MST) cluster in Plymouth Final Report April 2003, GHK & BMT, for the City of Plymouth

[62] Business Clusters in the UK – A First Assessment February 2001,Trends Business Research,

[63] UK Biotechnology Industry. Government response to the House of Commons Trade and Industry Committee's twelfth report of the session 2002-03 Appendix to Sixth Special report of Session 2002-03, November 2003, The Stationery Office Limited, London

[64] Science & innovation investment framework 2004-2014 July 2004 HM Treasury, DTI, DfES

The Government has established a number of targets, which are termed 'ambitions' in the document[65]. Ambitions relevant to marine biotechnology include ensuring the UK's competitive position in research excellence, growing the UK's share of internationally-mobile R&D investment and people, a stronger influence from end users of research on Research Council programmes and continued improvement of UK performance in knowledge transfer and commercialisation. It is widely accepted that the UK achieves a strong R&D showing internationally with lower average investment compared with other countries.

Other initiatives that are committed to by this document, and in which marine biotechnology could have a role, given greater or lesser degrees of ingenuity, include:

- responsibility of the Director General of RCUK for a strategic fund for emerging priorities and the health of disciplines (£70 million)
- far greater emphasis on multidisciplinary capabilities and actions in HEIs, driven by the Research Councils (therefore suggesting a greater cross-Council internal activity)
- establishment of a high-level horizon scanning centre of excellence within Government and RCUK, to be co-ordinated by the OST's (Office of Science and Technology's) Fore*sight* Directorate, complementary to the horizon scanning activities of individual departments
- the dedicated capital funding stream provided by SRIF (Science Research Infrastructure Fund) will be continued, with £500 million per year from 2005 onwards, and an additional £50 million will be provided for Research Council Institutes by 2007-2008.[66]

The investment framework document records the decision to continue with the building of a replacement for the research vessel *Charles Darwin*, scheduled for launch in 2007, and recognises the role of marine bioscience in completing the marine biodiversity inventory as a component of a Sustainable Earth systems multidisciplinary programme. These multidisciplinary programmes are seen to be of international importance and, implicitly, ones at which UK must excel. The examples given include:

- Systems biology - again something to which current marine bioscience, biology and biotechnology can contribute
- Cognitive systems - where the understanding of cell-to-cell signalling and consensus between cells of different types that has arisen from the study of biofilms and other mixed marine microbial communities may well give critical insights.

The RDAs (Regional Development Agencies) and Devolved Administrations (Scotland, Wales, Northern Ireland) are best placed to identify and support emerging companies with the potential for strong growth. That said, it is recognised that these might arise not in a cluster, but in a 'pocket of scientific brilliance'. DTI's Bioscience Unit has a role in promoting and facilitating collaboration between regions and devolved administrations in relation to

[65] *ibid.* page 6
[66] *ibid.* Chapter 2

bioscience. It will therefore be an important player in the development of a marine biotechnology networked community.

Industrial applications of biotechnology are the subject of the first report of the UK **Industrial Biotechnology Task Force** (IBTF) which was facilitated by DTI's Bioscience Unit.[67] The IBTF report highlights the potential that translation of biodiversity into new industrial products has. Because of their ability to cope with high and low temperatures, high pressure and salinity, enzymes and whole cells sourced from marine derived micro-organisms have numerous potential applications in industry. EU policy developers are increasingly recognising the significant potential for industrial applications of biotechnology, which should open up further opportunities for marine biotechnology. For example, the Environmental Technology Action Plan stresses the importance of industrial biotechnologies for the sustainable development of our society[68], the European Technology Platform on Sustainable Chemistry (launched July 2004) brings together leading chemical companies with the new, emerging biotechnology sector[69] and the European Plant Genomics and Biotechnology Platform[70]. Further developments could well include industrial biotechnology being featured in the next EU R&D Framework Programme (FP7).

Regional aspects

An effective strategy will need to take account of regionality and current approaches to support of economic performance in the regions. Scotland is better represented in academic excellence and business start-ups in marine biotechnology than other regions of the UK, a reflection of long-term commitment to marine economic enhancement. Nevertheless, Scotland ranks fourth for overall Gross Value Added (GVA, expressed as output *per capita per annum*), at £12,500. London dominates at £22,500, mainly contributed by service industries, followed by the South East at £16,000 and Eastern region at £14,000. Outside Scotland, marine biotechnology activity aimed at commercial exploitation is found mainly in the South-East, South-West and North-East, regions with GVA 10-25% lower than Scotland's. Generally speaking, higher-growth companies require better-trained people. Contribution to GVA mirrors the proportion of population and employees with higher education qualifications, which has considerable implications for the siting of new businesses and the potential impact of increased funding of science and engineering training for marine biotechnology in the regions. Investment is also required for development of commercial activities and, certainly in the private equity sector, investment per head of population is very much higher in London, the South East and East [71] compared with other regions.

Several programmes are now available to provide support for the relatively high-risk start-ups that will comprise marine biotechnology's exploitation efforts. In particular, the **Regional Venture Capital Funds** (RVCF) are intended to go some

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67 Industrial Biotechnology: Delivering Sustainability & Competitiveness, IBTF. 2 December 2004 (see www.dti.gov.uk/biowise for further details).

68 For further information see http://europa.eu.int/comm/environment/etap/

69 For further details see Europabio's press release http://www.europabio.org/PRWB.htm

70 For further information see Europabio's press release http://www.europabio.org/PRGB.htm

71 Competing in the global economy: the innovation challenge December 2003 The UK DTI, Chapter 6

way towards addressing disparities and, with Regional Innovation Funds, University Innovation Centre funding and application of European Structural Funding, should be explored for support of regional activities in marine biotechnology. The **Research Council Follow-on Fund**, operated by NERC, BBSRC and EPSRC (Engineering and Physical Sciences Research Council), which supports proof of concept activities, closed its pilot scheme earlier in 2004 and has recently issued a new call.

The **Regional Science and Industry Councils** will be involved in steering R&D according to strategic goals and the needs of regional industrial sectors, and it is vital that marine biotechnology and its potential are brought fully before these.

Scotland has been a strong supporter of aquaculture, marine sciences and marine biotechnology and this will continue. Looking to the other Devolved Administrations, there are opportunities in Wales, where an £8.5 million Research Capacity Development Fund includes biosciences in its remit, and Northern Ireland, where there is considerable activity, including:

- a Research and Technological Development Fund
- a pilot Proof of Concept Fund of £3 million, established by Invest Northern Ireland and the Department of Enterprise, Trade and Investment
- the promise of £50 million in the Support Programme for University Research from 2004-2007
- £21 million from the UK-wide SRIF
- HEI-industry technology transfer support from the Higher Education Innovation Fund (HEIF), of £9 million from 2004-2007.[72]

[72] Science & innovation investment framework 2004-2014 July 2004 HM Treasury, DTI, DfES Chapter 9

4. MARINE BIOTECHNOLOGY IN AN INTERNATIONAL CONTEXT

There is a great deal of activity in marine biotechnology and associated marine technology world-wide. **Annex D** includes some details of funding and support for marine biotechnology in the UK and elsewhere.

4.1 International competition

From the competitive point of view, in the specific activity of building added-value businesses based on fisheries and aquaculture output, **Canada**, **Norway** and **France** are ahead of the UK, as far as we can tell.

In marine biotechnology itself, we see **USA** being definitely ahead of the UK. Germany and France are ahead in certain areas: **France** as a result of specific government support for networks such as GENOMER, programmes of commercialisation and individual research centres (Roscoff, Pleubian); **Germany**, as a result of a specific focus on commercial opportunities in the main marine research centres of GBF Braunschweig and the Institute for Marine Biotechnology Greifswald.

We do not consider **Japan** and **Australia** as immediate threats: Japan has invested heavily in marine biotechnology, with substantial cutting-edge work in deep-sea submersibles and high-pressure, high-temperature bioreactors over the past 20-25 years, but so far has not been very productive in biological applications of knowledge or international commercialisation. Australia, despite heavy investment and an impressive range of international collaborations, has only recently begun to be really active in licensing-out technologies and establishing start-ups from AIMS (Australian Institute of Marine Science), but the main impact is still local. The screening and pre-clinical arrangements of AIMS with the US National Cancer Institute may yet yield world-beating products but they are still far from commercialisation and, with the exception of some work on agricultural applications and sun-screen uses of marine bioactives, there is little other evidence of diversification.

Commercial challenges to the UK's existing efforts are in two main areas – culture collections, which have been well-commercialised from USA and Australia, and prevalence of patents and prior art in pharmaceutical applications of bioactives, certainly the case for USA. The UK can, however, be regarded as internationally prominent in marine actinomycetes, marine virus and biofilm research and it makes sense to capitalise on these strengths and move forward into a current window of opportunity.

It is more difficult to overcome the commanding position of the USA in marine biotechnology and marine-derived resources, because the USA started its support activities much earlier and it has put more money into it.

4.2 The European Union (EU)

UK initiatives need to be considered in an EU context. The Marine Board of the **European Science Foundation** (ESF) has published two Position Papers concerning marine biotechnology and marine science. The first of these, *Marine Biotechnology*[73], provides a foundation for relevant activities and initiatives at European and national level. The second[74] has a broader sweep and examines integration of marine science, including biotechnology, in Europe.

Marine Biotechnology set out a vision of creating a 'concerted and focused initiative', extracting marine bioactives and using them in medicine, industrial processes and environmental monitoring. The key objectives[75] are of the nature that can be facilitated by strong, effective academic-industrial networks and cross-institution collaborative projects. The outputs of this report are more a list of desirable research and collaboration goals than a defined strategy, but these are set in a wealth of information showing that these goals are quite feasible. Elements of a strategy included in the paper are

- investment in enlarging the knowledge base on marine life
- funding focus on marine biology and biotechnological applications
- co-ordinated funding of interdisciplinary programmes
- focus on problem-driven research
- upgrading and efficient networking of European marine stations and centres
- developing systems for high-level specialist training
- effective encouragement of industrial involvement in the application of scientific research
- establishing new ways of obtaining technology transfer
- establishing a global network for dissemination of marine biotechnology discoveries to academic, industrial, business and public sectors
- promotion of public understanding of the use of marine organisms
- establish marine biotechnology firmly in EU Framework Programmes.

An important aspect of this is better use and deployment of infrastructure such as research vessels, remote undersea vehicles and other mechanisms for safely accessing and researching marine organisms.[76] A Marine Infrastructures Strategy Group is envisaged, which can contribute to the goals of creating an effective European Research Area (something that is of great importance in the context of the recent enlargement of the EU). Although the *Marine Research Infrastructures* report concerns the breadth of marine research, not just biosciences and biotechnology, it makes some points that are relevant, including the desirability of promoting regional centres of excellence and accessibility and co-ordination of infrastructure.

Active involvement of the UK in European Union projects, such as the **Network of Excellence in Marine Genomics**, has now increased. Investment in advanced

[73] Marine Biotechnology, a European strategy for marine biotechnology ESF Marine Board Position Paper 4, December 2001

[74] *Integrating Marine Science in Europe* ESF Marine Board Position Paper 5, November 2002

[75] see page 3, Executive Summary of the ESF report *Marine Biotechnology*

[76] *European Strategy on Marine Research Infrastructures* 2003, the Academy of Finland, for the European Strategy Forum on Research Infrastructure, Publications of the Academy of Finland 6/03

marine engineering for sampling, screening *in situ* and in Sea-Bed Observatories will help maintain the UK's position in Europe.

5. UK STRENGTHS, WEAKNESSES, OPPORTUNITIES AND THREATS (SWOT)

5.1 The SWOT Analysis

The UK marine biotechnology sector faces a number of challenges. One aim of this study was to establish a current view of the UK's strengths, weaknesses, opportunities and threats in the field of marine biotechnology. There have been a number of exercises at UK and European level, discussing and analysing the position with respect to development of marine biotechnology against what is perceived as its potential. The outcomes of some of these are presented and discussed in more detail elsewhere in this document. Our own work, based on a synthesis of existing information, a mid-project workshop and direct enquiry of interested parties, led us to the following analysis:

UK Strengths

- Excellent intra-national collaborations fostered by NERC (Natural and Environmental Research Council) and earlier BBSRC (Biotechnology and Biological Sciences Research Council) funded programmes.
- Good move to establish a M&FMB (Marine and Freshwater Microbial Biodiversity) Technology Translator.
- Individual centres of excellence exist (Southampton for deep-sea technologies, Plymouth for marine viruses, Newcastle for actinomycetes, Aberdeen for bioactives, Heriot-Watt for biofilm and applied marine biotechnology, SAMS for biocides and surfactants, for example).
- Overall:
  - Excellent activity in marine actinomycetes
  - Excellent activity in marine biofouling.
  - Excellent activity in marine viruses.
  - Potentially excellent culture collections.
  - Strengths in advanced engineering for ocean explorations.
  - Strengths in bioprocessing technology and some institutional desire to move ahead and fund this.
- Access to Faraday Partnerships for best practice and Knowledge Transfer Networks/Partnerships for enhancing science-base/industry collaboration.
- Ability to build on what natural resources activities we already have (mariculture, seaweed processing, aquaculture) and exploit added-value opportunities.

Note: ***Annex C*** *draws out the relevant conclusions of a report on the application of bioscience in the development of non-food crops, where there are some parallels which have helped inform our analysis.*

UK Weaknesses

- Lack of UK co-ordinated framework for marine biotechnology.

- Fragmented research community (in spite of NERC programme) with no planned cohesion, lacking clearly-visualised Centres of Excellence.
- Many research groups are small and lack critical mass compared with US (COMB or Scripps)
- Few large-scale or productive international collaborations.
- Still on the whole a mismatch between perceptions of value in the academic sector and in the commercial sectors.
- Not much follow-through from research findings to practical applications.
- Low investment base in business ideas arising from marine biotechnology or biosciences research.
- Few companies of any size and momentum to take new ideas forward.
- Reluctance of larger companies in pharmaceutical sector to take on marine bioactives.
- No inventory of resources.
- No integrated training programmes that start at base-line with marine biotechnology.

Opportunities for the UK

- Some viable business opportunities have already been identified that capitalise on the UK's science strengths in marine biotechnology; these include applications of biofilm knowledge in anti-fouling, use of marine viruses, development of new enzymes for biocatalysis, development of bioactives for infections (rather than cancers).
- The UK's work in marine bacteria and cell-to-cell signalling is highly relevant to R&D and commercial opportunities in other fields such as medicine and cancer prevention.
- Scientists working in marine biotechnology are aware that building a network will enhance interactions and improve opportunities for working with industry - the DTI's Knowledge Transfer Networks programme gives the opportunity to do this.
- There is an opportunity to use the SAMS experience of establishing the European Centre for Marine Biotechnology to explore the possibility of establishing other Centres of Excellence, either real or virtual, building on existing strengths.
- Funding programmes exist in Scotland (Proof of Concept projects, the Intermediary Technology Institutes, HIE provision of flexible funding) and the rest of the UK (Follow-on-Fund, Knowledge Transfer Partnerships, DTI Business Support Products) to move science-industry developments forward in application of the output of marine biotechnology
- The SBRI programme is a gateway for start-ups and SMEs to receive alerts on government procurement opportunities and to find out more about departmental and research council funding programmes[77].

[77] see www.sbri.org.uk

Threats to the UK

- France has significant strengths in deep-sea exploration and deep-sea bacteriology, which are somewhat in advance of ours.
- The French programme supporting exploitation of marine algae ('Valorisation des Algues') has also been important in legitimising commercial activity in this area.
- German investment in marine bioactives has been significantly greater and earlier than the UK's; Greifswald and other institutes are definitely focused on commercial opportunities; and MPI and GBF have strengths in genomics.
- If funding priorities are switched away from continuation of fundamental work to emphasise applied and exploitable aspects, there is a risk of falling away from the cutting-edge of science.
- The investment community currently fails to regard marine outputs with any seriousness; discussions are required.

5.2 Responses to the SWOT Exercise

To explore the relevance of these findings and to obtain feedback on the recommendations which those suggested, we sought responses from academic workers in the field and commercial or business support contacts. 66 questionnaires were sent out, 56 to academics and 10 to business and we received 10 detailed responses and 5 less-detailed responses, all of which provided insight into the goals and preferences. Of these, 11 were from the academic sector, 4 from the commercial or business support sectors. The main comments are summarised below:

- Respondents recognised the general panorama of strengths, weaknesses, opportunities, threats and recommendations as being comprehensive and were in general agreement with them.
- A priority of many respondents was identification of early- and mid-term opportunities for exploitation. Using Technology Translators was seen as a prime way forward. How to stimulate industry to invest in potential marine natural products was a prime challenge. A focus on microbial enzymes for biocatalysis might provide initial success and impetus.
- It was also seen as important to have a long-term commitment, to a 5-10 year programme, and one that allowed the advantages of devolved administrations to be deployed. Other preferred recommendations included investment seminars and partnering events, centralised support for fund-finding and applications, a Resources Review, using a network to raise awareness in the scientific community of the value of this type of activity to them as well as industry, and enhancing marine biotechnology training.

5.3 Initial Recommendations

Analysis of the SWOT findings resulted in recommendations in five activity areas:

- Maintaining and developing R&D base
- Sustaining networking
- Commercialisation and funding

- Scientific understanding of marine biotechnology and marketing
- Stimulate training and education

On further assessment, focus on funding was subsumed into the commercialisation element, leaving five major tasks to tackle (see **Chapter 6** for detailed discussion of recommendations, and **Volume 2** for background information, commentary, appendices and references).

6. STRATEGIC ANALYSIS AND RECOMMENDATIONS FOR ACTION

The following chapter focuses on the five key areas for action that were identified following the SWOT exercise (set out above). For each area, we have set out the suggestions that emerged during this study (see bulleted italicised list – in no particular order of importance), some further discussion, current activities and what we see as the key recommendations for action.

The remainder of this chapter then analyses the general approach to a strategy and reviews component parts, in the light of available programmes for support in the UK.

Figure 1 and **Figure 2** at the end of this section illustrate the linkages between the areas for action and those who might be involved.

6.1 Maintaining and Developing the Science Base

Review resources within the marine sciences including biotechnology, and create accessibility:

- create an inventory of marine biotechnology resources: map the expertise, equipment and other useful facilities of each research and development group or centre that could serve as a community-wide resource – MBA and FMP could perhaps collaborate on this.
- examine the feasibility of setting up virtual or real cross-sector resources that call on the strengths of individual researchers and organisations, evaluating the potential of each HEI or institute to form part of such centres:
    - a Centre of Excellence for Marine Biotechnology Chemistry and Analytics, which isolates, characterises, establishes synthetic methods and develops appropriate analytical tools for novel bioactives and biomaterials from marine sources.
    - a Bioprocessing and Scale-Up Centre, which finds the best ways to mass-culture source organisms, whether open cultivation, closed bioreactor or by use of genetic engineering, and builds and validates the industrial-scale systems required, as well as putting in place the relevant knowledge from chemistry and analytics.
    - a Centralised Marine and Industrial Culture Collection facility, with suitable depository, viable storage and validation facilities, running at commercial rates.
    - a Centre for Marine Biotechnology Pharmaceutics & Formulation, which establishes the commercially-viable forms for marine bioactive-based or biomaterials-based products, in collaboration with industry.

Discussion

The proposed approach is a way of drawing together the diversity of expertise and overcoming the geographic separations within the marine biotechnology community, also of recruiting assistance cross-discipline and of making strategic links with pre-existing activities in other sectors, such as the ITI (Intermediary Technology Institute) Life Sciences, the UK Centre for Tissue Engineering or the Advanced Bioprocessing Centre, Brunel University.

HIE/SE's Marine Science Strategy for Scotland recommends that major participants in marine biotechnology should hold periodic brainstorms to maximise enthusiasm and opportunities for synergy; this can easily be adopted on a nation-wide basis.

Key recommendation for action:

The FMP-Marine Biotechnology Group will consider further, in collaboration with a network of researchers and companies already established in the sector, the strengthening of one or more centres of excellence in discussion with appropriate bodies (e.g. RCUK - Research Councils UK, DTI and regional development and enterprise agencies).

6.2 Sustaining Networking

Create a community for scientists working in marine biotechnology:

- establish a new web-site or build on an existing one
- provide:
  - scientific content.
  - market information relevant to development and commercialisation of the outputs of marine biotechnology.
  - a discussion forum for scientists and industrialists.
  - virtual conferencing.
  - resource matching between science and industry.
- since Knowledge Transfer Network funding might be appropriate for this, make a case to DTI for support of this for marine biotechnology.

Discussion

Two aspects emphasised by respondents during this project were that, though there is a great deal of research going on, and the NERC has played an important catalytic role, there is no other effective platform for networking within the science community, especially to bring in people from disciplines other than marine biotechnology and biodiversity studies. There are also no platforms, networks or fora in which the science community and the industrial end-user communities can come together, which is possibly the main barrier to speedy uptake of new ideas by industry - a reason why a Knowledge Transfer Network approach may be particularly productive for this sector.

Effective networking can be encouraged by organised workshops, seminars and partnering events that deal with marine biotechnology in general, and presentations by marine biotechnologists at fora where end-users are in attendance, as well as the development of a dedicated web-site that serves the interests of the entire community.

Current activities:

Networking is in train through the M&FMB programme, as it brings diverse researchers together. NERC is also funding a Knowledge Transfer Network on microbial biodiversity and marine biotechnology and this can be built on to extend beyond microbial biodiversity to biotechnology, given suitable resources.

Key recommendation for action:

By building on existing funded networking activities by the research councils, such as the NERC M&FMB (Marine & Freshwater Microbial Diversity) programme, and new initiatives such as the Knowledge Transfer Network funded by the DTI (Department of Trade and Industry), a pan-UK approach to marine biotechnology will be developed.

6.3 Commercialisation and Funding

Identify viable business opportunities that the market wants, benchmark these and assess their feasibility:

- realistic candidates for the above process seem to us to be:
  - applications for marine biofilm knowledge in medical and other industrial anti-fouling.
  - marine viruses for environmental and industrial use.
  - microbial enzymes for biocatalysis, including those from marine viruses.
  - bioactives for infections (rather than cancers).
  - added-value materials from raw material processing.
- make full use of the Technology Translator concept.
- develop a technology transfer methodology that can be applied to future outputs.
- explore, at an early stage, the potential for transfer to other sectors of the UK's knowledge in marine bacteria and cell-to-cell signalling.
- identify technology gaps where marine biotechnology could meet areas of need for industry (including non-biomedical).
- make use of Scottish Proof of Concept projects and Intermediary Technology Institutes, using Scotland's marine scientists as the entrée.
- make use of HIE flexible approach to funding research and development.
- make use of UK Follow-on-Fund, Knowledge Transfer Projects and SBRI (Small Business Research Initiative) service for directed development of the research outputs of marine biotechnology.
- provide some centralised planning and assistance for marine biotechnology researchers and SMEs via information, web-site links and, if appropriate, a hands-on service.
- the investment community continues to be interested in innovative approaches to manufacture, healthcare and high-tech, and there should be no barrier to marine biotechnology feeding into this, provided that the targets are clear and the business strategies for reaching them are well-argued; this requires the marine biotechnology community as a whole to promote what is on offer to the investment community, using well-thought out seminars, conferences and partnering activities.

Discussion

With regard to delivering the needs of industry, a UK-based respondent has pointed out that:

> *"there's a kind of institutional or cultural void between the people with relevant academic competencies and the ultimate end users (oil companies, pharmaceuticals, etc). Other sectors have a fertile middle ground of "appliers" – IT, for instance. Academics who are good at being academics are not always the risk-coping entrepreneurs that these high-investment high-tech outputs demand, and experience seems to suggest that the market for one brilliant idea is more finite than university researchers expect."*

This is consistently a difficulty faced by an academic community seeking to exploit its discoveries. The most effective ways of overcoming the perceived and actual gaps are:

- industry-led contract-based work that springboards off the academic discovery.
- R&D centres funded by industry consortia that focus on industry problems.
- creation of networks, fora or platforms that bring academic researchers and industry together.

The latter has the capacity to pinpoint industrial problems, challenges, gaps and needs on a broader scale, review research innovations from diverse sources that could answer these, and develop collaborative projects to do this. We tend to favour this route as a better way forward; if nothing else, it also allows each community to make internal links (ie academic-academic or industry-industry) that otherwise might not happen.

Funding of basic knowledge in marine biodiversity and biotechnology is an issue. By 1995, the USA realised how far behind Japan it was falling. Only £22million in 1992 of Federal biotechnology research funding was going into the marine sector compared with £290 million in Japan, and this included infrastructure. The application of funds for research alone in marine biosciences and biotechnology in USA is now significant - The Sea Grants programme, the Microbial Observatories (see **Annex D**) and even the Californian BioStar/University of California Discovery Grants total almost £56 million. But these programmes are dwarfed by the Census on Marine Life programme, a >45-country collaboration, with core funding from the Alfred P Sloan Foundation and total funds of £600 million over 10 years.

The UK can take part in activities such as these but the research and applications communities cannot hope to receive funding at such a scale, even comparatively-speaking. The UK Research Councils have supported different aspects of marine science and biotechnology; currently, the most important activities in biosciences lie within the Marine & Freshwater Microbial Biodiversity programme, supported by the NERC with funding of approx. £7 million. Commercialisable results are arising from this programme. One target might be to persuade other research councils and government funding sources to include support for applied marine biotechnology in their budgets and policy thinking.

This needs to be addressed as a matter of urgency, and it may require some degree of flexibility on the part of government to respond; a way forward would be for the scientific and applications communities themselves to come up with proposals for support that stimulate the interests of more than one funding source in such a way that they feel able, perhaps obliged, to work together.

In order to accelerate development in this sector, creating projects in the new Knowledge Transfer Networks (KTNs) and Knowledge Transfer Partnerships (KTPs) programmes is one opportunity. Making use of existing integrative mechanisms such as transfer of best practice from Faraday Partnerships is another.

The investment community in UK is, on the whole, conservative. Biotechnology-based human health companies have produced some success stories but have also produced high-profile failures. Investing in this area is generally the province of a few high-profile specialists such as Prelude, Advent, Apax Partners in the UK, Soros Perseus in US, or technology consultancy-associated funds such as TTP Ventures in UK. There is no real precedent in the UK for involvement of such companies in marine biotechnology exploitation.

Current activities:

Some **commercialisation** is already underway, either as activities by individual scientists or organisations, or through the medium of technology translators devoted to one particular programme, as is the case for the NERC's M&FMB programme. Outcomes can be enhanced by appropriate support in a networked environment, such as provided by an interest grouping or partnering activity. There is no current specific focus on **funding** for exploitation of outputs of marine biotechnology. It is necessary for entrepreneurial researchers and start-ups to search for funding from a variety of sources, including existing public programmes and investor organisations. The establishment of regional venture capital funds and maintenance of the Enterprise Investment Scheme may assist SMEs, provided they have a good story to tell about why marine biotechnology offers good prospects to investors.

Key recommendation for action:

The FMP-Marine Biotechnology Group will develop a register of interested venture capitalists, and garner support from biotechnology trade associations (e.g. the BIA), to develop a portfolio of funding opportunities, with the assistance of the DTI.

6.4 Scientific Understanding of Marine Biotechnology and Marketing

Address concerns about the marketing and image of the sector:

- organise science missions, GlobalWatch missions, involve more scientists in trade missions.
- encourage and support the presence of UK marine biotechnology scientists at conferences and workshops that relate to end-users.
- prepare publicity using case studies of successful development and application of marine biotechnology, targeted at four sectors – academic, industrial, public and intermediaries (including government and funders).
- use whatever additional Government sponsorship is possible for disseminating information on biotechnology and innovation.

- enhance opportunities for the UK to reach level pegging and aim to overtake France and Germany using appropriate, strategic collaborations, funded by EC programmes or other instruments depending on scale and scope.
- use sensitive and consistent lobbying to ensure a realistic balance in support between fundamental marine bioscience, including biotechnology, and development and commercialisation of the sector.

Discussion

In order to establish the gravitas of the UK's research activity in the minds of stakeholders and demonstrate the contributions it can make to scientific excellence, competitiveness and economic progress, promotion activities are essential. Success breeds success. There are success stories in marine biotechnology, even if they do not always come from the UK (eg pseudopterosin). The UK has scientific excellence in several areas that are intrinsically fascinating (oceanic engineering, marine viruses, extremophiles from coastal areas, for example) and others that hold out great promise for environmental and health benefits, topics of current public and policy interest (eg biofouling, cell-to-cell signalling, actinomycetes and other microbes).

Though individual efforts should not be prevented, to make the most of the opportunities and the UK's strengths in an efficient way argues for a co-ordinated approach with a focal point for information on the science and benefits of UK marine biotechnology. Conferences, workshops and partnering events with the specific theme of products from marine science will also add to the impact of activities in this area, adding value to research funding and assisting commercial prospects.

Current activities:

Support of marine biotechnology GlobalWatch, Trade and other special missions are helpful.

Key recommendation for action

New initiatives in public understanding of science will be harnessed to develop readily accessible information that fulfils a promotion, PR and marketing objectives.

6.5 Stimulate Training and Education

Create a co-ordinated cross-disciplinary training effort

- build on existing excellent marine science and biology courses and the two marine biotechnology courses that are available.
- benchmark, review and if appropriate transfer best practice from within the Faraday Partnerships in establishing modular cross-institution courses.

Discussion

Training is a common theme in high-technology bioscience sectors. We believe that here, too, a collaborative approach is best, in order to make use of scarce resources. This is why we suggest reviewing existing marine bioscience and marine biotechnology courses and, by taking best practice from cross-institutional and/or modular higher education in other areas (eg from UHI Millennium Institute, Faraday Partnerships, inter-institutional centres of excellence or Open University), assess the feasibility of establishing similar training courses, which can be more effectively funded for this role than trying to establish a number of fully-formed but essentially competitive courses at several HEIs. Individuals in the marine biotechnology community may also benefit from training in the communication of science to other scientists, lay public and groups such as investors and policy-makers.

Current activities:

The Government has recognised the importance of training across the sciences and there is considerably more funding available for training programmes, including basic skills, scientific skills and business knowledge. Contact with RDAs and local Skills and Training Councils will enhance the possibility of obtaining financial support for training programmes geared to the special needs of marine biotechnology and companies based on this.

Key recommendation for action:

Working with the Funding Councils and Research Councils, the FMP-Marine Biotechnology Group will seek to identify opportunities for modular cross-institution courses in marine biotechnology, including specialist technical skills training.

7. DEVELOPING A STRATEGY FOR SUCCESSFUL SCIENTIFIC AND ECONOMIC DEVELOPMENT OF MARINE BIOTECHNOLOGY IN THE UK

7.1 Analysis

Any strategy for development of a technology-based sector needs to recognise both scientific and commercial aspects:

- Recognition that the field in question has made genuine scientific achievements.
- Showing that research in the field can contribute to economic advancement.
- Identifying the players and contributors necessary for a successful strategy.
- Capacity-building for promotion and marketing.
- Developing programmes of scientific support for innovation creation.
- Using programmes for economic development to transfer knowledge and technology and build marketable products and services.
- Harnessing willingness-to-fund.
- Establishing the best facilitation mechanisms.

7.2 Possible mechanisms

The DTI Innovation Report *Competing in the global economy: the innovation challenge* views innovation as the source of better products and services, cleaner and more efficient production processes and improved business models, with positive impacts on consumers, businesses and the economy alike.[78] A strong message in this report is the Government's commitment to realising the UK's potential through creating a more demand-led, responsive and flexible training system. It recognises that cross-departmental action on fostering innovation is still required, building on DTI and OST activities.

The report promises direct measures in seven key areas:

- generating new knowledge that is transferable.
- enabling companies to better transfer and embed that knowledge.
- filling gaps in access to funding.
- stimulating competition and entrepreneurialism.
- encouraging suppliers to Government and other public sector procurement agencies to become more creative.
- promoting appropriateness of regulation.
- enhancing networks and collaboration.

More recently, the Science and innovation investment framework document points the way to actions for 2004-2014. These initiatives are there to be taken

[78] Innovation Report: Competing in the Global Economy the UK DTI September 2003

advantage of by players in the marine biotechnology sector in moving towards an overall goal of enhancing UK's productivity and competitiveness.

In broad terms, scientific development includes actions such as support for integrated or directed programmes, cross-institute and trans-national projects in identified subject areas, increased focus on training and on knowledge transfer by placements and collaborations, science-oriented networks and scientific PR (public relations and communications). In the UK, these commonly fall within the remit of the research councils making up RCUK, private research funding organisations (Wellcome, for example), trans-national funding bodies such as the European Union (EU), and the HEIs (Higher Education Institutions) and PSREs (Public Sector Research Establishments) themselves.

Economic development includes actions such as support for technology transfer, prototyping and capacity-building for SMEs (small and medium-sized enterprises), academic-industry networks or platforms, investment funds targeted at a specific sector, export promotion and trade missions, cluster-building and infrastructure support, including training. Conventionally, DTI, Regional Development Agencies (RDAs) and Skills and Learning Councils are the supporting and organising bodies for such activity. A more recent actor on the scene is NESTA, the National Endowment for Science, Technology and the Arts.

The UK Government's approach to funding of technology innovation and economic development has been overhauled and there are considerable opportunities for marine biotechnology in this[79] (**Annex D** expands on possible sources of funding and support).

7.3 Targets

The targets are to:

- identify the elements and mechanisms for successful scientific and economic development of marine biotechnology in the UK
- scope the scale of requirements
- identify players and contributors to investment/funding packages
- define feasible investment/funding strategies
- make recommendations for achieving all this.

7.4 Possible next steps

A sequence of events in encouraging the development of marine biotechnology in the UK could therefore include the following:

- defining the sector, creating its message and engaging enthusiasm
- supporting a network as a facilitating mechanism
- instituting a directed or thematic programme of research that validates the commercial potential of scientific innovations, for example into identifying

[79] see Competing in the global economy: the innovation challenge December 2003 The UK DTI and Science & Innovation investment framework 2004-2014 July 2004 HM Treasury, DTI and DfES

and validating marine outputs for the chemical, pharmaceutical and biotechnological sectors

- supporting relevant centres of excellence
- supporting research-industry-investor knowledge and technology transfer as appropriate
- general support of communications, public relations, image-building, credentials of the sector.

7.5 Participants

The aim of facilitation mechanisms is primarily to encourage industry and research to work together, to enhance the credentials of research in terms of ability to fill technology gaps or answer some of industry's strategic needs, and to legitimise industry's needs in the eyes of researchers. Facilitation should also strengthen the partnership between academic and industry sectors in the areas of education and training and enhance the willingness-to-fund of investors. Mechanisms may be passive, in the sense that programmes are provided by government or locally and people may take advantage of them, or active, in the sense that there are protagonists driving activities forward. Establishment of a small, active team representing the interests of a particular academic-industry grouping is always more effective in focusing strengths and leveraging energy than moving immediately into a broad, dispersed kind of network. If Government identifies a particular area for action and undertakes to support such a group by targeted funding, this can be genuinely synergistic.

There is a complex connectivity between players and contributors in the marine biotechnology sector. If a centrally-active facilitation organisation is seen as key to establishing a successful strategy, it might work as shown in **Figure 2**.

IACMST, the Inter-Agency Committee on Marine Science and Technology, may have a role, in that it is possible to work with a member department such as DTI to encourage an Open Forum on the development and exploitation of marine biotechnology, or work with IACMST's marketing liaison function to set up an industry-research conference.

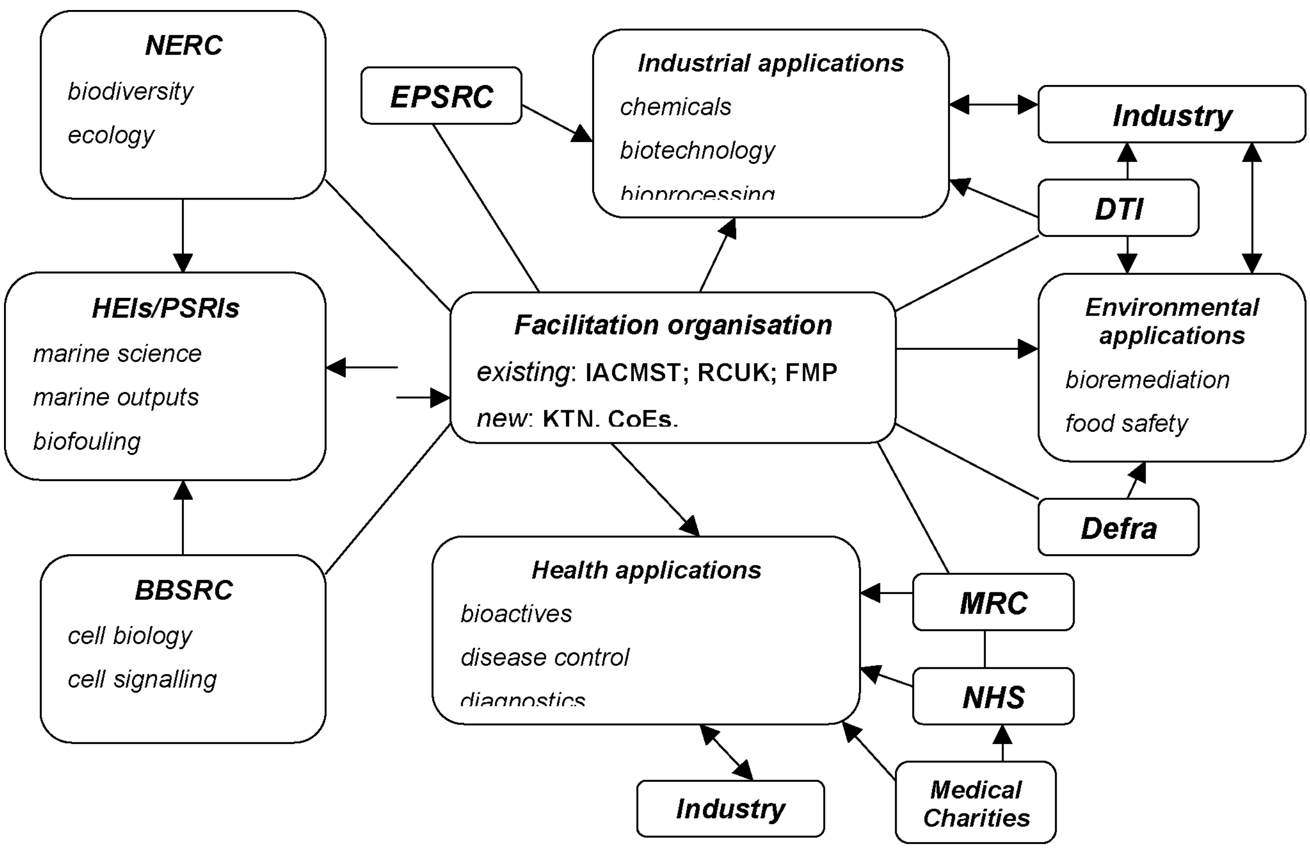
7.6 Costs

A cost estimate for a strategy support programme can be constructed from knowledge of the costs of reasonably comparable programmes and projects, including some marine science ones (see **Table 25** in **Annex D**). Following a decision on what strategy to follow, deeper analysis will allow the development of more accurate and coherent costings and a plan that identifies realistic sources of funding, nationally and internationally, public and private. **Annex D** also summarises potential sources of funding and support.

FIGURE 1: RECOMMENDATIONS AND POSSIBLE ACTIONS IN A MARINE BIOTECHNOLOGY STRATEGY

Maintaining and Developing R & D Base: Review resources, create accessibility to scientific and industrial communities	Create an inventory of marine biotechnology resources, map expertise, equipment Examine the feasibility of setting up virtual or real cross-sector Centres of Excellence	Explore and use all available Government Initiatives Identify initiatives in other sectors – chemistry and analytics, bioprocessing, pharmaceutics and formulation; Scottish ITI, UK equivalents Consider ways of improving Culture Collection economics
Networking: Create a community for scientists, influencers and end-users working in marine biotechnology	Test models for networks very actively Establish a web-site Create workshops, seminars and fora Bring together scientists and industry, plus funders, government, charities, patient groups, end-user groups Engage in brokerage and partnering events Build knowledge base of relevant science and business	Approach DTI about Knowledge Transfer Networks Read, understand and use all initiatives included in Government's Innovation strategies Consider Centres of Excellence – will they contribute?
Commercialisation and Funding: Identify viable business opportunities, benchmark, assess feasibility; identify and obtain funding	Applications for marine biofilm knowledge in medical sector Anti-fouling paints Marine viruses for environmental and industrial use Microbial enzymes for biocatalysis Bioactives for infections, inflammations, cancers Added-value materials from raw material processing Transfer UK knowledge in marine bacteria, cell-to-cell signalling Create a service providing centralised information on public and private funding and assistance with applications Increase interactions between researchers and investment community Improve the visualisation and communication of business concepts	Technology Translators User-friendly tech transfer methodology Identify technology gaps by dialogue with industry Focus on Markets Scope the opportunity Build a Network? Use web-site as open door Understand and use available Government initiatives Plan workshops, seminars and partnering events Training in communication skills for business
Scientific PR and marketing	Develop a coherent profile of UK marine biotechnology and a clear message that marine biotechnology can contribute to a better future and to the economy; get over the message to the people and organisations that count	Draft an agreed briefing paper Make use of Government initiatives in science communication and public understanding of science Co-ordinate UK Marine Biotechnology presence at overseas events
Training: undergraduate, graduate and post-graduate levels for marine biotechnology; business skills	Create a co-ordinated cross-disciplinary training effort	Build on existing marine bioscience and biotechnology courses If appropriate, transfer best practice from modular cross-institution courses eg FPs, OU Make use of Government initiatives in training

FIGURE 2: CONNECTIVITY BETWEEN RESEARCH AND SUPPORT IN SCIENTIFIC DEVELOPMENT AND COMMERCIALISATION



Notes:

In Figure 2, double-headed arrows refer to collaborative development; single headed to funding support, in the case of RCUK, NHS (National Health Service) and Government, or flow-through of knowledge/technology, in the case of applications. The linkages of RCs and DTI to a possible integrating body might be via funding, policy discussions, directed programming, eliciting of further Foresight activities or other scientific and economic development instruments.

The above does not take into account interactions with RDAs, Devolved Administration support bodies, Local Authorities or Government departments such as DfES.

ANNEX A: COMPANIES

TABLE 20: COMPANIES ACTIVE IN ASPECTS OF MARINE BIOTECHNOLOGY IN THE UK

COMPANY	CONTACT	SECTOR
Actinomed Ltd Newcastle	Alan Blakey; Prof Mike Goodfellow, Dr Alan Ward	A very new start-up looking at bioactives from novel marine actinomycetes; targeting antibiotic-resistant bacterial pathogens
Aquapharm Bio-Discovery Ltd European Centre for Marine Biotechnology, Dunstaffnage Marine Laboratory, Dunbeg, Oban, Argyll, PA37 1QA	Dr Andrew Mearns Spragg CEO T: 01631 559390 andrew@aquapharm.co.uk	Founded by Heriot-Watt University post-doc; has >1000 microbes in library and three candidates – AQP001, new source of astaxanthin for aquaculture feeds, APQ002, process for anti-oxidant flavonoids and APQ001, new antibiotic; gained a Smart:Scotland award in 2001 for the astaxanthin
BioDiversity Ltd Business Innovation Centre, Rm 23/24, Innova Park, Mollison Avenue, Enfield EN3 7XU	T: 020 8350 1278 F: 020 8350 1255 info@bdlabs.com	BioDiversity supplies microbial samples, fermentation biomass extracts and metabolites and has a focus on fungi, which may be relevant to marine bioactives
Biolitec Pharma Ltd Breasclete, Isle of Lewis, HS2 9ED Western Isles (HQ Heriot-Watt Research Park, Edinburgh)	T: 01851 707500 F: 01851 621368	Originally Scotia Pharmaceutical's photodynamic anti-cancer therapy division, sold to Singapore Technologies when Scotia folded and then bought in 2002 by BioLitec AG of Germany; down-sized in 2003-2004; was researching bioactives from seaweed
Carapacics Ltd c/o QUBIS Ltd Lanyon North, The Queen's University of Belfast, University Road, Belfast BT7 1NN, Northern Ireland	Ian Scade, MD c/o T: 028 9068 2321 F: 028 9066 3015	Founded in 1999 in Northern Ireland as a spin-out from Queen's University Belfast, Carapacics has developed technologies for producing added-value chitin, chitosans, collagen and biocomposites from prawn wastes. The company began a joint venture in 2000 with a US company Ovogen to carry out similar development and commercialisation work with egg shell membrane. Carapacics has a Scottish site in Ayrshire.
Coastal & Marine Biotechnologies Ltd Tamar Science Park, 1 Davy Road, Derriford Plymouth PL6 8BX	Ian McFadzen, Director John Wedderburn, Director T: 01752 764430 F: 01752 772227 cmb@cmbiotech.co.uk	A spin-out from the Plymouth Marine Laboratory & NERC, founded in December 2001; has developed water quality assays using shellfish embryos and itself spun-out **BioVault Ltd**, a human cell and tissue cryopreservation company, on the back of its proprietary freeze-drying technology; expanding to include 'UK's and EU's first bio-repository facility'

TABLE 20: CONT

COMPANY	CONTACT	SECTOR
Commercial Microbiology Ltd Kettock Lodge, Campus 2, Aberdeen Science Park, Bridge of Don, Aberdeen AB22 8GU Scotland	Stephen Maxwell, Managing Director; Alison Gardner General Manager T: 01224 706062 F: 01224 706012 info@commercialmicrobiology.com	Bioremediation: Development of biological products for odour control, oil spill clean-up, drill cutting remediation, effluent treatment
Croda International Plc Cowick Hall, Snaith, Goole, East Yorkshire DN14 9AA	T: 01405 860551 F: 01405 861767	Colloids company, originally animal-origin, now widely-sourced including marine; cosmetics formulations sold via subsidiary Sederma
Destiny Pharma Ltd Sussex Innovation Centre, Science Park Square, Falmer, Brighton, BN1 9SB	Dr Bill Love, CEO T: 01273 704 440 F: 01273 704 499 wl@destiny-pharma.demon.co.uk	Working with Prof Peter Revell (University College London-Royal Free Hospital) and Prof Andrew Lloyd (Brighton) on alginates and chitosans for tissue engineering scaffolds
Drug Discovery Ltd Royal College Building, 204 George Street, Glasgow G1 1XW	Dr Alan Harvey T: 0141 548 4534 info@drugdiscovery.co.uk	Strathclyde Institute for Drug Research's commercial arm – bioactives from marine sources, as well as other microbes and plants, specifically targeting asthma, arthritis, cancer and rejection of transplantation.
Hebridean Biotech Ltd		A new company, set up to commercialise essential fatty acids produced in marine algae; awaiting results of an application for SMART funding, currently dormant
Integrin Advanced Biosystems Marine Resource Centre, Barcaldine, Oban, Argyll PA37 1SE Scotland	Dr. Charles Bavington charlie@integrin.co.uk, Claire Moss claire@integrin.co.uk T: 01631 720 765	Marine Natural Products: international libraries of marine extracts, screening for interesting biological activity, bioactive characterisation, delivery into pharmaceutical drug development pipelines; tests for shellfish toxins; development of new culture methods for marine invertebrate cells and for bacterial symbionts to accelerate development of bioactives
ISP Alginates (UK) Ltd Ladyburn Works, Dipple, Girvan, KA26 9JN Strathclyde	T: 01655 333000 F: 01655 333100	Major producer of alginates and other marine hydrocolloids, using mainly imported raw materials. Contributes approx. £30m turnover to Scotland's marine economy.
Laxdale Ltd Kings Park House, Laurelhill Business Park, Stirling, UK FK7 9JQ.	T: 01786 476000 F: 01786 473137	Developing treatments for central nervous system diseases such as Huntington's and Alzheimer's diseases from polyunsaturated fatty acids (PUFAs). Being acquired by US company Amarin
Marine Biotechnology Products 125 Ramsden Square, Barrow-in-Furness, Cumbria LA14 1XA		Registered at Companies House but no further information available yet

TABLE 20: CONT

COMPANY	CONTACT	SECTOR
NCIMB Ltd 23 St Machar Drive, Aberdeen AB24 3RY	Ian Garner, Gordon McFarlane T: 01224 273332 F: 01224 272461 enquiries@ncimb.co.uk www.ncimb.co.uk	Commercial arm of the National Collection of Industrial, Marine and Food Bacteria, providing research and consultancy in microbiology; part-funded by BBSRC.
Novacta Biosystems Ltd Innovation Centre, University of Hertfordshire, College Lane, Hatfield, AL10 9AB	Fiona Marston, Brian Rudd, Mike Dawson T: 01707 281100 mail@novactabio.com, brian.rudd@novactabio.com	Drug discovery & development company using pathway engineering and chemistry to optimise the activity of natural products for the treatment of infectious diseases; though not exclusively focused on marine biotechnology, marine organisms are one source of compounds for the company.
Plymouth Marine Applications Prospect Place, The Hoe, Plymouth PL1 3DH	Carole Llewellyn T: 01752 633 100 F: 01752 633 101	Commercial arm of Plymouth Marine Laboratory; currently working on characterisation and exploitation of marine chlorophylls and carotenoids (Small Business Research Initiative)
Remedios Limited MacRobert Building, 581 King Street, Aberdeen AB24 5UA	Ian George Managing Director T: 01224 274255 F: 01224 274256 www.remedios.uk.com	Use of marine microbial *lux* gene as basis for land contamination sensor and remediation monitor; spin-out from University of Aberdeen
SAMS Research Services Ltd Dunstaffnage Marine Laboratory, Oban, Argyll, PA34 4AS	Prof Graham Shimmield T: 01631 559000 F: 01631 559001	Provides all the commercial services (including billing) for Scottish Association of Marine Sciences' (SAMS) scientific activities.
SEAS Ltd c/o Dunstaffnage Marine Laboratory, Oban, Argyll, PA34 4AS	Mr J Blackstock T: 01631 566877 F: 01631 564124 seas@wpo.nerc.ac.uk	Private consultancy and research company based at Dunstaffnage Marine Laboratory, specialising in analysis of marine benthic samples, polychaete taxonomy, benthic community structure and adaptive responses to stress; recently absorbed into SAMS Research Services Ltd.
X-Gnat Labs Limited Unit 11, Beta Centre, Stirling Innovation Park, Stirling FK9 4NF	T: 01786.442006 F: 01786.442006	X-Gnat specialises in insect and organism repellents, based on environmentally friendly materials; involvement in marine biotech is through being a partner with Grant Burgess of HWU on a project to develop an anti-fouling paint using marine microbial extracts.

Note: Plymouth Marine Laboratories is about to spin out two new companies[80], so that this number may change. Two companies are profiled below, since they illustrate the combination of public and private funding that is assisting start-ups in this area. The strategies of both companies are similar: to establish one stream of activity that is income-generating (contract work in shellfish toxin analysis for Integrin and in rapid screening for Aquapharm) whilst investigating novel bioactives from proprietary collections of marine microbes.

[80] pers. comm. D Robins 2004

CASE STUDIES: AQUAPHARM BIO-DISCOVERY AND INTEGRIN ADVANCED BIOSYSTEMS

Aquapharm Bio-Discovery *Ltd was founded in 2000, after Andrew Mearns Spragg, a PhD at Heriot-Watt University, had gained a Royal Society of Edinburgh-Scottish Enterprise Fellowship, which he continued at St Andrews University.*

The company was founded to commercialise antibacterial molecules from marine organisms; in the process of developing this, a faster assay and screening system was developed and new anti-oxidant and aquaculture feed pigments were discovered. Aquapharm also has its own culture collection.

The company has moved from Edinburgh to ECMB Oban because of favourable costs and facilities that allow the business and research sides of the company to co-locate.

Aquapharm has obtained funding from private sources and from public endowments, including the SE/RSE Enterprise Fellowship, SMART: Scotland funding (end-2001), NESTA (£50,000 in January 2003 and follow-on) and a BBSRC CASE award. Andrew has followed the strategy of getting potential licensees on-side by undertaking co-development projects. Aquapharm used the CONNECT Springboard conference in Scotland to begin the process of gaining almost £1.5 million in external funding, due to complete in 2004.

Integrin Advanced Biosystems *Ltd was founded in 1999, effectively as a spin-out from SAMS at Dunstaffnage. The company has two different streams of activity, drug discovery, focusing on anti-inflammatories from marine organisms & monitoring seafood for planktonic toxins.*

Early funding included a contract for PharmaMar SA, other service contracts and a Eureka grant of £170,000 to develop novel bacterial assays. Integrin has been active in seeking appropriate support grants from Argyll & the Islands Enterprise, receiving almost £47,000 for business development, product development and training between 2001 and 2003.

Revenues in 2001 were £250,000 from services and contracts and, by 2002, total capital raised approached £950,000. Integrin is now the UK leader in shellfish toxin testing and received the Pfizer Award for Innovation in Life Sciences in 2003 as recognition of this. Integrin is also working on a CRAFT project for European SME shellfish producers on detoxification of harvested product.

In January 2003 the company was successful in gaining £330,000 from a combination of HIE Ventures, Argyll & Islands Enterprise (£71,000) and private funds. It has been seeking up to £5 million in external funding.

ANNEX B: RESEARCH ACTIVITY

TABLE 21: MARINE BIOTECHNOLOGY RESEARCH ACTIVITIES IN HEIS AND ORGANISATIONS IN ENGLAND

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Aston University Chemical Engineering and Applied Chemistry,	Investigating the use of porous marine-origin structural biomaterials from corals, sponges and sea-urchins in the production of artificial cornea for keratoplasty techniques
Birmingham, University of School of Biological Sciences	The molecular and cellular basis of primary adhesion by *Enteromorpha* spores (Marine Biofouling Thematic Programme MBTP – NERC 1995-1998); Marine Biofouling, especially in relation to the control of algae which foul ships; core member of EU NoE Marine Genomics; Microbial interactions in natural assemblages, N-acylhomoserine lactones and *Ulva* zoospore adhesion (Marine & Freshwater Microbial Biodiversity programme M&FMB – NERC 2000-2005)
Brighton, University of Faculty of Science & Engineering	Working on glycine betaines and other marine-derived betaines for cryopreservation of biological systems
Bristol, University of School of Chemistry, School of Biological Sciences Biogeochemistry Research Centre	Prokaryotic ether lipid membranes, Picocyanobacteria communities & Novel molecular markers for sub-sea microbes (M&FMB); Bacterial populations in ocean sediments, palaeo-oceanography; synthesis of marine natural products (EC-funded 1997-2000)
British Antarctic Survey Cambridge	Genomic and metagenomic studies on Antarctic organisms, including extremophilic cyanobacteria and microbial communities. Exploitation will however be constrained by bioprospecting aspects of Antarctic Treaty. Member of EU NoE Marine Genomics
British Oceanographic Data Centre University of Liverpool	Central data repository and distributor for M&FMB project results
Buckingham, University of Clore Laboratory for Life Sciences	Biofouling
Cambridge, University of Dept of Chemistry	In the past has been a recipient of EPSRC grants for total synthesis of interesting marine bioactives including swinholide A, marine polyketides, squalestatins, scytophycin, aplyronine, bistheonellide and discodermolide
East Anglia, University of School of Environmental Sciences	Marine microbial ecology, Biogenic production of trace gases of atmospheric importance in marine waters. Biological oceanography, seaweed physiology and trace gas production; Viruses and biogeochemical cycling, Sulphur compounds and viral infection of phytoplankton & Virus-host dynamic during *Emiliania huxleyi* bloom (M&FMB); M&FMB Programme Science Co-ordinator for NERC
Essex, University of Dept of Biological Sciences	microbial interactions and the functioning of microbial consortia, application of microbial diversity, oil bioremediation, extremophiles esp. halophiles and their biotechnological applications; Novel *Archaea* in coastal marine sediments, Culture methods for novel marine and estuarine microbes (M&FMB with University of Reading); structure and function of complex microbial communities in aquatic systems and microbiology of polluted environments; atmospheric trace gas exchange by aquatic bacteria, cycling of C, N & S in coastal and Antarctic regions, ecology of aquatic and sedimentary organisms

TABLE 21: CONT

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Hull University	algal functional group ecology, techniques for monitoring algal communities, morphological variation and speciation of fucoid algae, general intertidal ecology and conservation biology; fisheries and biological oceanography and behaviour of krill; member of EU NoE Marine Genomics
Kent, University of Applied & Environmental Microbiology Group	Studying novel biotechnological applications provided by bacteria from the deep sea. Research collaborations with groups in Spain, France, Germany, Hungary, Japan, Indonesia, Greece, Norway, Italy, Portugal; Sedimentary actinomycetes (diversity and sampling methods), *Pseudonocardiae* from marine sediments & Marine *Micromonosporae* diversity (M&FMB, with Newcastle); Abyssomycins (with Eberhard Karls Universität Tübingen Germany and University of Newcastle-upon-Tyne)
King's College London	Surface active proteoglycan secretions from marine invertebrates and their role in modulating biofouling
Lancaster University Institute of Environmental and Natural Science	Trace metal metabolism and cycling in freshwater and marine environments (M&FMB with Marine Biological Laboratory Copenhagen University Denmark, Lucas Heights Science & Technology Centre Australia and University of Aberdeen); high resolution analysis of trace metal-sediment interactions
Leeds, University of Dept of Microbiology	Molecular biology of freshwater cyanobacteria & Biofilm-disrupting compounds from marine bacteria (M&FMB) (Biofilm work with Heriot-Watt)
Liverpool, University of School of Biological Sciences Port Erin Marine Laboratory IRC in Surface Science	Analysis of the structure and activity of bacterial populations in natural soil, sediment and water environments; development of molecular and DNA-based methods to profile bacterial communities; dynamics of microbial communities; gene fluxes and gene function in natural environments; Chemisorption studies related to reactive organic film growth; lysogenic phages in freshwater bacteria (M&FMB); commercial activity: Environmental Research and Consultancy's Marine Services
Manchester, University of **UMIST** Dept of Chemistry	Microbial adhesion and biofilm formation. Interbacterial adhesion in aquatic biofilms; Cytokine resuscitation of actinomycetes (M&FMB)
Marine Biological Association Plymouth	Active in NERC's MBTP programme: marine viruses; induction of barnacle larval settlement, settlement pheromones; modulation of marine invertebrate larval settlement and metamorphosis by eicosanoids; can bacterial metabolism self-regulate attachment to surfaces?; a partner in the EU NoE Marine Genomics; Viruses and biogeochemical cycling, Gene transfer via marine bacteriophages, Virus-host dynamics in *Emiliania huxleyi* blooms, Molecular biology of freshwater cyanobacteria, Sulphur compounds and viral infection of phytoplankton, Photosynthesis genes in marine viruses & Exploitation potential of marine viruses (M&FMB) (Photosynthesis genes with University of Warwick and MBA)

TABLE 21: CONT

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Newcastle-upon-Tyne, University of Centre for Coastal Management Dove Marine Laboratory School of Marine Science and Technology Centre for Molecular Ecology School of Civil Engineering and Geosciences School of Biology Agricultural & Environmental Science Postgraduate Institute, Newcastle Research Group	particular strengths in tropical and temperate marine biology; owns a research vessel. Departmental specialisms: environmental signal transduction in marine organisms; marine ecosystem dynamics; well-established marine engineering department; marine invertebrate reproduction and development, esp. larval settlement; marine biofouling/antifouling; invasive species; ecotoxicology (esp. endocrine disruption); seasonal variation of antifouling activities of marine algae from the Brittany Coast; research in behavioural ecology, ecophysiology, and biofouling, temperate and tropical ecosystems; Novel rhodococci, streptomycetes and actinomycetes from the deep sea (characterisation and exploitation), Diversity of sediment actinomycetes, Microbial N2 fixation, Diversity of diazotrophs in the Arabian Sea, Models for screening microbial biodiversity & Bioactive screening on a chip (M&FMB); microbial ecology and environmental microbiology, geomicrobiology, biodegradation of hydrocarbons, Microbiology of biogeochemical cycles; Abyssomycins (with Eberhard Karls Universität Tübingen Germany and University of Kent & Canterbury); member of EU NoE Marine Genomics
Nottingham, University of Centre for Biomolecular Sciences	Microbial interactions in natural assemblages & Natural antifoulants from actinomycetes (M&FMB)
Oxford, University of Dept of Zoology	marine taxonomy and distribution; Dispersal of free-living microbial species & Biodiversity and ubiquity of *Gymnamoebae* and *Cercozoa* (M&FMB); member of EU NoE Marine Genomics
Plymouth Marine Laboratory	an independent charitable company limited by guarantee, affiliated to NERC; Core research in estuarine and coastal function and health, scaling biodiversity and the consequences of change and microbially-driven biogeochemical processes, exchanges and controls; marine viruses, including those of microalgae and bacteria; cell signalling and nutrient uptake in biofilms and biofouling; bacterial-trace metal interactions, Characterisation of MeBr degraders, Bacteria-trace metal interactions, Virus-host interactions in *Emiliania huxleyi* bloom, Sulphur compounds and viral infection of phytoplankton, Molecular biology of freshwater cyanobacteria, Photosynthesis genes in marine viruses, Novel enzymes from marine viruses & Natural antifoulants from actinomycetes (M&FMB) (Photosynthesis genes with University of Warwick and MBA, Natural antifoulants with University of Nottingham) Commercial activity: Plymouth Marine Applications - Characterisation and exploitation of marine chlorophylls and carotenoids (Small Business Research Initiative)
Plymouth, University of Marine Algal Research Group Dept of Environmental Science	marine algae and environmental pollution; cellular responses to stress in algae; commercial and applied activity in seaweed and polyculture within the Centre for Applied Plant Research; Bromine cycling, Microbial interactions in natural assemblages, Bacteria-trace metal interactions & Diatom pigments (M&FMB)

TABLE 21: CONT

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Portsmouth, University of School of Biological Sciences Institute of Marine Sciences	Marine fungi; production of PUFAs by thraustochytrids; n-substituted imides as antifoulants; *Mytilus edulis* phenoloxidase; international collaborations on bioactives with Quimper and Concarneau, France; marine wood borers, Protection of wood in the sea, Impact of biocides used in wood protection on marine invertebrates, bivalve larvae, mangrove ecology in relation to the utilisation and the breakdown of wood; taxonomy and systematics of Brown Algae. Fouling/antifouling studies, pollution studies; the role of bacterial exopolymers in marine fouling and deterioration of steel surfaces: (MBTP); can bacterial metabolism self-regulate attachment to surfaces?; ecotoxicology and ecophysiology of fish and marine invertebrates, Fish endocrinology, Sensory biology of fish and invertebrates; environmental and endocrine control of reproduction in marine invertebrate, Ecotoxicology, Effects of pollutants and other human impacts (bait collection) on invertebrate reproduction, the role of chemical signalling in marine invertebrates.
Queen Mary, University of London	Nitrogen transformations in estuarine and coastal sediments; marine and estuarine benthic ecology and conservation
Reading, University of School of Animal and Microbial Sciences	Environmental Systems Science Centre PhD / MPhil (Departmental specialism includes Marine Science); Characterisation of non-extremophilic estuarine organisms & Novel *Archaea* in coastal marine sediments (M&FMB)
Royal Holloway, University of London School of Biological Sciences	Parasitology and aquatic toxicology: Ecology and epidemiology of parasites in aquatic and terrestrial hosts. Development of fish biosensors for early detection of pollutants in water. Fish and other aquatic host-parasite systems as indicators of water quality and environmental stress; ecology and physiology of aquatic, intertidal and marine invertebrates, especially amphipod crustaceans; adaptations to life in extreme environments; induction of barnacle larval settlement: the nature and perception of settlement pheromones (MBTP)
Sea Fish Industry Authority Hull	supports projects in improving sustainable seafish and shellfish farming, nutrition (possible role for microalgae, for example), microalgal-related shellfish toxins; seafood waste as composts; fish processing technologies and new product development
Sheffield, University of Biological and Environmental Systems Group	Applied research on extremophiles in culture, to investigate their physiology and biochemistry and make use of these for industrial processes, including new bioactives, halophiles, piezophiles, thermophiles; bioactives and hydrogen from marine cyanobacteria; solvent-tolerant marine microbes
Southampton, University of Southampton Oceanography Centre, School of Ocean & Earth Science The George Deacon Division for Ocean Processes, SOC	biomarkers, biogeochemistry of deep-sea animals, marine biofouling, carbon cycle, biosensors & chemical sensors; remote sensing methodology; effects of predation and nutrient recycling by protozoa on the development of communities of marine biofouling organisms (MBTP); a multidisciplinary research group of biological, physical and chemical oceanographers; The Oceanography Centre also hosts the Inter-Agency Committee on Marine Science and Technology, T:02380 596611, www.marine.gov.uk; physiological and environmental ecology of marine microalgae, phytoplankton, benthic microalgae, coccolithophore biology, physical-biological interactions at fronts, biostabilisation of intertidal sediments; larval biology of marine invertebrates, bathyphilic environments including hot vents and cold seeps, Antarctic invertebrates; Marine biogeochemistry of trace metals, carbon, and nutrients & Molecular ecology, physiology and genetic diversity of phytoplankton (M&FMB), functional genomics of bioluminescence in marine dinoflagellates; core member and partner of EU NoE Marine Genomics

TABLE 21: CONT

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Surrey, University of Microbial Physiology & Ecology Group	Research includes bioproduct physiology, microbe/surface interactions, microbe-microbe signalling and bioelectronics (interface between biosystems and electronics), advanced fermentation technology for production of bioactives, ecosystem function in attachment/biofilms [not clear if marine]; development of microarrays for characterising novel deep sea and coastal streptomycetes (collaboration with M&FMB project at University of Newcastle)
University College London Royal Free Hospital School of Medicine Dept of Chemistry & Molecular Biology	Working with Prof A Lloyd (Brighton) and Destiny Pharma Ltd on alginates and chitosans for tissue engineering scaffolds Phylogenetic analysis of biodiversity in deep marine and hydrothermal vent biotopes
Warwick, University of Dept of Biological Sciences	Cyanobacteria; phage ecology and exploitation; a partner in the EU NoE Marine Genomics; Bromine cycling, Characterisation of MeBr-degraders and assessment of potential as biocatalysts, Community structure of picoeukaryotes, Photosynthesis genes in marine viruses & Gene transfer via marine bacteriophages (M&FMB) (MeBr project with PML and University of Waikato New Zealand, picoeukaryote project with Station Biologique Roscoff France)
Wolverhampton, University of	Subcellular membrane transport processes studied in marine fungi; specialisms include gastropod oxidases [not clear if marine].
York, University of	marine biodiversity conservation, coral reefs, coastal management, tourism sustainability, marine reserves, threatened species, fishery management; pigments from diatoms (M&FMB 2004)

TABLE 22: MARINE BIOTECHNOLOGY RESEARCH ACTIVITIES IN HEIS IN SCOTLAND

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Aberdeen, University of Aberdeen Institute for Coastal Science & Management Dept of Zoology Marine Natural Products Lab Dept of Chemistry Oceanlab Dept of Molecular and Cell Biology Institute of Medical Sciences	ecology, physiology and *in situ* behaviour of deep-sea fauna; fundamental and applied studies in a wide range of ecosystems, intertidal to deep Arctic; marine natural products and marine biotechnology: novel fatty acids from marine algae, novel pharmaceutical agents from sponges; systems development: engineering of deep ocean instrumentation packages; lab studies on functional morphology and physiology using material retrieved by trap or trawl from the deep sea; work in MBTP; Viruses and plankton blooms & Trace metal cycling (M&FMB); spin-out Remedios, environmental biosensors; molecular analysis of marine bacterial communities. NCIMB (National Collections of Industrial, Food and Marine Bacteria) and NCIMB Ltd, the commercialisation activity relating to this, are hosted at Aberdeen.
Edinburgh, University of	microbial genomics and genotyping applied to foraminifera and other marine microbes
Fisheries Research Services Marine Laboratory, Aberdeen	fish diseases and disease diagnosis using molecular methodology; focus on diseases of turbot; biodiversity, microbiology, benthic studies and plankton; taxonomy of flatworm fish parasites using molecular methods; sea lice; bacterial and viral diseases of fish; viruses and phytoplankton blooms (M&FMB)

TABLE 22: CONT

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Glasgow, University of Institute of Biomedical and Life Sciences Dept of Civil Engineering UMBS Millport Glasgow Marine Technology Centre	work with Strathclyde on a library of natural materials, including some marine samples; Biofouling-resistant surfaces, functional biomimetics (including MAST project on antifouling), underwater sensors and reduced environmental impact of marine technologies; biodiversity, microbiology and benthic studies
Heriot Watt University Centre for Marine Biodiversity and Biotechnology, School of Life Sciences Dept of Chemistry, School of Engineering and Physical Sciences	marine biofouling, bacterial cell signalling, bioreactors and general aspects of marine biotechnology. Engaged in research aimed at the industrial and medical applications of marine bacteria and fungi. In particular interested in cell-cell signalling in marine gram-positive bacteria and its effect on the synthesis of antimicrobial compounds; production of bioactive compounds by marine fungi; chemical ecology of seaweed surface: antifouling activity of Epiphytic bacteria from intertidal and subtidal seaweeds (MBTP); Biofilm-disrupting compounds & Cell signalling system regulating antibiotic and pigment production (M&FMB); fluidisation systems; solid state fermentation; moisture in particulate systems; novel bioreactor technology; recipient of an award from the Royal Society for work on novel reactors for marine bacteria; project funding comes from EPSRC, Scottish Hospital Endowments Research Trust, BBSRC, Pfizer, SmithKline Beecham and NERC; fish diseases, vaccine development, marine bioactives as antibiotics; fish physiology, new treatments for sea lice
Napier University School of Life Sciences	Development of microbial biosensors for pollution and pollutant assessment, with prospects for commercialisation, biodiversity, plankton. Sources of funding: EU, Scottish Enterprise
Royal Botanic Garden	Diatom taxonomy, preservation of CCAP's voucher material for marine microbial strains (Marine algal characterisation and exploitation 'MACE' M&FMB with SAMS)
St Andrews, University of Gatty Marine Laboratory	Chemical and structural characterisation of invertebrate non-fouling surfaces; biofouling; planktonic barnacle larval distribution; Immune systems of crustacea; Aquapharm is a Gatty spin-out.
SAMS Dunstaffnage Marine Laboratory **European Centre for Marine Biotechnology**	fjordic systems, ocean margins, measuring and modelling change using sea sensors and information technology; Chemical and structural characterisation of invertebrate non-fouling surfaces & Surface active proteoglycans from marine invertebrates (MBTP); marine bacteria as a source of novel biosurfactants and bio-emulsifiers; The Culture Collection of Algae and Protozoa (CCAP-Marine); Marine algal characterisation and exploitation 'MACE' (M&FMB); Marine malcroalgal pathogens – phylogenetic affinities (with Dept of Biology University of Konstanz Germany, CNRS-Station Biologique Roscoff France and CNRS-Université Pierre et Marie Curie Roscoff) To be opened in June 2004
Stirling, University of Dept of Biological Sciences Machrihanish Marine Environment Research Laboratory	Diversity of diazotrophs in the Arabian Sea (microbial N2 fixation) (M&FMB) mariculture-related research
Strathclyde, University of Strathclyde Institute for Drug Research	in collaboration with Glasgow in the PharmaLinks initiative; maintains and works on over 6,500 natural extracts in the Natural Products Library, of which a few dozen are marine from overseas

TABLE 23: MARINE BIOTECHNOLOGY RESEARCH ACTIVITIES IN HEIS IN WALES

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Aberystwyth, University of Wales Institute of Biological Sciences	cytokine resuscitation of 'unculturable' actinomycetes (M&FMB)
Bangor, University of Wales School of Ocean Sciences, Centre for Applied Oceanography, Marine Science Laboratories	microbial communities in biofilms, bioremediation, marine microalgae, reef ecology; a partner in the EU NoE Marine Genomics
Cardiff, University of Wales Cardiff School of Biosciences, Cardiff School of Earth, Ocean and Planetary Sciences Wound Healing Research Unit, Cardiff Medicentre, Heath Park, Cardiff CF14 4UJ	A partner in the EU NoE Marine Genomics; Isobaric *in situ* sampling and collection device, Novel molecular markers for sub-sea microbes, Isolation of unculturable bacteria & Prokaryotic ether lipids (M&FMB) Using alginate derivatives in studies of wound healing; carrying out confidential commercial developments utilising marine-origin materials
Swansea, University of Wales Singleton Park, Swansea, SA2 8PP T: 01792 205678, F: 01792 295618	Modulation of marine invertebrate larval settlement and metamorphosis by eicosanoids with Dr A. Clare (Marine Biological Association) MBTP research

TABLE 24: MARINE BIOLOGY AND BIOTECHNOLOGY ACTIVITIES IN NORTHERN IRELAND

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Belfast, Queen's University School of Biology and Biochemistry, Depts of Pharmacy & Chemical Engineering	BSc in Marine Biology, PhD in Marine Biology including Molecular Ecology and Evolution, Molecular Microbiology & Marine Systems; projects in bioremediation using macroalgae and biomonitoring; Carapacics is a QUBIS spin-out in chitin products
Ulster, University of School of Biological and Environmental Sciences, Coleraine	offers Marine Science BSc (Hons) with Marine Biotechnology; has an Applied Microbiology and Biotechnology group working on bioremediation and biochemistry, stable marine-origin enzymes and physiology of marine organisms
Centre for Innovation in Biotechnology	joint venture between QUB and University of Ulster Coleraine
Department of Agriculture and Rural Development for Northern Ireland	Scientific studies on marine and freshwater fisheries and the environment

ANNEX C: PARALLELS WITH DEVELOPMENTS ON NON-FOOD CROPS

The challenge for the marine biotechnology community in capitalising on marine resources is somewhat similar to that faced by those researching and developing non-food uses of crops. This sector faces static investment in R&D and a need to enhance understanding of the capacity for contribution to UK economy, amongst policy, academic and industry communities. A report published at the beginning of 2004[81] recommends

- investment in bio-refining technology platforms (equivalent to bioreactors and bioprocessing for marine biotechnology)
- collaboration across the range of biosciences
- promoting the use of non-food crops for pharmaceuticals and specialist materials
- stimulating the application of venture capital to commercialisation
- maintaining research funding to ensure world-class performance
- developing statistical and other databases to support policy formation.

The report points out the growing demand for products and raw materials from renewable sources to replace petrochemical-based materials; this is also one target for marine biotechnology (microalgal or microbial surfactants, for example). Bioremediation is another target. Several of the recommendations for action are relevant to marine biotechnology.

The recommendations that seem most relevant to the marine biotechnology community at the moment, and that might be successfully transferred, are highlighted below:

- develop an integrated UK strategy through the medium of a working group
- develop technology roadmaps for different application areas, so that their specific needs are highlighted
- promote R&D investment and academic research in bio-processing, through a new HEI-industry collaborative programme
- secure full UK involvement in the design and development of European initiatives
- establish a programme of demonstration projects in containment culture for high-value outputs
- fund commercialisation studies for each demonstration project
- promote and support bioscience technology fairs
- encourage interchanges between investment and industrial companies by secondments
- foster links between investment organisations and HEI commercialisation units
- ask OST to urge BBSRC to explore the potential for cross-RC initiatives with MRC, EPSRC, NERC
- commission a statistical study that examines and differentiates between the different application areas and sectors of UK industrial biotechnology.

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[81] *Prospecting Bioscience for the future of non-food uses of crops* January 2004 A McMeekin, M Harvey *et al.* for the Government Industry Forum on Non Food Uses of Crops

ANNEX D: POTENTIAL SOURCES OF FUNDING AND SUPPORT FOR MARINE BIOTECHNOLOGY

The UK Government sees uptake of innovation as a critical element in stimulating UK manufacturers to match productivity levels in France, Germany and USA. *Investing in Innovation* [82] has announced additional investments by 2005-2006 in skills base (£100 million pa), science and engineering research (£400 million pa), equipment and capital spend (£100 million pa), the HEIF (to reach £90 million pa) and the PSRE Fund (£15 million extra), from which marine biotechnology should aim to benefit.

More specifically, there are relevant cases of capital expenditure (or estimates) to take into account in estimating costs of new initiatives. In the UK, these are the establishment of the European Centre for Marine Biotechnology (ECMB) at SAMS, Dunstaffnage and the proposed Plymouth MSTP.

- Including ECMB and related renovation of existing facilities, a total budget of £8.3 million has been spent at SAMS, including a contribution from EU funds of approximately £2.4 million and support from Highlands & Islands Enterprise, Argyll & the Islands Enterprise, the Scottish Executive and commercial lenders.
- In Plymouth, the very preliminary estimate for the establishment of the MSTP is £30-£50 million, based on the average level of investment in the UK's 10 largest Science Parks (£60 million) and expenditure on the first stages of the Tamar Science Park of just over £13 million.[83] The project has now moved onto a more detailed costing stage.

Elsewhere, various comparator figures for support of marine biotechnology programmes can be garnered from different sources:

- The budget of the Marine Institute **Ireland** and related institutions was Ir£13.5 million in 1998 (latest figures easily obtainable); a six-year plan was established in 2000 for marine research and technology development and innovation, of which the project budget was approximately £15 million (pounds sterling).
- Even fragmentary data for state and national support programmes in marine biosciences in **USA** suggest that over £300 million has been spent in the last 15 years; recently, a virtual centre of excellence in biomedical and marine biotechnology has been established in Florida, with state, national and HEI support totalling over £6 million[84]
- In **Australia**, the main effector of the Oceans Policy in biosciences is the Australian Institute for Marine Science (AIMS), with a total budget for 2004-2005 of about £11 million, about 25% from the sale of goods and services (contract projects and licensing); the departmental spend for the marine biotechnology group for 2003-2004 was about £2.7 million
- Current figures for **Japan** are difficult to find; however, the Marine Science and Technology Center's budget for marine engineering and sciences was £190 million in 2002, the Marine Biotechnology Institute's start-up investment from a public-private partnership between1988-1998 was almost £125 million, plus

[82] Investing in Innovation. A Strategy for science, engineering and technology July 2002, DTI, HM Treasury and DfES (Dept for Education and Science)

[83] Feasibility Study for the development of a marine science and technology (MST) cluster in Plymouth Final Report April 2003, GHK & BMT, for the City of Plymouth, page 51

[84] see http://www.floridabiotech.org/

significant funding from state R&D programmes, and in 2000 Takara Shuzo established Dragon Genomics Center, with 20% (approx £7 million) of its budget devoted to marine genomics and the search for useful genes and products.

For funding of specific marine biotechnology programmes, and at a more local level, the most accessible source is the EU's Framework Programme 6 (FP6). This has funded three relevant programmes:

- BlueBioNet, the Platform for European Blue Biotechnology, which is aimed at converting traditionally-structured maritime regions into European Knowledge Regions for applied biotechnology and has the goals of developing a number of commercial and international R&D collaborations by December 2005[85]
- Two Networks of Excellence with marine biodiversity themes, including one on Marine Genomics.

The Fore*sight* Marine Panel has noted that research funding may be available from the USA.[86] There are potential contributions of marine biotechnology to research, development and applications in diagnosis and management of biohazards and bioterrorism that also make it worthwhile exploring opportunities for funding within, for example, the BioShield programme, signed by the US President in July 2004[87].

Funding Virtual Institutes

Apart from conventional technology transfer functions in UK HEIs, there are several organisations that seek to add value to HEI resources and expertise by helping businesses and their advisors find the best mix of skills and facilities across institutions rather than within. Examples of two of these are given below, Scottish Biomedical and i10, since they could well provide models or best practice for similar efforts in marine biotechnology development and exploitation.

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85 *pers. comm.* G Shimmield 2004

86 *Marine Technology, report of the eighth Foresight Seminar, 13 May 1999*, with reference to the Department of Defense's Office of Naval; Research, see http://www.ma.hw.ac.uk/RSE/govt_responses/commercialisation/seminar_reports/foresight/f08may99.pdf

87 see http://www.whitehouse.gov/bioshield/

CASE STUDIES: SCOTTISH BIOMEDICAL & i10

__Scottish Biomedical__ was founded in 1994, acting as marketer, broker, project-former, project manager and negotiator on behalf of the biomedical science functions of six Scottish Universities, creating collaborative teams across disciplines to answer the specific needs of clients. It has had notable international successes with Japan, facilitating the establishment of the Kyorin Research Scotland Laboratories, the YRING Institute in Glasgow and a long-term cross-institute project for the Kowa Company. It has now established its own laboratories, gaining a SMART: Scotland award in 2000 for human tissue techniques that ensure stability of messenger RNA for gene analysis research. Scottish Biomedical's success in attracting an estimated £40 million in biomedical funding to Scotland has been recognised by the Biotech Scotland Award in 2002 and a SMART Achievement Award in 2003. Turnover in 2002-2003 was £5 million, with profits of over £125,000, and the Foundation completed a transition to a fully-independent company as a result of a leveraged management buy-out in 2002.[88]

__i10__, a collaboration between 10 HEIs in East of England, has received c. £3 million to help fund inter-institution projects that respond to regional and industrial sector needs. The i10 network is aimed at businesses and their advisors, and is a 'front-end' that then matches appropriate resources across the region's HEIs. This is co-ordinated through the University of Cambridge and served by a web-site, which also aids networking and information-finding. i10 is working on a standardised data-base of academic resources and expertise in the region to help the process. The i10 structure could provide a model for development of a marine biology, bioscience and biotechnology resource database and collaboration network, essentially web-based with a funded co-ordination centre at a relevant establishment.[89]

Funding Sector Support and Interest groupings

Sector support programmes have been quite successful in UK, in particular **Bio-WISE**, which targets the use of biotechnology in waste management, and the **National Non-Food Crops Centre** (NNFCC), which services farmers, processors, manufacturers and researchers in a wide range of unconventional non-food sectors. These are models for an interest grouping in marine biotechnology, as well as useful links for enhancing exploitation and partnering (for example, making use of the Rothamsted International Biomarket conferences.[90]) These are profiled below in more detail.

Investing in commercialisation and economic development

As part of its re-appraisal of its role in supporting innovation and economic development, the UK Government has established a number of innovative programmes aimed at

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88 see http://www.scottish-biomedical.com, http://www.ideas21.co.uk/317, http://www.scotland.gov.uk/news/2000/10/se2767.asp and other related sites

89 see http://www.i10.org.uk

90 see http://www.biomarket.rothamsted.ac.uk/index.php

starting-up and maintaining new businesses, which are relevant to marine biotechnology.[91] These include the DTI's Enterprise Capital Fund (ECF) programme, currently undergoing a pilot scheme, Pathfinder ECF, with up to £2 million of public and private funds.[92] The existing Enterprise Investment Scheme (EIS) will be maintained, extended to allow groups of business Angels to form funds - recent estimates are that the UK's angel funding may be as much as £500 million - £1 billion a year, 75% of this below £100,000 and 8% above £250,000[93], well within the range needed by embryo marine biotechnology companies. The Venture Capital Trusts scheme will also be maintained, to allow formation of funds for investment of more than £1 million in SMEs.[94]

Government-sponsored mechanisms for scientific and economic development

NERC programmes

NERC is supporting marine bioscience in 3 programmes for the period 2000-2005. These include:

- the M&FMB programme, cost £7 million (including a research cruise and SBRI grants for proof-of-concept and exploitation projects)[95]; this is now complete
- the Environmental Genomics Programme, cost £16.5 million, in which 4 of 28 projects involve marine or aquatic genomes[96]; there should be a third round of funding in this
- the Marine Productivity Programme, cost £6.5 million, which includes biology, modelling, behaviour, ecology, molecular identification and development of marine plankton.

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91 Science and innovation investment framework 2004-2014 July 2004 HM Treasury, DTI and DfES

92 see http://www.sbs.gov.uk/default.php?page=/financegap/default.php

93 Bridging the finance gap: a consultation on improving access to growth capital for small businesses April 2003, HM Treasury and DTI's Small Business Service

94 Bridging the finance gap: a consultation on improving access to growth capital for small businesses April 2003, HM Treasury and DTI's Small Business Service

95 see http://www.nerc.ac.uk/funding/thematics/mfmb/

96 see http://www.nerc.ac.uk/funding/thematics/envgen/

CASE STUDIES: BIO-WISE & NNFCC

Bio-Wise[97] *began in 1996 as Biotechnology Means Business, a DTI-funded programme aiming to support the increased use of biotechnology in British industry. Bio-Wise itself was launched in 1999, also funded by DTI, at £13 million over four years, to continue embedding the use of biotechnology for environmental management, often in relatively low-tech circumstances (such as reduction in the polluting power of fats and oils in fast-food restaurants, or providing bioremediation for dying and tanning effluents). 25% of eligible costs are covered, grants are in the range £25,000-£250,000. The programme has been very successful in creating case studies and bringing together research, applications, environmental consultants, system and process designers and businesses in a range of industrial sectors. This is all relevant to any effort to create a UK marine biotechnology community and, in particular, increased interaction between companies with a need for technological solutions to problems and HEIs or institutes with answers. The web-site for the Bio-Wise programme may provide insights into the structure of a web-site for marine biotechnology, since it has case studies, technological information for companies, on-line partnering, a user club section, and other more general information.*

The ***NNFCC***[98]***,*** *which took over the activities of ACTIN and the Plant Protein Platform, was launched in November 2003. It is based in York and has the slogan 'From crops to cashflow: building sustainable supply chains.' Its core funding is provided by Defra. NNFCC will become the UK's main information point for industry and academia, and will also advise government on future directions in this area. It has a major technology translation role, funded by DTI under contract until 2007. It is a subscription organisation and will also carry out commercial contract work. ACTIN, founded in 1995, was funded by a consortium of industry (ICI, Zeneca, DuPont, Dalgety, British Sugar, Cargill Seeds, PBI-Cambridge and PIRA International), farmer groups (Home Grown Cereals Authority and National Farmers' Union), BBSRC and government (DTI, Defra – then MAFF). It supported and developed a strong network of interest in alternative uses and alternative crops and worked closely with LINK in a £4 million programme for new uses for plants.*[99] *The LINK programme, sponsored by BBSRC, Defra, EPSRC, DTI and SEERAD (Scottish Executive Environment & Rural Affairs Dept), funded 21 projects from 1996 to 2002. This programme was successful in encouraging SMEs to become involved.*

NERC also funds a great deal of infrastructure and capital support for marine sciences, including research vessels, costs of many of the relevant culture collections and facilities development projects.

RCUK Follow-on Fund

The first stage of this closed in early 2004. The BBSRC fund is likely to continue and is aimed at developing proof of concept and prototypes from BBSRC-funded new knowledge and embryo products.

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[97] see http://www.biowise.org.uk/

[98] see http://www.nnfcc.co.uk

[99] Competitive Industrial Materials from Non-Food Crops LINK programme – see http://www.ost.gov.uk/link/foocim.html

HEI programmes

SRIF the Science Research Investment Fund and **HEIF** the Higher Education Innovation Fund are aimed at HEIs.

The **SRIF** (Science Research Investment Fund 2000-2002, Science Research Infrastructure Fund 2002-2004), jointly provided by HEFCE (Higher Education Funding Council of England) and the Wellcome Trust, is aimed at supporting capital infrastructure and facilities in which high quality research can be carried out, particularly in scientific areas of national strategic priority. The work within these is also intended to be collaborative, between HEIs, charitable bodies, NHS Trusts, Government and industry, and can encompass buildings, research equipment and support and communication networks. The first round was announced in 2000 and the second round closed in May 2003.

The **HEIF** (Higher Education Innovation Fund), a joint initiative between HEFCE and OST, has £186 million allocated for the period 2004-2006, and is aimed at individual or collaborating HEIs who wish to improve technology and knowledge transfer and the business awareness of their staff. The second round was announced in February 2004, resulting in 124 awards, including 22 ‘Centres for Knowledge Exchange Activities’. The decision has been made that this support will form a permanent ‘third stream of funding’ for HEIs, to stimulate and recognise the efforts at technology transfer that the usual assessment exercises ignore.

The HEIF absorbed the **University Challenge** and **Science Enterprise Challenge** activities from 2003 onwards. These achieved their first funding rounds in 1999 and second rounds in 2001. The University Challenge programme was the equivalent in England of the Proof of Concept Fund in Scotland. In the first round, £65 million was available, £20 million of this from HEI resources and other funds from the Wellcome Trust and Gatsby Charitable Foundation, for 28 HEIs and 9 PRSEs. The second round supported 17 institutions in 5 consortia with £21 million. In the Science Enterprise Challenge programme, 12 centres of excellence were established in the first round of £29 million, which attracted a further £28 million from external sources, and a further £15 was invested in 7 consortia in the second round.

The HEIF should be investigated as a source of funding for relevant marine biotechnology activity, especially as it includes HEIs, PSREs and the establishment of centres of excellence for proof of principle, knowledge transfer, and business development.

Programmes bringing HEIs and companies together

Newer initiatives bringing academic research, applications and businesses together include **Knowledge Transfer Networks** and **Knowledge Transfer Partnerships**. For SMEs, a useful ‘front door’ for support programmes is the SBRI Programme.[100]

Knowledge Transfer Networks (KTN) - These build on the Faraday Partnership experiences, and include a wider range of networking activities to enhance knowledge transfer from HEIs and PSREs into industry, targeting activities and sectors that can maximise productivity. They are targeted or thematic programmes and not responsive

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[100] see http://www.sbri.org.uk/aboutus.asp

mode; thus if marine biotechnology is to be eligible, it is dependent on the relevant RC or government department opening a call for the area. Notwithstanding this, it may be possible to present a position paper arguing for establishment of a KTN in marine biotechnology and exploitation.

A similar programme in Scotland, which is intended to support research-industry interactions that are not otherwise being supported, is Scottish Expertise Knowledge and Innovation Transfer, SEEKIT. This involves research institutes and technology transfer offices as well as HEIs.

Knowledge Transfer Partnerships (KTP) - These are direct collaborations between HEIs and specific companies, in which graduates and other recently qualified people undertake specialised knowledge transfer from the HEI to the company, building on the Teaching Company Scheme. A similar activity in Scotland, which involves R&D collaboration between HEIs and industry, is the SME Collaborative Research programme ScoRE.

Economic support programmes for companies

The work undertaken as part of the Government's innovation funding review revealed that about 87% of SMEs are generally able to obtain the financing they need. The remaining 13% find varying difficulty but, since a high proportion of these are high-risk, special attention needs to be paid to these. Marine biotechnology start-ups and resource development companies would, by their nature, fall into this class.

Regional Venture Capital Fund (RVCF) Programme - This group of 9 funds, RVCFs, was established in England in 2000 as a means of bridging early-stage equity gap and stimulating SMEs that demonstrate growth potential. Regional Fund Managers were chosen via open tender and work with the local RDA and the DTI's SBS (Small Business Service). The original plan was to source 50% of the funds from SBS plus European Investment Fund and 50% obtained from private sources by the Fund Managers. The eventual size at closing in 2003 was over £250 million, about 1/3 from public sources and 2/3 from private. The RVCFs vary in size from North East RVCF at £15 million to London RCVF at £50 million; most are in the £25-30 million range.

A Regional Venture Capital Fund can invest or co-invest up to a maximum of £250,000, following up with a further £250,000, whether or not there are other investors. Investment can be equity or debt and a wide range of companies can take part, exceptions being agricultural, horticultural, forestry and some other service companies. By November 2003, 70 companies had been supported; by April 2004 this had risen to 107 investments (including follow-ons) in 83 companies.[101]

Since marine biotechnology exploitation has not previously been classified as agriculture and algal farming is arguable, start-ups in England could be eligible for support, but this remains to be tested.

Grant for Investigating an Innovative Idea

Within SMART, funding was available to SMEs for Technology Reviews and Technology Studies. These were formally closed in May 2003 and are now replaced by **Grants for Investigating Innovative Ideas**, aimed at SMEs for sums up to £500,000, and available

[101] Chapter 12 of the DTI's Departmental Report for 2004, see http://www.dti.gov.uk/expenditureplan/report2004/

within the overall Small Business Services package of the DTI.[102] This scheme was used by over 350 businesses between June 2003 and April 2004. It would seem suitable for marine biotechnology businesses trying to establish new products or processes, and perhaps also for bioreactor investigation.

Other programmes are available in general for small companies, including the Small Firms Loan Guarantee Scheme, the Early Growth Funding project, providing between £50,000 and £100,000, and, for businesses starting in deprived areas with local impact, the Bridges Community Development Venture Fund. There is also an increased emphasis on provision of business training for start-ups and small businesses. A local Enterprise Agency is best-placed to advise on these.

NESTA

Although this programme is thought of as being more for the creative arts, NESTA is one of the instruments for support of innovative science and technology in design, manufacturing and start-up businesses. NESTA was established in 1998 with an endowment from the National Lottery of £200 million, extended in 2003 with a further £50 million. NESTA has so far invested £40 million in new activities and is concerned that the DTI's Innovation Report and the resulting National Technology Strategy completely omit the role of science and technology in the creative industries.[103] NESTA might be a route to funding of innovative PR and communications media for the marine bioscience and biotechnology sector.

TABLE 25: EXAMPLES OF COSTS OF COMPONENTS OF A SUPPORT PROGRAMME

COMPONENT	EXEMPLAR	COMMENTS
Defining the sector, creating the message and engaging enthusiasm	Fore*sight* Marine Panel Marine Biotechnology Group	Little overall costs – relies on volunteer time of group; secretariat should be funded; expenses for volunteers and budget for communications are recommended.
Networking (Academic-Academic)	Yorkshire Tissue Engineering Group[104]	Regional collaboration between Universities of York, Leeds, Sheffield and Bradford – runs an EPSRC-funded regional network on Post-Genomic Tissue Engineering, £64,000 over 3.5 years.
Networking (Academic-Industry)	Faraday Partnerships Knowledge Transfer Networks	>£2 million each, over 3-4 years, with expectation of securing further funding through 'commercial' activities (membership fees, meeting attendance fees, sponsorship, industry co-funding) as well as further public funding through project bids. The National Composites Network gained £4.74 million fromDTI and £14 million from RDAs in the first KTN round (april 2004), with a target of an additional £11.25 million from participating industry.
Industry support network	MDIS	Medical Devices in Scotland – funded by Scottish Enterprise at £480,000 over 3 years, plus subscriptions, meeting and mission fees and other private funding.

[102] see http://www.dti.gov.uk/innovative-idea/index.htm

[103] see http://www.nesta.org.uk/mediaroom/newsreleases/3904/

[104] see http://www.yteg.org.uk/

TABLE 25: CONT

COMPONENT	EXEMPLAR	COMMENTS
Thematic programmes	NERC Marine & Freshwater Microbial Biodiversity NERC Environmental Genomics Programme	>£7 million for 5 years 2000-2005 (including some SBRI grants). £16.5 million for 5 years 2000-2005; 4/28 current projects involve marine or aquatic genomes.
Case study programmes	Bio-WISE[105]	£3m provided for 21 case studies within a £13 million 4 years 1999-2003 programme, funded by DTI with European Regional Development Fund input.
Centres of Excellence	UK Centre for Tissue Engineering[106] European Centre for Marine Biotechnology	>£9.7 million 2001-2007 – Universities of Liverpool and Manchester, funded by a 6-year Interdisciplinary Research Collaboration Award (BBSRC, EPSRC, MRC). Approx. 2/3 of the total SAMS renovation and new buildings cost of £8.3 million.
Centres for Knowledge Transfer	BITE CIC[107] ITI Scotland[108]	Centre for Industrial Collaboration formed by combining biomaterials/tissue engineering skills of Universities of York, Leeds, Sheffield, but geared to industry collaboration – funded by the RDA Yorkshire Forward as part of a £11 million programme (includes >5 other CICs in other technology-driven industrial sectors). Intermediary Technology Institutes, virtual engines for transferring research knowledge and inventiveness into companies, to the tune of £450 million over 10 years (c. 1/3 for Life Sciences).
Communications programme	OST Science and Society Programme	£4.25 million 2005-2006, >£9 million 2006-2007 for projects that increase the public capacity to understand and appreciate science, and engage the public, science community and policy makers in dialogue.
Training	Knowledge Transfer Partnerships	Place graduates/PhDs in companies for technology/knowledge transfer to company, and acquisition of industrial knowledge/skills by graduate; company costs £14,000-£25,500 per placement, topped up by public funds

[105] see http://www.biowise.org.uk/
[106] see www.ukcte.org
[107] see http://www.bitecic.com/
[108] see http://www.itilifesciences.com/

ANNEX E: INDIVIDUALS CONTACTED FOR RESPONSES TO SWOT AND RECOMMENDATIONS

TABLE 26: CONTACTS

Research & Academics	
Contact	**HEI/Institute**
Dr Ivan Heaney	Department of Agriculture and Rural Development for Northern Ireland
Dr Frithjof Kuepper	CCAP, SAMS Dunstaffnage
Professor Graham Shimmield FIBiol	ECMB Dunstaffnage
Professor Brian Austin	Heriot Watt University
Dr J Grant Burgess	Heriot Watt University
Dr Michelle Tobin	Hull University
Professor Clive Page	King's College London
Dr Ian Joint	MBA Plymouth
Dr Willie Wilson	Plymouth Marine Laboratory
Professor Nick Christofi	Napier University
Dr Martin Embley	Natural History Museum
Dr Tony Clare	Newcastle University
Dr David Robins	Plymouth Marine Laboratory
Professor John W Lewis	Royal Holloway, University of London
Professor M. C. Thorndyke	Royal Holloway, University of London
Professor A F Rowley	University of Wales, Swansea
Professor Marcel Jaspars	University of Aberdeen
Professor Monty Priede	University of Aberdeen
Professor J. A. Callow	University of Birmingham
Professor Len V Evans	University of Buckingham
Professor John Parkes	University of Cardiff
Dr Sarah Cornell	University of East Anglia
Dr Gill Malin	University of East Anglia
Dr Phillip Williamson	University of East Anglia
Dr Kate Darling	University of Edinburgh
Professor David Nedwell	University of Essex
Dr Mark Osborn	University of Essex

Research & Academics	
Contact	**HEI/Institute**
Dr Tony Clare	University of Newcastle upon Tyne
Dr Ian Head	University of Newcastle upon Tyne
Dr Jeremy Thomason	University of Newcastle upon Tyne
Dr Alan Ward	University of Newcastle upon Tyne
Professor Paul Williams	University of Nottingham
Dr Peter Holland	University of Oxford
Dr Iwona Beech	University of Portsmouth
Mr Graham Bremer	University of Portsmouth
Dr Colin Waring	University of Portsmouth
Dr Keith Haines	University of Reading
Professor Phillip Wright	University of Sheffield
Dr Ralf Prien	University of Southampton
Dr Mark Varney	University of Southampton
Dr Chris Todd	University of St Andrews
Dr M Wyman	University of Stirling
Professor Jim Lynch	University of Surrey
Dr Derek Jackson	University of Ulster
Dr Aileen Moore	University of Ulster
Professor Michael Young	University of Wales, Aberystwyth
Dr Jonathan King	University of Wales, Bangor
Professor Nick Mann	University of Warwick
Dr Alan J Blakey	Actinomed
Dr Andrew Mearns Spragg	Aquapharm Bio-Discovery Ltd
Steve Rumford	AstraZeneca
Dr Barbara Blaney	BIA Scotland

TABLE 26: CONT

RESEARCH & ACADEMICS	
CONTACT	HEI/INSTITUTE
Professor Kenneth Timmis	University of Essex
Professor Mike Cowling	University of Glasgow
Dr Rupert Ormond	University of Glasgow
Professor Alan Bull	University of Kent
Professor Don Ritchie	University of Liverpool
Dr Mark Trimmer	University of London Queen Mary
Dr Pauline Handley	University of Manchester

COMMERCIAL	
CONTACT	COMPANY
Ian Scade	Carapacics Ltd
Robin Teverson	Finance Cornwall
Dr Dave Woodwark	FIRST Faraday Partnership
Michelle Scott	Glaxo Smith Kline
Dr Charles Bavington	Integrin Advanced Biosystems
Alasdair Munro	Top Country Development

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Foresight Marine Panel

Marine Biotechnology Group

A STUDY INTO THE PROSPECTS FOR MARINE BIOTECHNOLOGY DEVELOPMENT IN THE UNITED KINGDOM

VOLUME 2 – BACKGROUND & APPENDICES

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The project team also included Dr Ambili Nair of BioBridge Ltd, with contributions from Dr Grant Burgess of Heriot-Watt University – their assistance is gratefully acknowledged.

This report is the starting point for discussion of a strategy for the development of the UK's Marine Biotechnology sectors. As such, it does not pretend to be complete and exhaustive, but is aimed at providing the nuclei or kernels on which further useful information and actions can be built. Examples might include using the tables on forthcoming conferences and useful associations as a basis for web-based resources that are dynamic.

While we hope that it is accurate, we welcome our attention being drawn to any inadvertent errors, via the FMP Marine Biotechnology Group or by email to mlloydevans@biobridge.co.uk; *comments on the conclusions and recommendations are also welcome, in the interests of expanding discussion within the marine biotechnology community.*

Meredith Lloyd-Evans, BioBridge Ltd, December 2004.

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FIGURES AND TABLES

ABBREVIATIONS

AFEN	Atlantic Frontier Environmental Network
AIMS	Australian Institute for Marine Science
AUV	Autonomous Underwater Vehicle
BBSRC	Biotechnology and Biological Sciences Research Council
CCAP	The Culture Collection of Algae and Protozoa
CEFAS	Centre for Environment, Fisheries and Aquaculture Science
COMB	Center for Marine Biotechnology, University of Maryland
DARD	Department for Agriculture and Rural Development
DEFRA	Department for Environment, Food and Rural Affairs
DFES	Department for Education and Skills
DTI	Department of Trade and Industry
ECF	Enterprise Capital Fund
ECMB	European Centre for Marine Biotechnology, Dunstaffnage
EMSB	ESF Marine Science Board
EIS	Enterprise Investment Scheme
EPSRC	Engineering and Physical Sciences Research Council
ERMS	European Register of Marine Species
ESF	European Science Foundation
EU	European Union
EU NoE	EU Network of Excellence
EU RTD	EU Research & Technology Development
FP6	The EU's Framework Programme 6, of Research and Technology Development
GBF	Gesellschaft für Biotechnologische Forschung
GDP	Gross Domestic Product
GMP	Good Manufacturing Practice
GVA	Gross Value Added
HEFCE	Higher Education Funding Council of England
HEI	Higher Education Institution
HEIF	Higher Education Innovation Fund
HIE	Highlands & Islands Enterprise
HWU	Heriot Watt University
IACMST	Inter-Agency Committee on Marine Science and Technology
IFREMER	Institute for Research in Marine Sciences

IMAREST	Institute of Marine Engineering, Science and Technology
IMBC	International Marine Biotechnology Conference
IP	Intellectual Property
ITI	Intermediary Technology Institute
KTN, KTP	Knowledge Transfer Networks and Partnerships
LEC	SE Local Enterprise Company
M&FMB	NERC Marine and Freshwater Microbial Biodiversity programme
MBA	Marine Biological Association of the UK
MBG	Fore*sight* Marine Panel - Marine Biotechnology Group
MDIS	Medical Devices in Scotland
MRC	Medical Research Council
MSTP	the proposed Plymouth Marine Science and Technology Park
NERC	Natural Environment Research Council
NESTA	National Endowment for Science, Technology and the Arts
NGO	Non-Governmental Organisation
NHS	National Health Service
NNFCC	National Non-Food Crops Centre
OST	Office of Science and Technology, DTI
PML	Plymouth Marine Laboratory
PMSP	Plymouth Marine Sciences Partnership
PSRE	Public Sector Research Establishment
R&D	Research & Development
RCUK	Research Councils UK
RDA	Regional Development Agency
RSE	Royal Society of Edinburgh
RVCF	Regional Venture Capital Fund
SAMS	Scottish Association for Marine Science
SBRI	Small Business Research Initiative
SBS	DTI's Small Business Service
SE	Scottish Enterprise
SEERAD	Scottish Executive Environment and Rural Affairs Department
SME	Small and medium-sized enterprise
SRIF	Science Research Infrastructure Fund

1. INTRODUCTION

This report (Volume 2) constitutes the background information gathered during the course of the study and should be used in support of Volume 1 of the report for those who require more detailed background information.

The report serves two different functions

- one, to provide a profile of activity in the UK and the rest of the world, so that we can put the UK into the context of marine biotechnology activities elsewhere
- two, to focus on some strategic issues that have an impact on whether supporting UK's marine biotechnology might produce a genuine competitive position and result in added economic value for the UK.

These two aims have somewhat diametrically-opposed requirements, the former requiring detail and the latter being to a large extent obscured by it. The information for the UK is included in the main report, and for the other parts of the world is presented in the Appendices.

An early question is a definition of marine biotechnology, not only from the scientific point of view, but also reflecting the fact that it is origin-defined, which may give the impression that it can only take place in or near the sea, or be applied to oceanic activities. Other biotechnology has been defined in terms of the end-market applications – food biotech, healthcare biotech, agribiotechnology and so on. This indicates the relative immaturity of the sector but could lead to some unconstructive pigeon-holing.

1.1 What is Marine Biotechnology?

The definition of marine biotechnology that has been endorsed by the Fore*sight* Marine Panel's Marine Biotechnology Group is 'The exploration of the capabilities of marine organisms, at the whole, cell, and molecular level, to provide solutions to today's problems, coupled with the use of technology to advance the understanding and accessibility of marine biological materials.'

"Marine biotechnology is the use of marine organisms, at the whole, cell, or molecular level, to provide solutions, thereby benefiting society."

The above is the simplest definition and ignores subsidiary questions such as what disciplines then make up marine biotechnology and where does molecular science-based endeavour stop and 'mere' technology-based endeavour begin. To skate over this question, we propose to use the term '<u>marine biotechnology</u>' to refer to marine biosciences that specifically involve molecular approaches, and use a portmanteau term '<u>marine bio[techno]logy</u>' to refer to activities which are aimed at a marine biotechnological outcome but need to involve other disciplines such as biochemistry, physiology, biodiversity studies, ecology, toxicology and so on, when the exact borderline cannot be determined or when an overall sector term is required.

Also, for the purposes of this study, we have excluded vertebrate animals as subjects of marine biotechnology, on the grounds that this project is not aiming to address the genetic modification of fin-fish, sharks, dolphins and whales.

Generally speaking, it is microbial fauna and flora of the sea that seem to offer the most excitement and promise in terms of their exploitation through technology, including but not limited to extraction and purification of bioactives, genetic engineering of the microbes themselves, or transfer of their genes to conventional organisms, and the biotechnology of bioreactors. This has also been the focus of much recent funding.

What we know already supports the view that marine micro-organisms and the larger marine plants and invertebrates are qualitatively so different from terrestrial organisms that they do indeed inhabit 'a different world':

- The seas cover about 70% of the Earth.
- More than 80% of the Earth's phyla are found only in the sea.
- Marine micro-organisms are responsible for 90% of the nutrient cycling that occurs
- There are probably 10^9 bacteria per litre of seawater and 10 times that many viruses.

Macroalgae offer a reasonably accessible and relatively easily-farmed marine resource. There are some exciting avenues such as actives with potential in inflammation, heart disease and coagulation disorders but, on the whole, seaweeds are regarded by industry as a source of commodities such as agar, alginates and carrageenan. Invertebrates are also of interest (ziconotide, for example), but pose problems in terms of sustainable harvesting or biotechnology production compared with micro-organisms, though farming of mussels and oysters is well-established and of sponges is becoming possible. In addition, we are also only just beginning to realise the full implications of many of the unique commensal or symbiotic relationships that occur between marine microbes and more complex organisms.

There are four aspects in particular that make marine biotechnology an exciting area, but also provide significant challenges:

- The range of habitats, from hot-water vents to polar ice and high-pressure depths to sea surface films, has led to a diversity of biochemistries, physiologies and metabolic processes that are often very distinct from those of land organisms.
- With recent bioreactor and culture developments, it becomes feasible to grow extremophiles as well as marine life from shallower depths, under controlled conditions.
- Advances in genomics and in techniques for genetic engineering of marine micro-organisms and invertebrates now allow enrichment or transfer of desirable products and characteristics.
- The nature of most if not all of the bioactives from marine organisms gives chemists an unparalleled opportunity to develop exciting new total synthetic or semi-synthetic methods, in the interests of sustainable production and exploitation.

The challenges posed by these four areas include:

- The resources (money, people, time, equipment) required to reach those habitats and then to collect and conserve materials from them, suggesting that the risk might be spread across the scientific, industrial and naval sectors already going to sea that collect material, deliberately or as a by-product of other activities.

- The risk of focusing on what is doable in marine bioculture, rather than what is productive, and the costs of continuing bioprocess development, suggesting that the 'appliance of science' already underway in marine bio[techno]logy will benefit from continued reinforcement and that a centralised or shared bioprocessing development facility would be tremendously beneficial.
- The typical challenges of the gene revolution, in terms of making sense and use of the information that arises from genomics, transcriptomics, proteomics, metabolomics, suggesting strategic emphasis on high-density information management and high throughput contextual screening, perhaps in a network of resources rather than duplicated facilities.
- The conflict between the perceptions of sea as nature and genetic enhancement techniques as the opposite, suggesting a careful choice of 'flagship' products and a strong, coherent sector branding.
- Natural products synthesis and chemistry on the one hand, and advanced engineering on the other, need to stay within the continuum of marine bio[technology], suggesting that cross-discipline collaborations and networks are vital to achieving outputs from marine biotechnology.

In addition, advances have been made in tools for identification of difficult-to-culture organisms or those in assemblages and communities such as in biofilms and symbionts in invertebrate tissues. The use of 16S ribosomal gene analysis has revolutionised the study of microbial biodiversity and was possibly the single biggest step forward in this area. Other tools and techniques such as fluorescent *in situ* hybridisation (FISH, an appropriate acronym for marine studies), matrix-assisted laser desorption-time of flight mass spectrometry (MALDI-TOF MS) and pulsed field gel electrophoresis are now contributing. No doubt other techniques, possibly allied to remote vehicles with on-board sensors, will enter the field. One aim is a complete 'lab-on-a-chip' concept, that allows *in situ* taxonomic, genomic and metabolomic analysis of mixed populations in mid-ocean, interfaces, extreme environments and sediments. Algorithmic analysis of complex genomic patterns will allow probability-based taxonomic analysis of mixed populations without microscopy or culture. Communities can be profiled using amplified ribosomal DNA restriction analysis, for example.

In many cases, the term 'blue biotechnology' encompasses advanced managed cultivation of fish, new techniques and technologies in aquaculture, mariculture and food from fish, and environmental biotechnology as applied to marine and freshwater. However, The Technology Foundation of Schleswig-Holstein produced an excellent report in June 2003 entitled Blue Biotechnology[1], covering bio[techno]logical utilisation of marine resources, and a recent report from the European Commission makes it clear that microbial technologies and bioprocess engineering using marine microbes should be considered as 'blue biotechnology'[2].

[1] *Blaue Biotechnologie: Stand und Perspektiven der marinen Naturstoffe*, N Kube and U Waller June 2003, Technologiestiftung Schleswig-Holstein, Kiel Germany

[2] see http://www.nf-2000.org/publications/york0401.pdf

The work of Remedios Ltd, a spin-out from University of Aberdeen using bioluminescence as a monitoring tool for the environment, has also been described as 'blue biotechnology' in its press releases. The *Blaue Biotechnologie* report incidentally restricts its attention to marine natural compounds, not to bioprocesses or bioengineering, although it refers to novel enzymes and biofouling.

1.2 Products[3]

The table below shows the vast range of end-markets for products from different marine organisms. including some that are not, strictly speaking, the products of marine biotechnology.

TABLE 1: END-MARKETS FOR PRODUCTS FROM DIFFERENT MARINE ORGANISMS

MARINE SOURCE	MARINE-DERIVED PRODUCTS
actinomycetes	antibiotics and other bioactives, pesticidal molecules
birds	food (eggs, meat), guano
cartilaginous fish	collagens, cartilage extracts, pharmaceuticals, PUFAs
crustacea	food, food and feed ingredients, chitin, chitosans, glucosamine, biomaterials, anti-fungals, soil conditioners, cosmetics, research reagents
diatoms	nanostructures, bioceramics, industrial uses
fin-fish	food, food and feed ingredients, gelatins, collagens, oils, PUFAs, cosmetics, fertiliser
mammals	meat, ambergris, oils, clothes
microalgae	food, food and feed ingredients, colorants, anti-oxidants, bioactives of various types, PUFAs, cosmetics, research reagents, surfactants
seaweeds	food, food and feed ingredients, medical biomaterials, anti-viral agents, soil conditioners, maerl, cosmetics, research reagents
soft invertebrates and corals	food, anti-pain products, bioadhesives, bone replacements, tissue engineering scaffolds, health supplements, cosmetics, research reagents; other activities may be associated with symbionts
symbiotic microbes	cytotoxic, anti-inflammatory, anti-viral drugs, and others
viruses	no uses yet established (?phage treatments for algal blooms?)

Marine-origin raw and processed materials have a long history of use in food and agriculture. In tonnage terms, seaweeds are the second most-traded products of the sea after finfish; most are the output of marine farming rather than harvesting from the wild. Carrageenan, alginates and agar are heavily used as thickeners, texturisers and bulking agents in food and in industries where liquid management is required (eg oil). Marine-origin materials certainly have applications in many sectors besides food and feed processing – microbiology has been dependent on agar, and the quality control of products generated using microbes, including

[3] see Chapter 5 for more detail

vaccines and many biopharmaceuticals, has depended on the LAL (*Limulus* amoebocyte lysate) test to detect bacterial endotoxins.

Marine wastes have also been a source of interesting and useful materials – crustacean shells yield chitin and chitosans, which have applications in agriculture as anti-fungal and soil conditioning agents and plant growth factors, in industrial applications such as filtration, remediation and ion-chelation, and in wound healing as dry dressing components. Further processing yields glycosaminoglycans, which are of growing interest as health supplements, nutraceuticals and borderline medical products for healthy joints and mobility. Even the previously-discarded melt-water from frozen prawns and shrimps is a source of the enzyme alkaline phosphatase. The crustacean colorant astaxanthin is used in its synthetic and natural forms as an anti-oxidant component of healthfoods and cosmetics and as a colorant for fish-food and flamingo-feed, and commands a market of at least $200 million per year.

Other relatively simple and accessible products of relevance to the focus of this report are fatty acids from marine algae, developed for use in baby foods by Martek, and bone-repair material from coral skeletons, launched in the USA in 1992 by Interpore International (now Interpore Cross International). But most interest and funding has focused on isolating novel bioactives from marine sources.

Activity in the USA has already yielded a number of exciting anti-inflammatory, pain management, anti-parasitic and anti-cancer agents from marine biota. Pseudopterosin, isolated from the Caribbean sea-fan *Pseudopterogorgia elisabethae* by Fenical and others at University of California San Diego (Scripps Institution of Oceanography), is one of these, a strong anti-inflammatory already launched in cosmetics by Estée Lauder that, to date, has returned about $2 million in royalties to the University of California[4].

What is clear at the moment is that, of the marine phyla, sponges have the highest productivity and, of the 15 marine natural products in clinical trials[5], one-third come from sponges collected in Australia or Papua New Guinea. Cold waters are under-represented in a way that has led some commentators to dismiss them. It is, however, more realistic to note that coldwater environments are more difficult and less pleasant to investigate, the organisms of interest are often in deeper water than those to be found in the tropics, and the preponderance of bioactives from warm water simply reflects the late start and, until recently, low funding applied to colder areas (with the possible exception of the Antarctic).

The range of products from marine biotechnology is expanded on the previous page. In a report of this scope and resource, it will not be possible to find data on each of these categories and, indeed, reliable data in most of these fields is difficult or impossible to obtain cheaply. The aim of the market assessment part of this project is to highlight those sectors where there may be opportunities that appear to match the UK's current-to-mid-term activities in marine biotechnology.

[4] *California Sea Grant Strategic Plan 2001-2005*, New Marine Products, p35

[5] according to *Modern Drug Discovery*, 2002, **22**, 419 – other sources say 20 or 30 depending on their own data collection

1.3 The Development of Marine Biotechnology

Interest in making technological use of marine organisms rather than simply eating them began some centuries ago in the west and probably much earlier in the east. In Scotland, the harvesting of kelp for its potash content was a thriving industry during the 18th and 19th centuries as a result of needs in the chemical industries. Maerl, a calcium rich seaweed harvested from offshore in Brittany and parts of the British Isles, is still collected for use as a soil fertiliser and conditioner. Seaweeds have been used therapeutically for their iodine content and for uses that are similar to those promoted by health and food supplement companies now. Homeopathy has also made use of marine extracts for disease management and re-balancing.

The 1960s saw the beginnings of serious interest in the potential of marine organisms for human health. The anti-viral and anti-cancer arabinoside molecules Ara-A and Ara-C were chance discoveries that stimulated a whole generation of chemists into exploring the vast undersea world. It was not until 1989 that the first International Marine Biotechnology Conference (IMBC) was held, in Tokyo. The IMBCs spawned regional groupings, including the Asian-Pacific, European (ESMB) and Pan-American (PAMBA) societies and associations for marine biotechnology. ESMB was founded in 1995. The first UK Marine Biotechnology Conferences was held at Heriot-Watt University in 1996. In Europe, a broad support for R&D activities also comes from the European Science Foundation's Marine Board, which published its European Strategy for Marine Biotechnology in December 2001.

Developing and exploiting discoveries in these sectors is difficult without a coherent strategy for investing in research and in proof of principle, an effective technology and knowledge transfer system, and a sensitivity to existing and emerging markets. Funding these processes can be extremely costly - Japan has invested billions of pounds in research and the establishment of dedicated research institutes in Kamaishi, Shizuoka, Yokosuka and Tokyo, Australia is strongly funding AIMS at Townsville Queensland, and the US, after a rather slow start, has put several hundreds of millions of dollars into the marine biotechnology sector in Hawai'i, Maryland (COMB), Massachusetts, California and other states.

In a UK context, the NERC is currently the strongest supporter of marine biotechnology efforts and its support is mentioned in more detail later. The NERC is funding the UK's involvement in the European Science Foundation's Marine Science Board (EMSB). The EMSB's Marine Biotechnology Feasibility Study Group published a European Strategy for Marine Biotechnology two years ago, to "promote the development of marine biotechnology in Europe in order to extend and enhance existing marine and biotechnology industries".

The Strategy document recognised that no concerted or focused initiative had yet materialised in Europe. Leading lights in European activity include several centres in Norway (Oslo, Bergen, Trondheim and Tromsø), the Netherlands (Wageningen, Groningen), Germany (IMaB Greifswald, Braunschweig), France (Roscoff, Concarneau, Brest-Nantes and IFREMER), Italy (Sardinia and Naples), Greece (Athens and Crete) and Ireland. Portugal hosts the European Centre for

Information on Marine Science and Technology (EurOcean), which provides a wide internet-based space for knowledge on many aspects of marine exploitation.

The European Union has supported marine biotechnology and the bringing-together of these resources through its Framework Programmes (FPs) of Research and Technology Development. Marine Science and Technology (MAST) received €390m support in FP2-FP4. The EMSB Strategy document highlights 13 projects supported under FP4 and FP5, in areas such as natural products from organisms, environmental monitoring and anti-fouling compounds. In FP6, there are two relevant Networks of Excellence, in Marine Genomics co-ordinated from Roscoff France and Marine Biodiversity co-ordinated from the Netherlands, and Integrated Projects in various areas of marine science and biotechnology are underway or foreseen.

TABLE 2: THE PRODUCTS OF MARINE BIOTECHNOLOGY

SECTOR	PRODUCTS
FOODS	• food additives such as new colorants, anti-oxidants, texturing agents • functional foods for general healthy lifestyles • nutraceuticals for specific health focus – cardiovascular, joint problems, osteoporosis
NUTRACEUTICALS	• carotenoids • calcium products • other trace elements • anti-oxidants • marine organisms as probiotics
MEDICINE	• pain management products • anti-inflammatory agents • growth factors • hormones • anti-viral agents • anti-cancer agents
HEALTHCARE	• biomaterials, including biopolymers and bioceramics • novel adhesives • anti-fouling agents for implants and catheters • components of medical devices • encapsulating drug delivery systems
COSMETICS	• collagens • anti-oxidants and sunscreens • revitalisers and anti-ageing
RESEARCH TOOLS	• reagents including enzymes • new tools for discovery and testing • libraries of organisms and extracts • model organisms for safety and toxicity tests • marker genes and gene products for molecular biology research e.g. bioluminescence •
NEW ENERGY SOURCES	• light-capture • microbial batteries • energy-rich oils • hydrogen-producers •

SECTOR	PRODUCTS
INDUSTRIAL	• novel adhesives • foams for oil industry • non-polluting metal extraction • anti-fouling materials • polymers • enzymes such as haloperoxidase • surfactants • ceramics • algae and other microbes as feedstock for biotechnological and chemical processes • thickeners and other materials for textile and paper industries • nanotechnological developments using diatoms
PROCESSING TECHNOLOGIES	• extremophile management • improved bioreactor technology • improved purification methods and reagents
ENVIRONMENT ENHANCEMENT	• desalination • heavy metal removal from mine wastes • marine phage viricides for use in microbial films • background pollution removal • removal of toxic microalgae
ENVIRONMENT & FOOD SAFETY	• diagnostics for toxins in seafood • pollutant detection
AGRICULTURAL	• seed coatings • pesticides, such as toxin from nereid worms or insecticide from sponges • animal feed additives • proteins and oils as animal feed ingredients • probiotic organisms in aquaculture • new vaccines and disease preventatives

In the UK, activity in marine bioscience and biotechnology is taking place at a surprisingly large number of Universities and other centres, including the Marine Laboratories at Plymouth and Dunstaffnage, Heriot-Watt University (notably), the Universities of Aberdeen, Stirling, Wales Bangor, Warwick, Essex and Hull and the British Museum and Natural History Museum. The new European Centre for Marine Biotechnology at Dunstaffnage hopes to act as the linchpin of a network of facilities, individuals, groups and companies that can develop the promise of marine biotechnology together. However, there are relatively few companies in the UK exploiting marine resources, twenty at most, and nearly all of these are small or even start-ups waiting for funding. The best-established, such as ISP Alginates, process algal raw materials such as carrageenan and alginates.

Internationally, there are a number of support programmes that have funded work in marine bioscience, biodiversity and marine biotechnology. As far as we know, no comprehensive listing of international marine bio[techno]logy support programmes exists or is widely available. **Table 3** shows a few of these programmes:

TABLE 3: SOME SUPPORT PROGRAMMES FOR MARINE BIOSCIENCES AND BIOTECHNOLOGY

COUNTRY	PROGRAMME	FUNDS	COMMENTS
USA	National Sea Grant Program www.nsgo.seagrant.org funding 2/3 from National Oceanic and Atmospheric Administration NOAA; 1/3 state or private	marine bio and biotech projects about $35 million in NOAA and matching funds	Each state operates its own Sea Grant programme; 29 coastal programs + inland projects Established a Marine Biotechnology Initiative in early 90s.
USA	BioSTAR (now University of California Discovery Grant)	approx. $30 million over 8 years	Marine biotechnology is a minority of projects, mainly at Fenical's Scripps Institution labs
EU	Framework Programmes for RTD (FP3, FP4, FP5, FP6), funded by the European Union via the European Commission for marine biotechnology, ecology, biodiversity, applications	total? has to be laboriously added up with lots of cross referencing	Somewhat stringent requirements for eligibility; tough requirements for proposal construction; a challenge to manage the large programmes and participant groups that result; no comprehensive and coherent list of projects seems easily available
UK	Marine and Freshwater Microbial Biodiversity programme, funded by NERC	approx. £7m	funds available for smaller-scale demonstration or application projects
International	Census of Marine Life	$1 billion over 10 years, mainly from the Alfred P Sloan Foundation	marine biodiversity is main aim; no focus on exploitation except in the context of sufficient knowledge to allow sustainability or prohibition
Ibero American Network	brings together researchers and government scientific institutions in Spain, Portugal, Central and South America Including Mexico, Cuba, Dominican Republic	? not immediately obvious how to create a total	very broad programme, marine biotechnology represented with some networks and sub-projects but not prominent

1.4 Markets and Prospects

A recent market sector report[6] gives an estimate for the world market for marine biotechnology products and processes as $2.4b in 2002, though this may be potential, rather than actual sales, and may certainly be based on a stretched definition of biotechnology (for example, including non-food uses of algal raw materials). Certainly there are substantial existing markets for products from macroalgae (seaweeds) in food and healthcare, mainly as agars, alginates, carrageenan and alternatives to animal biopolymers (collagens, gelatins). The biopolymer woundcare sector alone, in which alginates and chitosan are already found, is estimated to be worth at least $800m per year. Natural pigments and anti-oxidants such as astaxanthins are also of interest, with a market for synthetic colorants of about $200m per year.

So far, the focus on the use of advanced technologies in exploiting marine resources has been on cultivation processes and extraction and purification methods. The most promising avenue for high-value utilisation of marine resources, and the one with the greatest input of effort and funding, is to isolate and characterise novel metabolites that might be useful medicines, nutraceuticals or cosmetics.

The application of biotechnology *per se* to marine resources has been relatively limited, though there is considerable interest in adding value by genetic enhancement, either to marine organisms themselves or, having identified genes of interest, by transfer to more conventional organisms such as *E. coli* or yeasts. As always, this is accompanied by regulatory, ethical and environmental concerns, which may well be crystallised by the recent marketing of 'Glo-Fish'™ in the USA.

Areas in which the UK could become a major force in the use of marine biotechnology include:

- Monitoring and prevention of fish disease.
- Pigment production for the food and aquaculture industries.
- Novel enzymes for food processing and other industrial uses
- Novel foods and snacks based on the 'healthy' image of products from the sea.
- Marine microbial biotechnology *per se.*
- Bioactives from marine organisms.
- Marine bioprocess engineering.
- Environmental remediation[7].

As analysed below, it is clear that the UK has major strengths in bio-fouling, marine actinomycetes, synthetic chemistry, marine viruses and advanced marine engineering.

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6 *Biomaterials from Marine Sources*, BCC Inc February 2003.

7 Derived from *UK Marine Industries World Export Market Potential*, Institute of Marine Engineers on behalf of the Marine Fore*sight* Panel 2000, ISBN 1-902536-38-X p87

1.5 Issues & Opportunities[8]

In October 2001, Professor Graham Shimmield conducted a workshop, sponsored by the Fore*sight* Marine Panel, at which there was a strong feeling of commitment to the idea of a marine biotechnology strategy in the UK but considerable surprise that a strategy exercise had not taken place earlier and that many fundamental strategic issues remained unresolved.

The workshop identified a number of issues for action that would need to be taken into account in formulating a credible strategy:

- Highlighting marine biotechnology as an area of potential and excellence.
- Focusing on existing strengths in marine biotechnology and the natural advantage of carrying out this area of science in the UK, as the fastest route to excellence.
- Differentiating UK marine biotechnology from its overseas competitors by creating excellence in specialist niches.
- Developing Centres of Excellence to host research and commercialisation of specialisms.
- Redressing the lack of trained scientists with a track record in marine biotechnology and provide more encouragement in education and awareness of employment opportunities.
- Accessing government support for and investment in the chosen specialisms.
- Ensuring that culture collections were regarded as a key growth area, for public and private sectors
- Establishing existing and likely demand for the outputs of marine biotechnology within the UK using market research.
- Encouraging exchanges between university and businesses through workshops, placements and staff exchanges.
- Invest effort in establishing a closer, systematic relationship with the government and the business community.
- Creating a network of effective relationships with links into providers of specialist technologies that are needed to exploit marine biotechnology.
- Establishing long-term objectives for marine biotechnology that provide a feasible basis for its support.
- Increasing the rate of new business formation for small businesses that use the outputs of marine biotechnology.
- Identifying an effective champion for this sector in the UK.

Feedback from our interviewees indicates that there is some momentum that can be grasped, but some problems that still need to be tackled. These are discussed in more detail in Chapters 6, 7 & 8.

[8] see Chapters 6, 7

2. THE UK

2.1 Introduction

The UK has made industrial use of marine resources for several centuries: the use of kelp harvested in Scotland for the extraction of minerals, especially potash, started in the 18th century and seaweed extraction for hydrocolloids is still the largest contributor to Scotland's marine biosciences economy[9].

The UK has a strong biotechnology sector focused mainly on biopharmaceuticals, bolstered by the rather 'invisible' earnings from service industries supplying into the sector. The UK's biotechnology sector is the largest in Europe, with about 500 dedicated biotechnology businesses in the UK employing around 23,000 people. Although revenues exceed £3 billion, and there are 17 profitable listed UK companies (e.g. Acambis, Shire and Cobra, and Celltech – now bought by UCB of Belgium for £1.5 billion), many UK businesses are very small, employing less than five people and still at venture capital stage. However, the UK is second only to the US, where the sector is more mature. UK companies also account for almost three-quarters of European's publicly quoted biotechnology companies and 45% of the biotechnology drugs in late stage clinical trials (Phase III)[10].

Marine biotechnology is still an invisible part of this sector, largely because its promise has not yet reached the wider industrial and investment communities or the general public consciousness. The Fore*sight* Marine Panel's Marine Biotechnology Group has focused on some of the actions necessary to achieve this, as well as to raise the profile of the sector in terms of support for the science and research.

Fore*sight *Marine Panel

The Fore*sight* Marine Panel was established in 1995, reporting into the Office of Science and Technology, with a brief to identify and assess commercial opportunities for the UK's science & technology base, and identify R&D requirements that underpin strategic economic development areas. It is one of 10 Sector Panels focused on emerging opportunities in markets and technologies and involves business and academic interests in engineering, science and technology, and policy.

The Panel developed four Marine Task Forces in the second Fore*sight* exercise. Three are potentially relevant - Energies from the Sea, Aquaculture 2010 and Management of Marine Resources and the Marine Environment. The Marine Panel, now independent from Government, is also concerned with education and training to overcome a shortage of marine skills.

The Marine Biotechnology Group within the Fore*sight* Marine Panel is responsible for considerations of marine biotechnology and exploitation of biotech-derived products, and for moving forward these aspects in the new round launched in April

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9 see *Marine Science in Scotland, a Strategy for developing its potential*, for HIE and SE Feb 2004

10 see http://www.uktradeinvest.gov.uk/biotechnology/profile/index/overview.shtml

2002. The MBG is responsible for commissioning this report, supported by DTI and SWRDA (South West of England Regional Development Agency).

Brief overview[11]

Marine-related activities in the UK accounted for £39 billion or 4.9% of GDP in 1999-2000. As expected, oil and gas is the most important single sector, contributing about £15 billion value-added; fish farming and fish processing contribute £180 million and £825 million added-value respectively. Turning to the research and education sector, the estimated contribution to value-added was £292 million. Of the 17 Schools or Departments with a significant presence, i.e. identified as having more than 40 researchers in marine-related areas, 9 are relevant to this study:

TABLE 4: IACMST RANKINGS OF UK HEIS INVOLVED IN MARINE SCIENCE

INSTITUTION	RANKING BY SIZE	REGION
University of Southampton School of Ocean and Earth Science	1	E
University of Wales Bangor School of Ocean Sciences	2	W
University of Plymouth Dept of Biological Sciences	4	E
University of Aberdeen Dept of Zoology	5	S
University of Plymouth Institute of Marine Studies	6	E
University of St Andrews School of Biology	7	S
SAMS Dunstaffnage/UHIMI	8	S
University of Newcastle Marine Sciences and Coastal Management	13	E
University of Liverpool Marine Laboratory	14	E

note rankings given not staff numbers – in fact 1 = 188 and 14 = 53

Heriot-Watt's marine biotechnology activities were numerically too small to be included in the analysis. If Plymouth researchers were summed, the University would rise to 3rd place. HEIs involved in marine research of any sort received about £58 million in grants, in addition to basic funding from HEFCE or the Welsh and Scottish equivalents. In all 17 HEIs, Life Sciences obtained the lion's share of the funding, 36%. The 16 most popular research topics are all relevant to a proper development and exploitation of marine biotechnology, including estuarine, coastal zone and seabed studies (1, 2 & 3). Although marine biological studies and physiology of marine organisms came low on unweighted scores, at 11th (8=) and 13th (8=) respectively, when the rankings were weighted to account for department

[11] derived from *A New Analysis of Marine-related activities in the UK economy with supporting science and technology*, D Pugh and L Skinner, Inter-Agency Committee on Marine Science and Technology Information Document No. 10, August 2002

size, marine biological studies leapt to 1st place and indeed this topic remained at the top of the HEIs forward research priorities.

In a report specifically focusing on Scotland[12], the bioscience, ecology and marine technology sectors were estimated to contribute £33 million in added value from gross turnover of £70 million, to which ISP Alginates, the seaweed processors, contributed some £30 million. During the project, interviewees were asked to position the UK in global perspective. The general consensus was that the US was the leader, and Scotland came second, with about half the UK's research activity. Scotland's quality was perceived as high but lacking in infrastructure. In particular, improved co-ordination and integration of research was highlighted as a need.

We have identified 21 companies that are active, or have been established in the UK, that deal with exploitation of marine bio[techno]logy. There are clearly others, such as Seven Seas, which exploit marine resources, but products such as fish liver oils do not fall within the scope of this report. The companies are described below in section 3.3.

2.2 UK Research – HEIs and Other Organisations

As the Appendices show, we found 64 HEIs and other organisations involved in researching and/or teaching marine sciences. Many of these focus more on biology, ecology and biodiversity than on marine biotechnology *per se*, but it is undeniable that these elements will be required for balanced, sustainable and managed exploitation of marine resources. The total does not take into account individual units, centres, marine laboratories or other departments within an HEI or research institute.

Many of these institutions have undertaken collaborative work. The NERC's M&FMB programme has encouraged this, as have EU projects. For example, of the 41 organisations involved in the recently-started EU-funded Network of Excellence on Marine Genomics, 11 are from the UK, including 2 core partners, the University of Birmingham and the Antarctic Genome Laboratory at the School of Ocean and Earth Science, Southampton. The other 9 partners are the Universities of Newcastle, Hull, Oxford, Wales-Bangor, Wales-Cardiff and Warwick, the Marine Biology Association Plymouth, Southampton Oceanography Centre and CEFAS Weymouth. This NoE will also contribute to intra-UK networking and collaboration as well as trans-European work in this very important area, plus the opportunity for contact with the eastern Mediterranean through the 7 Israeli partners.

We identified a total of 49 HEIs and other organisations more closely involved in marine biotechnology or related research, of which many are or were active contributors to the NERC-funded Marine & Freshwater Microbial Biodiversity and Biofouling programmes (see tables below and Appendices 1-4). 33 HEIs and organisations are in England, 10 are in Scotland, 4 are in Wales and 2 are in Northern Ireland. The RAE ratings for the Scottish HEIs and institutions, reported

[12] *Assessment of Marine Science Activities and Capability in Scotland (Abridged Version)* Scientific Generics Limited October 2001, for Highlands and Islands Enterprise and Scottish Enterprise

in the Marine Science in Scotland strategy document[13], are very favourable – Aberdeen, St Andrews, Glasgow and the Gatty score 5, UMBS Millport, HWU Marine Biotechnology and SAMS Dunstaffnage score 4, and it would seem they generally 'punch above their weight'.

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13 see *Marine Science in Scotland, a Strategy for developing its potential*, Feb 2004, for HEI and SE pp31-32

TABLE 5: MARINE BIOTECHNOLOGY RESEARCH ACTIVITIES IN HEIS AND ORGANISATIONS IN ENGLAND

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Aston University Chemical Engineering and Applied Chemistry,	Investigating the use of porous marine-origin structural biomaterials from corals, sponges and sea-urchins in the production of artificial cornea for keratoplasty techniques
Birmingham, University of School of Biological Sciences	The molecular and cellular basis of primary adhesion by *Enteromorpha* spores (Marine Biofouling Thematic Programme MBTP – NERC 1995-1998); Marine Biofouling, especially in relation to the control of algae which foul ships; core member of EU NoE Marine Genomics; Microbial interactions in natural assemblages, N-acylhomoserine lactones and *Ulva* zoospore adhesion (Marine & Freshwater Microbial Biodiversity programme M&FMB – NERC 2000-2005)
Brighton, University of Faculty of Science & Engineering	Working on glycine betaines and other marine-derived betaines for cryopreservation of biological systems
Bristol, University of School of Chemistry, School of Biological Sciences Biogeochemistry Research Centre	Prokaryotic ether lipid membranes, Picocyanobacteria communities & Novel molecular markers for sub-sea microbes (M&FMB); Bacterial populations in ocean sediments, palaeo-oceanography; synthesis of marine natural products (EC-funded 1997-2000)
British Antarctic Survey Cambridge	Genomic and metagenomic studies on Antarctic organisms, including extremophilic cyanobacteria and microbial communities. Exploitation will however be constrained by bioprospecting aspects of Antarctic Treaty. Member of EU NoE Marine Genomics
British Oceanographic Data Centre University of Liverpool	Central data repository and distributor for M&FMB project results
Buckingham, University of Clore Laboratory for Life Sciences	Biofouling
Cambridge, University of Dept of Chemistry	In the past has been a recipient of EPSRC grants for total synthesis of interesting marine bioactives including swinholide A, marine polyketides, squalestatins, scytophycin, aplyronine, bistheonellide and discodermolide
East Anglia, University of School of Environmental Sciences	Marine microbial ecology, Biogenic production of trace gases of atmospheric importance in marine waters. Biological oceanography, seaweed physiology and trace gas production; Viruses and biogeochemical cycling, Sulphur compounds and viral infection of phytoplankton & Virus-host dynamic during *Emiliania huxleyi* bloom (M&FMB); M&FMB Programme Science Co-ordinator for NERC
Essex, University of Dept of Biological Sciences	microbial interactions and the functioning of microbial consortia, application of microbial diversity, oil bioremediation, extremophiles esp. halophiles and their biotechnological applications; Novel *Archaea* in coastal marine sediments, Culture methods for novel marine and estuarine microbes (M&FMB with University of Reading); structure and function of complex microbial communities in aquatic systems and microbiology of polluted environments; atmospheric trace gas exchange by aquatic bacteria, cycling of C, N & S in coastal and Antarctic regions, ecology of aquatic and sedimentary organisms
Hull University	algal functional group ecology, techniques for monitoring algal communities, morphological variation and speciation of fucoid algae, general intertidal ecology and conservation biology; fisheries and biological oceanography and behaviour of krill; member of EU NoE Marine Genomics

TABLE 5: CONT

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Kent, University of Applied & Environmental Microbiology Group	Studying novel biotechnological applications provided by bacteria from the deep sea. Research collaborations with groups in Spain, France, Germany, Hungary, Japan, Indonesia, Greece, Norway, Italy, Portugal; Sedimentary actinomycetes (diversity and sampling methods), *Pseudonocardiae* from marine sediments & Marine *Micromonosporae* diversity (M&FMB, with Newcastle); Abyssomycins (with Eberhard Karls Universität Tübingen Germany and University of Newcastle-upon-Tyne)
King's College London	Surface active proteoglycan secretions from marine invertebrates and their role in modulating biofouling
Lancaster University Institute of Environmental and Natural Science	Trace metal metabolism and cycling in freshwater and marine environments (M&FMB with Marine Biological Laboratory Copenhagen University Denmark, Lucas Heights Science & Technology Centre Australia and University of Aberdeen); high resolution analysis of trace metal-sediment interactions
Leeds, University of Dept of Microbiology	Molecular biology of freshwater cyanobacteria & Biofilm-disrupting compounds from marine bacteria (M&FMB) (Biofilm work with Heriot-Watt)
Liverpool, University of School of Biological Sciences Port Erin Marine Laboratory IRC in Surface Science	Analysis of the structure and activity of bacterial populations in natural soil, sediment and water environments; development of molecular and DNA-based methods to profile bacterial communities; dynamics of microbial communities; gene fluxes and gene function in natural environments; Chemisorption studies related to reactive organic film growth; lysogenic phages in freshwater bacteria (M&FMB); commercial activity: Environmental Research and Consultancy's Marine Services
Manchester, University of **UMIST** Dept of Chemistry	Microbial adhesion and biofilm formation. Interbacterial adhesion in aquatic biofilms; Cytokine resuscitation of actinomycetes (M&FMB)
Marine Biological Association Plymouth	Active in NERC's MBTP programme: marine viruses; induction of barnacle larval settlement, settlement pheromones; modulation of marine invertebrate larval settlement and metamorphosis by eicosanoids; can bacterial metabolism self-regulate attachment to surfaces?; a partner in the EU NoE Marine Genomics; Viruses and biogeochemical cycling, Gene transfer via marine bacteriophages, Virus-host dynamics in *Emiliania huxleyi* blooms, Molecular biology of freshwater cyanobacteria, Sulphur compounds and viral infection of phytoplankton, Photosynthesis genes in marine viruses & Exploitation potential of marine viruses (M&FMB) (Photosynthesis genes with University of Warwick and MBA)
Newcastle-upon-Tyne, University of Centre for Coastal Management Dove Marine Laboratory School of Marine Science and Technology Centre for Molecular Ecology School of Civil Engineering and Geosciences School of Biology Agricultural & Environmental Science Postgraduate Institute, Newcastle Research Group	particular strengths in tropical and temperate marine biology; owns a research vessel. Departmental specialisms: environmental signal transduction in marine organisms; marine ecosystem dynamics; well-established marine engineering department; marine invertebrate reproduction and development, esp. larval settlement; marine biofouling/antifouling; invasive species; ecotoxicology (esp. endocrine disruption); seasonal variation of antifouling activities of marine algae from the Brittany Coast; research in behavioural ecology, ecophysiology, and biofouling, temperate and tropical ecosystems; Novel rhodococci, streptomycetes and actinomycetes from the deep sea (characterisation and exploitation), Diversity of sediment actinomycetes, Microbial N2 fixation, Diversity of diazotrophs in the Arabian Sea, Models for screening microbial biodiversity & Bioactive screening on a chip (M&FMB); microbial ecology and environmental microbiology, geomicrobiology, biodegradation of hydrocarbons, Microbiology of biogeochemical cycles; Abyssomycins (with Eberhard Karls Universität Tübingen Germany and University of Kent & Canterbury); member of EU NoE Marine Genomics

TABLE 5: CONT

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Nottingham, University of Centre for Biomolecular Sciences	Microbial interactions in natural assemblages & Natural antifoulants from actinomycetes (M&FMB)
Oxford, University of Dept of Zoology	marine taxonomy and distribution; Dispersal of free-living microbial species & Biodiversity and ubiquity of *Gymnamoebae* and *Cercozoa* (M&FMB); member of EU NoE Marine Genomics
Plymouth Marine Laboratory	an independent charitable company limited by guarantee, affiliated to NERC; Core research in estuarine and coastal function and health, scaling biodiversity and the consequences of change and microbially-driven biogeochemical processes, exchanges and controls; marine viruses, including those of microalgae and bacteria; cell signalling and nutrient uptake in biofilms and biofouling; bacterial-trace metal interactions, Characterisation of MeBr degraders, Bacteria-trace metal interactions, Virus-host interactions in *Emiliania huxleyi* bloom, Sulphur compounds and viral infection of phytoplankton, Molecular biology of freshwater cyanobacteria, Photosynthesis genes in marine viruses, Novel enzymes from marine viruses & Natural antifoulants from actinomycetes (M&FMB) (Photosynthesis genes with University of Warwick and MBA, Natural antifoulants with University of Nottingham) Commercial activity: Plymouth Marine Applications - Characterisation and exploitation of marine chlorophylls and carotenoids (Small Business Research Initiative)
Plymouth, University of Marine Algal Research Group Dept of Environmental Science	marine algae and environmental pollution; cellular responses to stress in algae; commercial and applied activity in seaweed and polyculture within the Centre for Applied Plant Research; Bromine cycling, Microbial interactions in natural assemblages, Bacteria-trace metal interactions & Diatom pigments (M&FMB)
Portsmouth, University of School of Biological Sciences Institute of Marine Sciences	Marine fungi; production of PUFAs by thraustochytrids; n-substituted imides as antifoulants; *Mytilus edulis* phenoloxidase; international collaborations on bioactives with Quimper and Concarneau, France; marine wood borers, Protection of wood in the sea, Impact of biocides used in wood protection on marine invertebrates, bivalve larvae, mangrove ecology in relation to the utilisation and the breakdown of wood; taxonomy and systematics of Brown Algae. Fouling/antifouling studies, pollution studies; the role of bacterial exopolymers in marine fouling and deterioration of steel surfaces: (MBTP); can bacterial metabolism self-regulate attachment to surfaces?; ecotoxicology and ecophysiology of fish and marine invertebrates, Fish endocrinology, Sensory biology of fish and invertebrates; environmental and endocrine control of reproduction in marine invertebrate, Ecotoxicology, Effects of pollutants and other human impacts (bait collection) on invertebrate reproduction, the role of chemical signalling in marine invertebrates.
Queen Mary, University of London	Nitrogen transformations in estuarine and coastal sediments; marine and estuarine benthic ecology and conservation
Reading, University of School of Animal and Microbial Sciences	Environmental Systems Science Centre PhD / MPhil (Departmental specialism includes Marine Science); Characterisation of non-extremophilic estuarine organisms & Novel *Archaea* in coastal marine sediments (M&FMB)
Royal Holloway, University of London School of Biological Sciences	Parasitology and aquatic toxicology: Ecology and epidemiology of parasites in aquatic and terrestrial hosts. Development of fish biosensors for early detection of pollutants in water. Fish and other aquatic host-parasite systems as indicators of water quality and environmental stress; ecology and physiology of aquatic, intertidal and marine invertebrates, especially amphipod crustaceans; adaptations to life in extreme environments; induction of barnacle larval settlement: the nature and perception of settlement pheromones (MBTP)

TABLE 5: CONT

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Sea Fish Industry Authority Hull	supports projects in improving sustainable seafish and shellfish farming, nutrition (possible role for microalgae, for example), microalgal-related shellfish toxins; seafood waste as composts; fish processing technologies and new product development
Sheffield, University of Biological and Environmental Systems Group	Applied research on extremophiles in culture, to investigate their physiology and biochemistry and make use of these for industrial processes, including new bioactives, halophiles, piezophiles, thermophiles; bioactives and hydrogen from marine cyanobacteria; solvent-tolerant marine microbes
Southampton, University of Southampton Oceanography Centre, School of Ocean & Earth Science The George Deacon Division for Ocean Processes, SOC	biomarkers, biogeochemistry of deep-sea animals, marine biofouling, carbon cycle, biosensors & chemical sensors; remote sensing methodology; effects of predation and nutrient recycling by protozoa on the development of communities of marine biofouling organisms (MBTP); a multidisciplinary research group of biological, physical and chemical oceanographers; The Oceanography Centre also hosts the Inter-Agency Committee on Marine Science and Technology, T:02380 596611, www.marine.gov.uk; physiological and environmental ecology of marine microalgae, phytoplankton, benthic microalgae, coccolithophore biology, physical-biological interactions at fronts, biostabilisation of intertidal sediments; larval biology of marine invertebrates, bathyphilic environments including hot vents and cold seeps, Antarctic invertebrates; Marine biogeochemistry of trace metals, carbon, and nutrients & Molecular ecology, physiology and genetic diversity of phytoplankton (M&FMB), functional genomics of bioluminescence in marine dinoflagellates; core member and partner of EU NoE Marine Genomics
Surrey, University of Microbial Physiology & Ecology Group	Research includes bioproduct physiology, microbe/surface interactions, microbe-microbe signalling and bioelectronics (interface between biosystems and electronics), advanced fermentation technology for production of bioactives, ecosystem function in attachment/biofilms [not clear if marine]; development of microarrays for characterising novel deep sea and coastal streptomycetes (collaboration with M&FMB project at University of Newcastle)
University College London Royal Free Hospital School of Medicine Dept of Chemistry & Molecular Biology	Working with Prof A Lloyd (Brighton) and Destiny Pharma Ltd on alginates and chitosans for tissue engineering scaffolds Phylogenetic analysis of biodiversity in deep marine and hydrothermal vent biotopes
Warwick, University of Dept of Biological Sciences	Cyanobacteria; phage ecology and exploitation; a partner in the EU NoE Marine Genomics; Bromine cycling, Characterisation of MeBr-degraders and assessment of potential as biocatalysts, Community structure of picoeukaryotes, Photosynthesis genes in marine viruses & Gene transfer via marine bacteriophages (M&FMB) (MeBr project with PML and University of Waikato New Zealand, picoeukaryote project with Station Biologique Roscoff France)
Wolverhampton, University of	Subcellular membrane transport processes studied in marine fungi; specialisms include gastropod oxidases [not clear if marine].
York, University of	marine biodiversity conservation, coral reefs, coastal management, tourism sustainability, marine reserves, threatened species, fishery management; pigments from diatoms (M&FMB 2004)

TABLE 6: MARINE BIOTECHNOLOGY RESEARCH ACTIVITIES IN HEIS IN SCOTLAND

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Aberdeen, University of Aberdeen Institute for Coastal Science & Management Dept of Zoology Marine Natural Products Lab Dept of Chemistry Oceanlab Dept of Molecular and Cell Biology Institute of Medical Sciences	ecology, physiology and *in situ* behaviour of deep-sea fauna; fundamental and applied studies in a wide range of ecosystems, intertidal to deep Arctic; marine natural products and marine biotechnology: novel fatty acids from marine algae, novel pharmaceutical agents from sponges; systems development: engineering of deep ocean instrumentation packages; lab studies on functional morphology and physiology using material retrieved by trap or trawl from the deep sea; work in MBTP; Viruses and plankton blooms & Trace metal cycling (M&FMB); spin-out Remedios, environmental biosensors; molecular analysis of marine bacterial communities. NCIMB (National Collections of Industrial, Food and Marine Bacteria) and NCIMB Ltd, the commercialisation activity relating to this, are hosted at Aberdeen.
Edinburgh, University of	microbial genomics and genotyping applied to foraminifera and other marine microbes
Fisheries Research Services Marine Laboratory, Aberdeen	fish diseases and disease diagnosis using molecular methodology; focus on diseases of turbot; biodiversity, microbiology, benthic studies and plankton; taxonomy of flatworm fish parasites using molecular methods; sea lice; bacterial and viral diseases of fish; viruses and phytoplankton blooms (M&FMB)
Glasgow, University of Institute of Biomedical and Life Sciences Dept of Civil Engineering UMBS Millport Glasgow Marine Technology Centre	work with Strathclyde on a library of natural materials, including some marine samples; Biofouling-resistant surfaces, functional biomimetics (including MAST project on antifouling), underwater sensors and reduced environmental impact of marine technologies; biodiversity, microbiology and benthic studies
Heriot Watt University Centre for Marine Biodiversity and Biotechnology, School of Life Sciences Dept of Chemistry, School of Engineering and Physical Sciences	marine biofouling, bacterial cell signalling, bioreactors and general aspects of marine biotechnology. Engaged in research aimed at the industrial and medical applications of marine bacteria and fungi. In particular interested in cell-cell signalling in marine gram-positive bacteria and its effect on the synthesis of antimicrobial compounds; production of bioactive compounds by marine fungi; chemical ecology of seaweed surface: antifouling activity of Epiphytic bacteria from intertidal and subtidal seaweeds (MBTP); Biofilm-disrupting compounds & Cell signalling system regulating antibiotic and pigment production (M&FMB); fluidisation systems; solid state fermentation; moisture in particulate systems; novel bioreactor technology; recipient of an award from the Royal Society for work on novel reactors for marine bacteria; project funding comes from EPSRC, Scottish Hospital Endowments Research Trust, BBSRC, Pfizer, SmithKline Beecham and NERC; fish diseases, vaccine development, marine bioactives as antibiotics; fish physiology, new treatments for sea lice
Napier University School of Life Sciences	Development of microbial biosensors for pollution and pollutant assessment, with prospects for commercialisation, biodiversity, plankton. Sources of funding: EU, Scottish Enterprise
Royal Botanic Garden	Diatom taxonomy, preservation of CCAP's voucher material for marine microbial strains (Marine algal characterisation and exploitation 'MACE' M&FMB with SAMS)
St Andrews, University of Gatty Marine Laboratory	Chemical and structural characterisation of invertebrate non-fouling surfaces; biofouling; planktonic barnacle larval distribution; Immune systems of crustacea; Aquapharm is a Gatty spin-out.

TABLE 6: CONT

HEI	ACTIVITIES (HISTORIC AND CURRENT)
SAMS Dunstaffnage Marine Laboratory	fjordic systems, ocean margins, measuring and modelling change using sea sensors and information technology; Chemical and structural characterisation of invertebrate non-fouling surfaces & Surface active proteoglycans from marine invertebrates (MBTP); marine bacteria as a source of novel biosurfactants and bio-emulsifiers; The Culture Collection of Algae and Protozoa (CCAP-Marine); Marine algal characterisation and exploitation 'MACE' (M&FMB); Marine malcroalgal pathogens – phylogenetic affinities (with Dept of Biology University of Konstanz Germany, CNRS-Station Biologique Roscoff France and CNRS-Université Pierre et Marie Curie Roscoff)
European Centre for Marine Biotechnology	To be opened in June 2004
Stirling, University of Dept of Biological Sciences	Diversity of diazotrophs in the Arabian Sea (microbial N2 fixation) (M&FMB)
Machrihanish Marine Environment Research Laboratory	mariculture-related research
Strathclyde, University of Strathclyde Institute for Drug Research	in collaboration with Glasgow in the PharmaLinks initiative; maintains and works on over 6,500 natural extracts in the Natural Products Library, of which a few dozen are marine from overseas

TABLE 7: MARINE BIOTECHNOLOGY RESEARCH ACTIVITIES IN HEIS IN WALES

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Aberystwyth, University of Wales Institute of Biological Sciences	cytokine resuscitation of 'unculturable' actinomycetes (M&FMB)
Bangor, University of Wales School of Ocean Sciences, Centre for Applied Oceanography, Marine Science Laboratories	microbial communities in biofilms, bioremediation, marine microalgae, reef ecology; a partner in the EU NoE Marine Genomics
Cardiff, University of Wales Cardiff School of Biosciences, Cardiff School of Earth, Ocean and Planetary Sciences	A partner in the EU NoE Marine Genomics; Isobaric *in situ* sampling and collection device, Novel molecular markers for sub-sea microbes, Isolation of unculturable bacteria & Prokaryotic ether lipids (M&FMB)
Wound Healing Research Unit, Cardiff Medicentre, Heath Park, Cardiff CF14 4UJ	Using alginate derivatives in studies of wound healing; carrying out confidential commercial developments utilising marine-origin materials
Swansea, University of Wales Singleton Park, Swansea, SA2 8PP T: 01792 205678, F: 01792 295618	Modulation of marine invertebrate larval settlement and metamorphosis by eicosanoids with Dr A. Clare (Marine Biological Association) MBTP research

TABLE 8: MARINE BIOLOGY AND BIOTECHNOLOGY ACTIVITIES IN NORTHERN IRELAND

HEI	ACTIVITIES (HISTORIC AND CURRENT)
Belfast, Queen's University School of Biology and Biochemistry, Depts of Pharmacy & Chemical Engineering	BSc in Marine Biology, PhD in Marine Biology including Molecular Ecology and Evolution, Molecular Microbiology & Marine Systems; projects in bioremediation using macroalgae and biomonitoring; Carapacics is a QUBIS spin-out in chitin products
Ulster, University of School of Biological and Environmental Sciences, Coleraine	offers Marine Science BSc (Hons) with Marine Biotechnology; has an Applied Microbiology and Biotechnology group working on bioremediation and biochemistry, stable marine-origin enzymes and physiology of marine organisms
Centre for Innovation in Biotechnology	joint venture between QUB and University of Ulster Coleraine
Department of Agriculture and Rural Development for Northern Ireland	Scientific studies on marine and freshwater fisheries and the environment

There are also organisations which, whilst their activities are not marine microbial biotechnology in a strict sense, are relevant. These include CEFAS, Essex, involved in fish health and a partner in the EU NoE Marine Genomics; the Inter-Agency Committee on Marine Science and Technology, which reports to the Office of Science & Technology (OST) on matters including support strategies; the Lairdside Maritime Centre in the Wirral, which has a land-based ship simulator that could be important for RV training; Ocean Scientific International, which provides marine services; the Proudman Oceanographic Laboratory, with coastal modelling and data provision on in-sea marine activities, and the Sir Alister Hardy Foundation for Ocean Science SAHFOS, which is a world leader in plankton-environment interaction.

The UK has 33 Public Sector research and survey vessels[14], from 'Aora' (and, appropriately in the present context, 'Aplysia') to 'Water Guardian'. Of these, 8 are capable of operating world-wide: four are Ministry of Defence vessels; two, 'Charles Darwin' and 'Discovery', are NERC Research Ship Units; and the remaining two, 'Ernest Shackleton' and 'James Clark Ross', are NERC British Antarctic Survey ships for polar sea work. These four could probably be counted as 'world-class'. The 25 other vessels work estuarine, coastal, shelf or sectoral waters around the UK, although 2 of these go further afield into the Atlantic.

A profile of other support sectors, including advanced marine engineering, wider biodiversity and ecology activities and marine vertebrate sciences, is beyond the scope of this study. It can be taken for granted that constructive interactions with these activities will be beneficial for UK marine bio[techno]logy.

[14] according to IACMST web-site

TABLE 9: UNITED KINGDOM PUBLIC SECTOR RESEARCH AND SURVEY VESSELS

ORGANISATION	N° OF VESSELS
NERC	9
Ministry of Defence	8
Environment Agency	4
CEFAS	2
Port Erin Marine Laboratory	2
SERAD	2
UMBS Millport	2
DANI (now DARD)	1
Dove Marine Laboratory	1
Southampton Oceanographic Centre	1
University of Wales Bangor	1

2.3 UK Companies

With the exception of Croda and ISP, hydrocolloid producers and users, all companies are small or even of start-up status. It has not been possible within the constraints of the project to include food companies, healthfood manufacturers or health and nutritional supplement manufacturers who might use ingredients from macroalgae or microalgae, or diagnostic or research reagent companies who might be selling marine-origin materials. Of the 21 listed below, 13 are Scottish, 7 are English and one (Carapacics) has its head office in Northern Ireland although it has a site in Ayrshire. Again, Scotland is proportionately over-represented.

TABLE 10: COMPANIES ACTIVE IN ASPECTS OF MARINE BIOTECHNOLOGY IN THE UK

COMPANY	CONTACT	SECTOR
Actinomed Ltd Newcastle	Alan Blakey; Prof Mike Goodfellow, Dr Alan Ward	A very new start-up looking at bioactives from novel marine actinomycetes; targeting antibiotic-resistant bacterial pathogens
Aquapharm Bio-Discovery Ltd European Centre for Marine Biotechnology, Dunstaffnage Marine Laboratory, Dunbeg, Oban, Argyll, PA37 1QA	Dr Andrew Mearns Spragg CEO T: 01631 559390 andrew@aquapharm.co.uk	Founded by Heriot-Watt University post-doc; has >1000 microbes in library and three candidates – AQP001, new source of astaxanthin for aquaculture feeds, APQ002, process for anti-oxidant flavonoids and APQ001, new antibiotic; gained a Smart:Scotland award in 2001 for the astaxanthin
BioDiversity Ltd Business Innovation Centre, Rm 23/24, Innova Park, Mollison Avenue, Enfield EN3 7XU	T: 020 8350 1278 F: 020 8350 1255 info@bdlabs.com	BioDiversity supplies microbial samples, fermentation biomass extracts and metabolites and has a focus on fungi, which may be relevant to marine bioactives

TABLE 10: CONT

COMPANY	CONTACT	SECTOR
Biolitec Pharma Ltd Breasclete, Isle of Lewis, HS2 9ED Western Isles (HQ Heriot-Watt Research Park, Edinburgh)	T: 01851 707500 F: 01851 621368	Originally Scotia Pharmaceutical's photodynamic anti-cancer therapy division, sold to Singapore Technologies when Scotia folded and then bought in 2002 by BioLitec AG of Germany; down-sized in 2003-2004; was researching bioactives from seaweed
Carapacics Ltd c/o QUBIS Ltd Lanyon North, The Queen's University of Belfast, University Road, Belfast BT7 1NN, Northern Ireland	Ian Scade, MD c/o T: 028 9068 2321 F: 028 9066 3015	Founded in 1999 in Northern Ireland as a spin-out from Queen's University Belfast, Carapacics has developed technologies for producing added-value chitin, chitosans, collagen and biocomposites from prawn wastes. The company began a joint venture in 2000 with a US company Ovogen to carry out similar development and commercialisation work with egg shell membrane. Carapacics has a Scottish site in Ayrshire.
Coastal & Marine Biotechnologies Ltd Tamar Science Park, 1 Davy Road, Derriford Plymouth PL6 8BX	Ian McFadzen, Director John Wedderburn, Director T: 01752 764430 F: 01752 772227 cmb@cmbiotech.co.uk	A spin-out from the Plymouth Marine Laboratory & NERC, founded in December 2001; has developed water quality assays using shellfish embryos and itself spun-out **BioVault Ltd**, a human cell and tissue cryopreservation company, on the back of its proprietary freeze-drying technology; expanding to include 'UK's and EU's first bio-repository facility'
Commercial Microbiology Ltd Kettock Lodge, Campus 2, Aberdeen Science Park, Bridge of Don, Aberdeen AB22 8GU Scotland	Stephen Maxwell, Managing Director; Alison Gardner General Manager T: 01224 706062 F: 01224 706012 info@commercialmicrobiology.com	Bioremediation: Development of biological products for odour control, oil spill clean-up, drill cutting remediation, effluent treatment
Croda International Plc Cowick Hall, Snaith, Goole, East Yorkshire DN14 9AA	T: 01405 860551 F: 01405 861767	Colloids company, originally animal-origin, now widely-sourced including marine; cosmetics formulations sold via subsidiary Sederma
Destiny Pharma Ltd Sussex Innovation Centre, Science Park Square, Falmer, Brighton, BN1 9SB	Dr Bill Love, CEO T: 01273 704 440 F: 01273 704 499 wl@destiny-pharma.demon.co.uk	Working with Prof Peter Revell (University College London-Royal Free Hospital) and Prof Andrew Lloyd (Brighton) on alginates and chitosans for tissue engineering scaffolds
Drug Discovery Ltd Royal College Building, 204 George Street, Glasgow G1 1XW	Dr Alan Harvey T: 0141 548 4534 info@drugdiscovery.co.uk	Strathclyde Institute for Drug Research's commercial arm – bioactives from marine sources, as well as other microbes and plants, specifically targeting asthma, arthritis, cancer and rejection of transplantation.

TABLE 10: CONT

COMPANY	CONTACT	SECTOR
Hebridean Biotech Ltd		A new company, set up to commercialise essential fatty acids produced in marine algae; awaiting results of an application for SMART funding, currently dormant
Integrin Advanced Biosystems Marine Resource Centre, Barcaldine, Oban, Argyll PA37 1SE Scotland	Dr. Charles Bavington charlie@integrin.co.uk, Claire Moss claire@integrin.co.uk T: 01631 720 765	Marine Natural Products: international libraries of marine extracts, screening for interesting biological activity, bioactive characterisation, delivery into pharmaceutical drug development pipelines; tests for shellfish toxins; development of new culture methods for marine invertebrate cells and for bacterial symbionts to accelerate development of bioactives
ISP Alginates (UK) Ltd Ladyburn Works, Dipple, Girvan, KA26 9JN Strathclyde	T: 01655 333000 F: 01655 333100	Major producer of alginates and other marine hydrocolloids, using mainly imported raw materials. Contributes approx. £30m turnover to Scotland's marine economy.
Laxdale Ltd Kings Park House, Laurelhill Business Park, Stirling, UK FK7 9JQ.	T: 01786 476000 F: 01786 473137	Developing treatments for central nervous system diseases such as Huntington's and Alzheimer's diseases from polyunsaturated fatty acids (PUFAs). Being acquired by US company Amarin
Marine Biotechnology Products 125 Ramsden Square, Barrow-in-Furness, Cumbria LA14 1XA		Registered at Companies House but no further information available yet
NCIMB Ltd 23 St Machar Drive, Aberdeen AB24 3RY	Ian Garner, Gordon McFarlane T: 01224 273332 F: 01224 272461 enquiries@ncimb.co.uk www.ncimb.co.uk	Commercial arm of the National Collection of Industrial, Marine and Food Bacteria, providing research and consultancy in microbiology; part-funded by BBSRC.
Novacta Biosystems Ltd Innovation Centre, University of Hertfordshire, College Lane, Hatfield, AL10 9AB	Fiona Marston, Brian Rudd, Mike Dawson T: 01707 281100 mail@novactabio.com, brian.rudd@novactabio.com	Drug discovery & development company using pathway engineering and chemistry to optimise the activity of natural products for the treatment of infectious diseases; though not exclusively focused on marine biotechnology, marine organisms are one source of compounds for the company.
Plymouth Marine Applications Prospect Place, The Hoe, Plymouth PL1 3DH	Carole Llewellyn T: 01752 633 100 F: 01752 633 101	Commercial arm of Plymouth Marine Laboratory; currently working on characterisation and exploitation of marine chlorophylls and carotenoids (Small Business Research Initiative)
Remedios Limited MacRobert Building, 581 King Street, Aberdeen AB24 5UA	Ian George Managing Director T: 01224 274255 F: 01224 274256 www.remedios.uk.com	Use of marine microbial *lux* gene as basis for land contamination sensor and remediation monitor; spin-out from University of Aberdeen

TABLE 10: CONT

COMPANY	CONTACT	SECTOR
SAMS Research Services Ltd Dunstaffnage Marine Laboratory, Oban, Argyll, PA34 4AS	Prof Graham Shimmield T: 01631 559000 F: 01631 559001	Provides all the commercial services (including billing) for Scottish Association of Marine Sciences' (SAMS) scientific activities.
SEAS Ltd c/o Dunstaffnage Marine Laboratory, Oban, Argyll, PA34 4AS	Mr J Blackstock T: 01631 566877 F: 01631 564124 seas@wpo.nerc.ac.uk	Private consultancy and research company based at Dunstaffnage Marine Laboratory, specialising in analysis of marine benthic samples, polychaete taxonomy, benthic community structure and adaptive responses to stress; recently absorbed into SAMS Research Services Ltd.
X-Gnat Labs Limited Unit 11, Beta Centre, Stirling Innovation Park, Stirling FK9 4NF	T: 01786.442006 F: 01786.442006	X-Gnat specialises in insect and organism repellents, based on environmentally friendly materials; involvement in marine biotech is through being a partner with Grant Burgess of HWU on a project to develop an anti-fouling paint using marine microbial extracts.

Note: Plymouth Marine Laboratories is about to spin out two new companies[15], so that this number may change. Two companies are profiled below, since they illustrate the combination of public and private funding that is assisting start-ups in this area. The strategies of both companies are similar: to establish one stream of activity that is income-generating (contract work in shellfish toxin analysis for Integrin and in rapid screening for Aquapharm) whilst investigating novel bioactives from proprietary collections of marine microbes.

2.4 UK Infrastructure

Research Councils

The most active Research Council in UK is NERC (National Environmental Research Council), which supports the Centre for Coastal and Marine Services (Proudman Research Laboratory and the Marine Laboratories at Plymouth and Dunstaffnage), the Sea Mammal Research Unit, Southampton Oceanography Centre and activities at other institutions. Marine biotechnology and resource exploitation *per se* form a relatively small part of overall marine research expenditure. NERC's total budget was approx. £42 million in 1998-9. NERC's total support of marine sciences increased from 2002 to 2003, with terrestrial, freshwater and marine science and technology gaining at the expense of earth and atmospheric sciences.

NERC's Marine and Freshwater Microbial Biodiversity (M&FMB) programme is the most important and influential research activity with relevance for biotechnology. It underpins the strengths of the UK in marine microbiology, culture collections, research on microbial diversity and biofouling and its prevention. NERC has allocated £6.98 million to the M&FMB programme for 2000-2005 and 27 projects have been approved to date.

15 pers. comm. D Robins 2004

The M&FMB programme began life as a marine-only co-operative programme led by Ian Joint of Plymouth Marine Laboratory. Later, NERC funded expansion of the programme to include freshwater studies. The biotechnology component of the programme has been slow to emerge but has been assisted greatly by the decision to appoint a Technology Translator, Dr Dave Woodwark, to assist in bringing M&FMB-funded research to the attention of the commercial user community. These efforts are currently ongoing.

Three themes are emerging as being further along the commercialisation track than others and these are:

- Marine viruses.
- Biofilms and cell-cell signalling.
- Marine natural products from novel actinomycetes.

NERC is in discussions with the BBSRC to look at an expanded programme of cross-research-council funding of marine biotechnology, also involving the DTI if appropriate. The United States has a similar marine microbial diversity programme (Microbial Observatories), funded by the NSF, and some communication between the programmes has taken place, catalysed by the M&FMB science co-ordinator Phil Williamson of the University of East Anglia.

The NERC M&FMB programme's awards for 2004 concentrate on demonstration-type projects of £25-30,000 each, lasting 6-15 months:

TABLE 11: TT PROJECTS IN NERC'S M&FMB PROGRAMME 2004

PROJECT	PARTNERS
Characterisation of novel methyl bromide degrading bacteria and assessment of their potential as biocatalysts	University of Warwick, Department of Biological Sciences Plymouth Marine Laboratory
Biofilm disrupting compounds from marine bacteria	Heriot-Watt University, Department of Biological Sciences & School of Engineering and Physical Sciences
Determining the exploitation potential of novel algal virus enzymes	Marine Biological Association, Plymouth
Natural product screening on a chip in streptomycetes – linking taxonomy to function	University of Newcastle-upon-Tyne, Agricultural and Environmental Science
Diversity of novel, technologically useful, pigment-producing diatoms in estuaries of South Devon, UK	University of Plymouth, School of Environmental Sciences University of York, Department of Chemistry
Natural products from marine actinomycetes and bacteria that attract and kill Ulva (Enteromorpha) zoospores	Plymouth Marine Laboratory University of Nottingham, School of Pharmaceutical Sciences
Marine Algal Characterisation and Exploitation (MACE)	SAMS, Dunstaffnage Marine Laboratory, Culture Collection of Algae and Protozoa Royal Botanic Garden Edinburgh

NERC's Marine Biofouling thematic programme[16] ran from 1996 to 1999 and focussed on mechanisms of fouling in the marine environment. The total budget for this programme was £1.17m. It was a stated objective that basic research would be funded but commercial and technical development of antifouling coatings would not be tackled as part of the programme. Market size and regulatory hurdles are the current bottlenecks in this field but significant scientific advances were made which might have allowed the UK to compete in this arena, had the opportunities been grasped. Important projects within the programme included studies on the settlement and fouling caused by barnacles, bacteria and algae, corrosion of steel in seawater, and chemicals that prevent fouling by invertebrates.

There appear to be opportunities for marine biotechnology to take part in the NERC's Environmental Genomics programme and the cross-Research Council programme on the UK Energy Research Centre, if appropriate proposals can be constructed.

TABLE 12: NERC FUNDING OF MARINE SCIENCE ACTIVITIES 2002 & 2003

SUPPORT CATEGORY	NERC FUNDING BY CATEGORY AND YEAR	
	2002	2003
Research grants for marine science and technology	£11.7 m	£13.5 m
Other research funding	£7.4 m	£13.5 m
Studentships and fellowships	£19.8 m	£20.4 m
Total spend	£99.8 m	£103.4 m

Note: funding rounded up or down to nearest decimal place

TABLE 13: NOTABLE 2002-2003 GRANTS AND SUPPORT FROM NERC FOR MARINE BIOTECH-RELATED ACTIVITIES

INSTITUTION	PROGRAMME	FUNDING
SAMS	overall programmes and infrastructure (within this, for CCAP: £109,000	£2,235,000
Plymouth Marine Laboratory	support and infrastructure	£5,980,000
British Antarctic Survey	'Antarctic Biodiversity past, present and future'	£340,000
SBRI	environmental genomics and marine microbial diversity	£216,000
National Marine Biological Laboratory		£270,000
Marine Biology Association	grants and infrastructure support	£770,000
Southampton Oceanographic Centre	Platform and Sensor Technologies for Marine Sciences	£628,000
	AquaGene programme	£62,000

16 see www.nerc.ac.uk/funding/thematics/mbiof & www.biosciences.bham.ac.uk/external/biofoulnet

EPSRC provides some funding for marine biotechnology activities: examples include:

- New routes to total synthesis of bioactives at University of Cambridge.
- A project on nanoscale sensors for genomic and proteomic analysis inside the living cell, co-ordinated by the Natural Sciences Dept at the University of Newcastle.
- A project on conotoxin mimics involving peptide synthesis, based on the Chemistry Dept at the University of Reading.
- A network of relevance to marine biofilms, Surface Science of Biologically Important Interfaces, co-ordinated by the Eastman Dental Institute, London, which finished in December 2003.

EPSRC also funded the Marine Bioprocess Engineering Network, based jointly at Heriot-Watt University and University of Sheffield, which ran from 2000-March 2004.

A Follow-on-Fund, jointly supported by BBSRC, NERC and EPSRC, was announced in 2003 that allows an individual to spin out based on research council-funded projects. The deadline for the pilot call for this was 30th January 2004. The total for the programme is £1.5m, typically for grants of £25,000 to £50,000, maximum of £100,000, over a 12-24 month period. It is not yet known how many applications managed to get submitted in the rather short deadline and how much has been committed of the overall funds. The KTP (Knowledge Transfer Partnership) programme is still available, for collaborations between academic and industrial researchers, and the SBRI (Small Business Research Initiative) portal to sources of government funding for commercial development of R&D is also accessible. NERC has used SBRI for demonstration projects arising from M&FMB programme work.

Capital expenditure can pose a problem, especially if each site for marine biotechnology research in UK wishes to establish bioprocessing or advanced analytical laboratories. The UK’s Science Research Investment Fund (SRIF), to which HEFCE and the Wellcome Trust have contributed, provided an opportunity for creating physical infrastructure for science and technology. This joint initiative by OST and the Department for Education and Skills (DfES) was announced in July 2000 with a second round in December 2002. It remains to be seen whether there will be another round; if so, then this will be an opportunity for marine biotechnology.

Support Societies, Associations and other Organisations

The most relevant societies, associations and other organisations that support or are actively involved in marine biotechnology are:

The Society for Underwater Technology SUT is an international organisation based in London and Aberdeen that is almost 40 years old. Although its main focus is on underwater technology, ocean science and offshore engineering, SUT has a remit for marine biology and marine resource exploitations. Its Ocean Resources Committee has responsibility for SUT’s activities in the identification, exploration and exploitation of marine and sub-floor living, non-living and energy resources. SUT has as one of its major aims the encouragement of cross-fertilisation and dissemination of ideas, experience and information between workers in academic research, applied research and technology, industry and government. Its role as a recognised interdisciplinary forum in the UK should be built on in carrying out any strategy for marine resource utilisation.

Examples of initiatives it supports include development of techniques and tools to explore, study and exploit the oceans; submersible design and operation; subsea systems; marine resource exploitation; oceanography; environmental studies; pollution management; and marine biology.

The Scottish Association for Marine Science SAMS[17] was founded as the Scottish Marine Station in 1884 and is a membership organisation with over 500 corporates, individuals and students as well as members of the public. Research interests are extensive and not confined to Scotland, including ecology and behaviour of marine life, impact of artificial reefs, deep-sea coral dynamics, marine biodiversity, mariculture, marine algae, CCAP and biosurfactants. SAMS is in the long Scottish tradition of independent research organisations, exemplified by the Moredun Institute, and has a similar mission of training and education. SAMS took over the Ardtoe research station of Seafish on November 1st 2003. Interactions with marine biotechnology and fish research may come from one of the activities that will continue at Ardtoe, of early-stage fish nutrition. SAMS is collaborating with The Deep, a sub-ocean aquarium in Hull, to work on *Lophelia pertusa*, the predominant hard coral of the North Atlantic mounds.

The Marine Biological Association of the United Kingdom MBA[18] was founded in 1883 as a charity with the aim of promoting scientific research into all aspects of life in the sea, including the environment on which it depends, and to disseminate to the public the knowledge gained. It has about 1200 professional marine biologist members world-wide and encourages visiting scientists to take part in its research programmes. The MBA's Plymouth Laboratory was opened in 1888. MBA was transferred to NERC in 1965 and, in 1988, MBA's environmental work was merged with the NERC Institute for Marine Environmental Research to form the Plymouth Marine Laboratory PML. Collaborative work is common.

MBA's current research areas include Ecology, Biology of invertebrates, Cellular and molecular processes in plants and algae, Phytoplankton productivity and dynamics, and Phytoplankton/virus interactions. The MBA is a member of the Plymouth Marine Sciences Partnership, along with the Plymouth Marine Laboratory, the University of Plymouth, the Sir Alister Hardy Foundation for Ocean Science SAHFOS and the National Marine Aquarium.

The Plymouth Marine Laboratory PML was a collaborative centre of NERC and became an independent charity in April 2002. It now includes a trading subsidiary to assist in exploitation and work with industry. It is widely involved in EU collaborative projects and in the NERC programmes, and is also a centre of expertise in advanced marine engineering for ecological and diversity studies.

So far, there is little or no marine biotechnology-oriented activity or interest from societies, associations and trade bodies working in potential end-use sectors; this

17 see www.sams.ac.uk

18 see www.mba.ac.uk

suggests that part of a development strategy will be to increase contacts, discussion and networking with these. IMarEST, the Institute of Marine Engineering, Science and Technology in London (until recently the Institute of Marine Engineers), is still focused on engineering-associated technologies.

Networks and industry groups

There are a number of networks and industry groups that are relevant to building a strategy for marine biotechnology at local, regional and national level. These include:

- England:
  - the UK BioIndustry Association
  - the Plymouth Marine Science Partnership
  - ERBI (Eastern Region Biotechnology Initiative)
  - the White Rose Consortium
  - BioApproaches South West
- Scotland:
  - Nexxus, which has replaced the Ayrshire and Glasgow bioscience networks, to cover the south-eastern parts of Glasgow, Lanarkshire, Renfrewshire, Dunbartonshire and Ayrshire
  - BIA Scotland
  - BioDundee
  - the Edinburgh Bio-Alliance
  - MDIS (Medical Device Industry Scotland)
  - the Scottish Biomedical Foundation
  - the Scottish Subsea Technology group
- Wales:
  - There is no specific network – approaches would be made to WDA
- Northern Ireland:
  - BioNorthern Ireland exists to create an Ulster biotechnology community

The Marine Bioprocess Engineering Network has now finished. It was based at Heriot Watt University and was managed by Dr Grant Burgess. Equivalent activities in other industrial sectors are embedded in the Faraday Partnerships.

A Centre for Process Innovation has been established as part of the North-East's techno-economic development programme, at Wilton, Cleveland. This could be of value as a collaborator for embedding new biocatalysis in industry. The EPSRC-funded UK Centre of Excellence in Biocatalysis is another potential source of technology translation.

Again, the new DTI Knowledge Transfer Networks Programme provides a good opportunity for marine biotechnology interests to come together and build a shared understanding of the commercial potential of R&D in this area, and what avenues are worth following up.

2.5 The UK Regions – Balance or Imbalance?

We identified 33 HEIs and organisations in England, 10 in Scotland, 4 in Wales and 2 in Northern Ireland that are involved in some aspects of marine biotechnology and its support. The IACMST identified 24 departments and/or HEIs in marine biology, 10 in marine ecology, 5 in marine biofouling and 3 in marine biotechnology (Heriot-Watt, Newcastle and Bangor – see **Appendix 8**, taken from IACMST's website). Of the 24 individual HEIs identified, 15 were English, 8 Scottish and 2 Welsh.

There are 10 sites that we believe can be defined as pre-eminent in marine biotechnology:

- Aberdeen
- Heriot-Watt
- Marine Biological Association Plymouth
- Newcastle
- Plymouth Marine Laboratory
- European Centre for Marine Biotechnology at SAMS as it comes on-stream later in 2004
- Birmingham
- Essex
- Glasgow
- the Gatty Marine Laboratory at St Andrews

5 of these are in Scotland (50% of Scotland's establishments) and 5 are in England (15% of England's). This imbalance should tell us immediately about pre-eminence of one region, Scotland, over the others.

The Marine Science Strategy for Scotland identifies Aberdeen, St Andrews, Dundee and the Deep Sea Benthic group at SAMS as leaders in marine biology and Heriot-Watt and the forthcoming ECMB as leaders in Marine Biotechnology *per se*. Genomics and genotyping of marine biota at Edinburgh can also be mentioned[19].

However, this analysis does not take account the effects of involvement in NERC's M&FMB programme and EU projects and NoEs on establishments in England, Wales and Northern Ireland – suggesting that regular nation-wide benchmarking of perceived excellence may be of value in deciding on relative regional strategic progress.

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19 see *Marine Science in Scotland, a Strategy for developing its potential*, Feb 2004, for HEI and SE

The distribution of companies involved in marine biotechnology exploitation and services round the UK

In Chapter 3.3, we identified 21 companies active in exploiting some aspect of marine bio[techno]logy or serving the sector in some way. Of these, 13 are based in Scotland, one (Carapacics) is based in Northern Ireland but has a facility in Scotland, and 7 are based in England. Scotland is strongly represented in this list. Only two companies (Croda and ISP Alginates) are large, and they manufacture alginates and industrial products from marine sources.

- England:
  - Actinomed Ltd, Newcastle
  - BioDiversity Ltd, Enfield
  - Coastal & Marine Biotechnologies Ltd, Plymouth
  - Croda International Plc, Goole
  - Destiny Pharma Ltd, Brighton
  - Marine Biotechnology Products, Barrow-in-Furness (dormant)
  - Novacta Biosystems Ltd, Hatfield
- Scotland:
  - Aquapharm Bio-Discovery Ltd , Roslin
  - biolitec Pharma Ltd, Isle of Lewis
  - Commercial Microbiology Ltd, Aberdeen
  - Drug Discovery Ltd, Glasgow
  - Hebridean Biotech Ltd, Hebrides
  - Integrin Advanced Biosystems, Oban
  - ISP Alginates (UK) Ltd, Girvan
  - Laxdale Ltd, Stirling
  - NCIMB Ltd, Aberdeen
  - Remedios Ltd, Aberdeen
  - SAMS Research Services Ltd, Oban
  - SEAS Ltd (now merged with SAMS)
  - X-Gnat Labs Limited, Stirling
- Wales:
  - none identified
- Northern Ireland:
  - Carapacics Ltd, c/o QUBIS Belfast (also in Scotland)

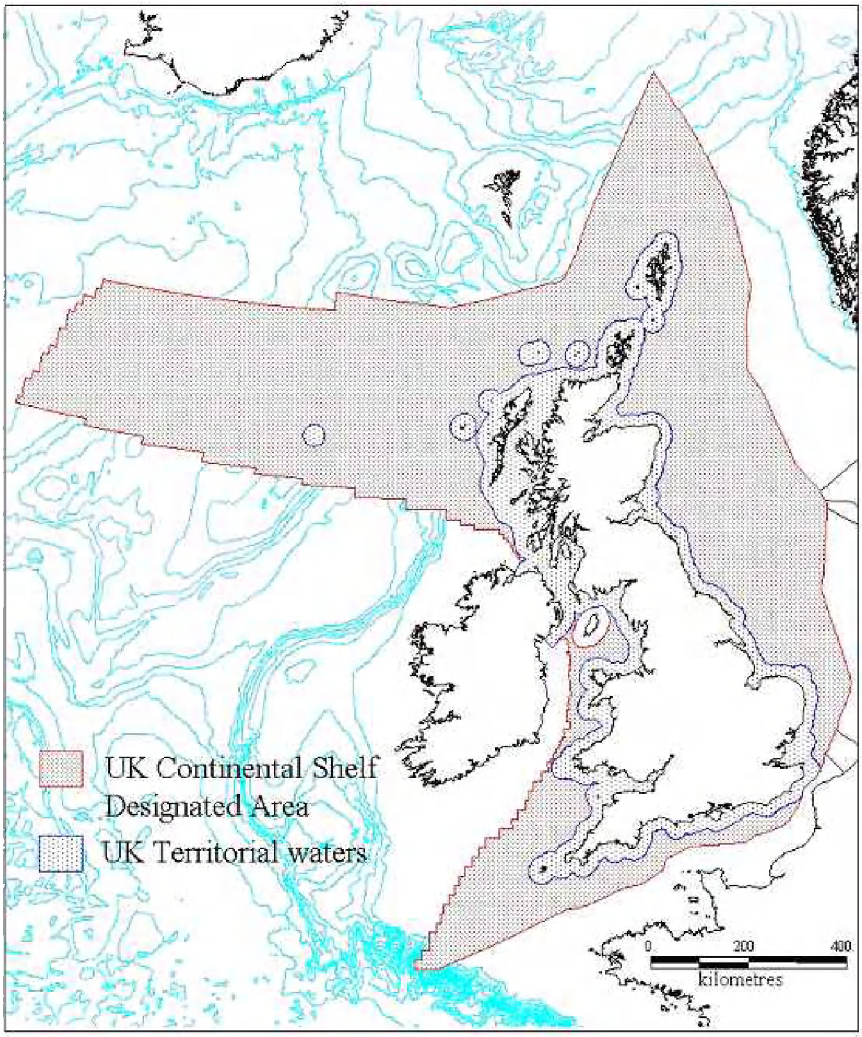
It will be noted that there is little association with recognised marine bioscience or biotechnology 'clusters' in companies based in England (only CMB Ltd in Plymouth). In Scotland, 7 are in island or coastal environments, with no real economic clustering, although Aberdeen has three companies. The others are associated with inland Universities or Innovation Parks. The two largest companies are sited close to ports for access to import-export flow. On the basis of economic development so far, it could be argued that access to research development expertise, investment sources and tailored start-up accommodation is more important for commercialising marine biotechnology than favouring a specific regional and cluster-building round coastal centres of marine biosciences. This may pose a conflict between the drivers for economic development of marine and coastal areas and the natural environment of market forces encouraging start-ups to establish and grow.

Access to the seas and oceans

The UK shares access to the North Atlantic with the Republic of Ireland and Iceland, and the North Sea with Sweden, the Netherlands, Denmark and Germany. Ireland provides a barrier to immediate westward access and the Atlantic oceanic 'fin-print' of the UK is therefore somewhat irregular, with considerably further extent north of Ireland than south – see **Figure 1**.

In terms of logistics of access, and the fact that Scotland's share of the UK's Economic Exclusion Zone is 63% of the total area, one would expect Scotland to have a larger influence and impact on Atlantic marine research, bioprospecting and biotechnology-based exploitation than England or Wales, and for matters of the sea to have a correspondingly larger profile on the radar-screens of economic and policy development organisations in Scotland. As far as we can tell, Northern Ireland is not well-represented in marine biotechnology.

FIGURE 1: UK'S TERRITORIAL WATERS AND DESIGNATED AREA OF CONTINENTAL SHELF



source: Joint Nature Conservation Committee web-site – Background to Special Areas of Conservation Selection, www.jncc.gov.uk 2004, with acknowledgement.

Differentials in support

Scottish Enterprise is strongly supportive of marine-based economic development and there is a good focus on marine biotechnology, especially from Highlands & Islands Enterprise – of the 5 winners of HIE's 2002/03 Research Challenge Fund prizes, 3 were for companies working in marine biotechnology, biolitec Pharma, Integrin Advanced Biosystems and SAMS. Biolitec's project concerned pharmaceutical compounds from a commercially-cultivated macroalga; Integrin's was on Bioprospecting in the marine environment, creating a library of characterised extracts from Scottish marine animals to be made commercially available to pharmaceutical companies, as well as used for internal research programmes; the SAMS project concerned novel biosurfactants from naturally occurring marine bacteria. The most recent strategic study, finished in early 2004, very strongly supports further development of marine biotechnology in Scotland[20].

SEEDA (South East) and SWRDA (South West) have both commissioned work looking at marine science and economic development. These have mainly concerned general activities, of which leisure boating, marine engineering and associated services form the largest sector. Marine biosciences and marine biotechnology have been given minor attention with one exception: the City of Plymouth commissioned a feasibility study in April 2003 for a marine science and technology cluster in Plymouth[21]. This included biotechnology in its assessment. It highlighted approx. £21 million in revenue to Plymouth from science and technology activity, of which the Plymouth Marine Laboratory contributed 40%, about £8 million, and the Marine Biology Laboratory contributed a further £2.5 million. Marine Biotechnology and biosciences is thus a strong contributor to the Plymouth region, providing strengths in coastal and off-shore shelf work. Southampton Oceanography Centre's focus on deep-water sciences makes it less of a nucleus for a marine biotechnology initiative, more an important and complementary partner to Portsmouth's activity.

SEEDA commissioned a report on the South East Marine Sector in April 2003[22]. Research and development and New Technologies were included in this overview. 10 or 11 companies (unidentified in the report) classed themselves as being involved in marine biotechnology. The report suggests a value to the UK of marine biotechnology of approx. £3 million by 2004 (p21 of report). The South East's biotechnology *per se* is not seen as strong in the market; relative strengths in biomolecular science, plankton science, marine chemistry and ecotoxicology give it an overall rating of '*well-positioned, possibly requiring further development*'. By contrast, fishing, aquaculture, marine science education and training are seen as strongly positioned. A lack of significant active exploitation was, however, noted.

In SWRDA's case, the activities in Plymouth give some basis on which to build a marine biotechnology activity, that will also bring in other aspects of marine industry. BioApproaches South West is an organisation funded by SWRDA to develop a Regional Strategy for the biotechnology sector in the South West of England, organise networking for SMEs within and outside the South West, support graduate development for technical, research and managerial staff and promote the sector in general, including career opportunities in biotechnology. Part of its remit includes marine biotechnology.

SWRDA and Marine SouthWest commissioned a report on skills needs in the south west of England in July 2003[23]. The report is useful in confirming that traditional marine business sectors are declining and that most businesses are SMEs, even in the equipment and service provider sectors, which make up 75% of

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20 *Marine Science in Scotland, A Strategy for developing its potential*, HIE and SE Feb 2004

21 *Feasibility Study for the Development of a Marine science and technology (MST) cluster in Plymouth*, GHK and British Maritime Technology April 2003, for the City of Plymouth

22 *South East Marine Sector: Business Issues, Prospects for Clustering. The Research Report*, A Mair April 2003, for South East Marine Task Force and South East England Development Agency

23 *Skills Needs of the Marine & Maritime Sector in the South West of England, Final Report*, J Beer, K Meethan, J Grant and A Mair July 2003, for SWRDA and Marine SouthWest

the employment. There is no specific or useful focus on marine biotechnology in this report, and it is hardly surprising that most of the gaps noted are in relatively basic business skills such as IT and customer-care, or the mandatory skills of safety and first aid, and not the higher degree of training needed to sustain a buoyant science-based business. However, the concept was put forward of a Networked Centre of Excellence for Marine & Maritime Training. Since a network of colleges of Cornwall already exists, this could be grafted onto that and then some use made of it to train eligible local people in the skills necessary for marine biotechnology.

Invest Northern Ireland has responsibilities for business growth as well as inward investment in Northern Ireland, but there is little or no mention of biotechnology business building in Invest Northern Ireland's plans and no mention at all of the potential of marine biotechnology, underlining the low profile of this activity in Northern Ireland. The Welsh Development Agency is responsible for activities in Wales and there seems a similar low level of recognition of marine biotechnology as an economic driver.

3. PROSPECTS FOR THE OUTPUTS OF MARINE BIOTECHNOLOGY – PRODUCTS, MARKETS, FUTURES

3.1 Introduction

A recent report[24] estimated the 2002 market for marine biotechnology products and processes as $2.4 billion, of which one-third was in the USA, and projected growth of about 9% p.a. 2002-2007.

TABLE 14: PRODUCTS FROM MARINE BIOTECHNOLOGY, ESTIMATES OF WORLD MARKETS[25]

REGION	YEAR AND MARKET US$ MILLIONS					AVERAGE
	1999	2000	2001	2002	2007	ANNUAL ↑
USA	555	626	719	804	1010	4.7%
rest of world	1329	1416	1519	1634	2230	6.4%
total	1884	2043	2229	2438	3240	5.9%

A further breakdown (**Table 15**) shows that the proposed components of this market are certainly of marine origin, either being processed raw materials or originally derived from marine organisms. However, the output of new biotechnology is not included; the remainder of this section looks at the potential markets in which advanced processing, production and biotechnologies could be applied to marine-origin molecules and materials. As such, it must be taken as conjectural, though possible.

TABLE 15: LEADING MARINE-ORIGIN PRODUCTS[26]

PRODUCTS	SALES EST. 2002 $M	SALES EST. 2007 $M
salmon calcitonin	800	1290
Ara-A	100	93
Ara-C	100	93
astaxanthin	6	40
petroleum emulsifier/surfactant	3	4
pseudopterosin	1	1.5
chitin/chitosan	625	655
carrageenan	319	422
alginates	257	285
agarose	178	175
docosahexaenoic acid	16	100
hydroxyapatite	15	15

[24] *Biomaterials from Marine Sources*, Business Communications Company Inc Report No. RC-184R, February 2003, $3800-$4500 depending on source; this report has not been purchased for this work because of the cost.

[25] source Business Communications Company Inc 2003

[26] approx. figures, based on *ibid.* page 37

This market looks substantial but in context is tiny – the value of the ship-related, leisure-boating, port services, naval-related and energy-related sectors, estimated at over £700 billion world-wide, dwarfs it.[27]

For the UK, the Marine Science and Technology Inter-Agency Committee's recent estimate of the contribution of the marine and maritime sector to the economy in 1999-2000 is £39 billion, almost 5% of GDP[28]. About one-third came from tourism, and much of the remainder was marine engineering-related. Marine biosciences, biotechnology and marine resource-utilisation scarcely appear and the difficulty of providing an estimate for this is underlined by the diversity of products and services that would make up this sector. A more optimistic estimate of world-wide potential of UK marine biotechnology activities of £2.0-2.6 billion has been provided, subject to development of added-value products and sufficient financial support to achieve exploitation[29]. This market could evolve from £0.5 billion in 1999 to £1.5 billion by 2004[30]. In contrast, established mariculture of edible produce contributed £14.7 billion in 1999 to the aquaculture total of £27.7 billion, 10-fold greater than the foreseen potential of marine biotechnology.

The potential products of marine biotechnology seem boundless and indeed there is progress and success in the development of bioactives for medical and cosmetic use. By 1995, 30 bioactives from USA Sea Grant-funded research had reached clinical trials and the market potential for the first five was estimated at $2 billion[31].

Pseudopterosin, one of the early wave of developed bioactives had, by 1995, brought in royalties of more than $1.2 million to the University of California and cosmeceutical products containing the anti-inflammatory molecule had sales estimates of $100 million per annum. The relationship between the sales of pseudopterosin (see **Table 15**) and the sales of the final cosmetic product give some ideas of the relative value of an active ingredient in such products.

A summary of potential applications is given in **Table 16** below, based on current industry commentaries. The breadth of applications suggests that what is required for fruitful development and commercialisation of the products of UK marine bio[techno]logy is focus and a cross-industry/academic network, to establish for the scientific researchers and developers what, from industry's viewpoint, are the most-needed developments.

The following section focuses on some opportunities within these areas:

- marine products as raw materials
- food, including health foods and nutraceuticals
- cosmetics

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27 *UK Marine Industries World Export Market Potential*, Institute of Marine Engineers (on behalf of Marine Fore*sight* Panel 2000, ISBN 1-902536-38-X p7; in addition, the ocean technologies sectors are estimated to be worth Can$1.5 trillion world-wide (www.nati.net)

28 IACMST web-site www.marine.gov.uk/jottings.htm

29 *UK Marine Industries World Export Market Potential* p10

30 *ibid.* p86

31 US NOAA's proposal for more significant funding of marine biotechnology

- pharmaceuticals
- medical devices and biomaterials
- regenerative medicine
- diagnostics
- research tools
- agriculture
- industrial uses
- environmental management
- bioengineering

TABLE 16: POTENTIAL APPLICATIONS OF THE PRODUCTS OF MARINE BIOTECHNOLOGY

SECTOR	POTENTIAL CONTRIBUTIONS
FOODS	• new colorants, anti-oxidants, texturing agents, preservatives • enzymes for food processing • edible coatings for foods • functional foods for general healthy lifestyles
NUTRACEUTICALS	• specific targets – e.g. heart, joints, osteoporosis • calcium products and other trace elements • anti-oxidants, astaxanthin, carotenoids • marine organisms as probiotics
MEDICINE	• pain management products • anti-inflammatory agents • anti-infectives • growth factors • hormones • anti-viral agents • anti-cancer agents
HEALTHCARE	• biomaterials, including biopolymers and bioceramics • novel adhesives • biocompatible anti-adhesion coatings for vascular devices • anti-fouling agents for implants and catheters • components of medical devices • encapsulating drug delivery systems
COSMETICS	• collagens • anti-oxidants and sunscreens • revitalisers and anti-ageing products
RESEARCH TOOLS	• reagents including enzymes • bioactive molecules for growth media • new tools for discovery and testing • libraries of organisms and extracts • model organisms for safety and toxicity tests • marker genes and gene products for molecular biology research

TABLE 16: CONT

SECTOR	POTENTIAL CONTRIBUTIONS
PROCESSING TECHNOLOGIES	• extremophile management • improved bioreactor technology • improved purification methods and reagents
NEW ENERGY SOURCES	• light-capture • microbial batteries • energy-rich oils • hydrogen-producers
AGRICULTURAL	• seed coatings • pesticides, such as toxin from nereid worms or insecticide from sponges • additives, proteins and oils as animal feed ingredients • probiotic organisms in aquaculture • new vaccines and disease control in aquaculture
INDUSTRIAL	• novel adhesives • foams for oil industry and other surfactants • non-polluting metal extraction • anti-fouling materials • polymers for general use, thickeners and coatings for textiles and paper • new enzymes for chemical, food, household and other industries • ceramic materials • organisms and wastes as feedstock for biotech and chemical processes • nanotechnological developments
FOOD SAFETY	• diagnostics for toxins in seafood • materials for preserving and decontaminating foods and feeds
ENVIRONMENT ENHANCEMENT	• pollutant and toxin detection and removal by biocatalysis or digestion • desalination • metal removal and retrieval from soils, water and mining • marine phage viricides for use in microbial films

3.2 Marine Products as Raw Materials

Marine products are well-established in many sectors of industrial activity, mainly food, healthcare and agriculture. The three primary groups of product are seaweeds and their constituents, chitin and chitosans from crustacean shells, and vitamins, colorants and lipids from microalgae.

Seaweeds[32]

Seaweeds, marine macroalgae or macrophytic algae, are used in food, as natural products, ingredients or food additives, and for other industrial uses including pharmaceutical, healthcare and research reagents. They include three types, brown, red and green. The commonest species are given in the table below.

[32] based on *The State of World Fisheries and Aquaculture*, The Food and Agriculture Organisation of the United Nations, Rome 2002, ISBN 92-5-104842-8

The production of farmed seaweed reached 10 million tonnes in 2000, a 50% increase over 1995, representing about 90% of all traded supplies. China is the largest producer, although its farmed output has diversified over the past 25 years, from a reliance on *Laminaria japonica* (Japanese kelp), *Porphyra tenera* (purple laver or nori) and some mussel culture to a broader mix of shellfish and prawns. Most of the seaweeds are used domestically in China, Korea and Japan, but there is also considerable trading between the markets in East Asia and import, especially of red seaweeds, into USA and the EU from countries such as the Philippines, Tanzania and Indonesia. The total EU imports of seaweed were 61,000 tonnes in 2000. Unlike the situation with global freshwater culture, where almost 98% of output is finfish, in mariculture, molluscs and seaweeds contribute about 45% each to the output. Seaweed farming is an attractive prospect in many parts of the world – in warmer waters, a phaeophycean such as Brown Kelp can increase its length by 50 cm a day. European producers sell most types of edible seaweed (see **Table 18**). Most of the product sold in the UK comes from Brittany or Scotland "as it relies upon particularly clean water"[33].

TABLE 17: COMMONEST TRADED SPECIES OF SEAWEED

BROWN SEAWEEDS	*Phaeophyceae*	kelps (*Laminaria* of North Europe and Japan, *Macrocystis* , *Durvillea*), wakame (*Undaria*), *Cladosiphon*
RED SEAWEEDS	*Rhodophyceae*	*Phyllophora, Gracilaria, Chondrus crispus* (Carragheenan*), Gigartina, Iridaea, Porphyra* (Laver, nori*)*, *Gelidiella*, *Gelidiopsis*, *Gelidium*, *Gracilaria*
GREEN SEAWEEDS	*Chlorophyceae*	*Ulva (Enteromorpha) pertusa* (Sea Lettuce)

TABLE 18: MAJOR WHOLESALE SOURCES OF EDIBLE SEAWEEDS AND COASTAL PLANTS IN EUROPE[34]

COUNTRY	SEAWEED OR SEA PLANT SPECIES
FRANCE	dulse, nori (*Porphyra*), sea lettuce (*Ulva pertusa*), wakame (*Undaria*)
IRELAND	carragheenan (*Chondrus crispus*), dulse, kombu, riseach, sloke, wakame
THE NETHERLANDS	Haricot de Mer, red sea cabbage, sea lavender, sea lettuce, *Salicornia*
SPAIN	'various'
UK	dulse, Haricot de Mer, kombu, laver/nori, sea lettuce, wakame

Seaweeds are a source of three very important hydrocolloids used across many of the market sectors that are included in this report, agar (agar agar), alginates and carrageenan. Agar, which contains agarose and agaropectin, is produced by processing of the Rhodophyacean seaweeds *Gelidium sesquipedale*, *Gracilaria* spp. and *Pterocladia*. Alginates, composed of polyguluronate and polymannuronate, are produced by *Laminaria* spp., *Ascophyllum* and *Durvillea*.

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33 *The fishproduce deskbook 2004,* fishproduce Journal 2003, ISBN 0-9539851-4-8 pp 385-386

34 *ibid.*

Alginates are also produced as high-performance products – NovaMatrix[35], the Norway-based new division of FMC BioPolymers, sells pure sodium alginate at $55/gram, and freeze-dried sterile sodium alginate for pharmaceutical formulations at $340/gram. These alginates are also used in bead encapsulation processes for cells, for research, drug delivery and tissue engineering. NovaMatrix sells equipment for preparing alginate solution in microbead form, at prices of $1100 or $9100 depending on the type.

TABLE 19: SEAWEEDS USED FOR AGAR AND AGAROSE[36]

GENUS	SPECIES	SOURCES
Phillophoraceae	*Ahnfeltia spp*	Sakhalin Russia
Gelidiaceae	*Pterocladia spp* *Gelidium amansii* *G. sesquipedale* *G. japonicum* *G. cartilagineum* *G. nudifrons* *G. spinulosum* *G. pristoides*	Azores & Mediterranean Japan Morocco & Spain Japan South Africa California Morocco Madagascar
Gracilariaceae	*Gracilaria verrucosa & G. confervoides* *G. foliifera & G. cornea* *G. chilensis* *G. bursa-pastoris* *Gracilariopsis chorda* *G. estedtii* *Acanthopeltis japonica* *Gelidiella acerosa* *G. edulis* *Gelidiopsis rigida*	Italy USA Chile Hawai'i Japan Florida Japan Japan India Indonesia

Margins seem rather tight in the marine hydrocolloids food ingredients sector and a certain amount of corporate condensation is going on. This year, Danisco will be completing the purchase of Rhodia's food ingredient business, for approx. € 250-300 million; though Rhodia made an operating profit of € 250 million in 2002, it made a loss of almost € 160 million in 2003.

Chitin and chitosans; glycosaminoglycans

Chitin and chitosans are already widely used in a wide range of market sectors, including health (especially wound-healing), food, food packaging, healthfoods, flocculation of impurities in liquids, antifungal and soil conditioner in agriculture. The higher-volume low-value uses are in agriculture, higher-value in medical devices, and high-volume, high-value in health and food supplements. Because

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35 see www.novamatrix.biz

36 source: B&V srl, Gattatico Italy

chitosans can be sprayed onto surfaces, they are also used as edible moisture-retaining coatings for fruit, foods and meat, as a means of removing egg yolk from processed egg white, and have been investigated as carcass surface antimicrobial sprays in abattoirs.

Chitosan and chitin can act as chelators and as reservoir materials for slow release; chitosan has been used in the diet as a cholesterol-lowering agent and, because they also sequester heavy metal ions, they are being used as treatments in humans exposed to long-term background radiation (for example, from Chernobyl). Other healthcare uses are growing, including wound healing, tissue engineering and tissue repair, and local delivery of cells, drugs, proteins, genes, and other therapeutics. Currently, nasal delivery technology with chitosan shows great potential, with several applications in phase III clinical trials. Ultrapure chitosan for intranasal drug delivery and other medical uses is produced by NovaMatrix in Norway from crustacean exoskeleton and is sold at $40/gram.

Glucosamine is a further derivative of chitosan. Chondroitin is also a health supplement, recommended for skin and joints, which can come from a marine source, in this case processed sea cucumbers. Sales of chondroitin, glucosamine and chitosan based products in US alone were $250 million in 1996, rising to $2.4 billion in 2000 as a result of their heavy promotion as nutritional supplements.

Products from microalgae

The most attractive products from microalgae are PUFAs, beta-carotenoids and surfactants. PUFAs and pigments have a combined global market of >several $ billions per year – astaxanthins are approx. $200 million per year.

The current market for surfactants is >4 x 10^6 tonnes pa. Surfactants from microalgal sources are produced not by the algae themselves but by their symbiotic micro-organisms, giving rise to the possibility that surfactants can be produced in bioreactors, either by the micro-organisms if culturable or by gene cluster transfer into a conventional fermentation organism. Manipulation of energy and hydrocarbon sources during fermentation leads to changes in the output. Currently, the cost is too high compared with conventional petrochemicals but their safety and environmental profile is better and much more structural diversity is possible than from petrochemicals[37]. SAMS is leading R&D of microalgal surfactants in UK.

Marine-origin oils have also been used in water-repellent and impermeable paints.

Products from marine invertebrates

A number of products extracted from marine invertebrates have applications or potential. The most famous of these is Limulus Amoebocyte Lysate, from *Limulus* horseshoe crabs, which gels when mixed with bacterial endotoxins and has been extensively used in quality control as the LAL test for bacteria-derived human and veterinary products, including biopharmaceuticals and vaccines. More recently, great interest has been roused in marine biotechnology potential as a result of the development of ziconotide, a synthetic analogue of the *Conus* neurotoxin, as a

[37] based on a presentation by Dr Jo Oliver at CORDIA Dec 2003 Vienna

treatment for severe pain. As noted previously, shells from shrimps, prawns, lobsters and crabs are used as a source of chitin, chitosan and chitosan derivatives including glycosaminoglycan products.

In addition to ziconotide, there are a number of antibacterial peptides that have been extracted from marine invertebrates:

TABLE 20: PEPTIDES FROM MARINE INVERTEBRATES

PEPTIDE	SOURCE
bactenecin-like	shore crab haemolymph (similar to bovine neutrophil bactenecin)
mytilin	mussel haemolymph
pleurocidin	*Pseudopleuronectes americanus* winter flounder skin
polyphemusin	*Limulus* haemocytes
protamine	salmon and herring sperm – as the sulphate, used medically as a heparin antagonist but can produce fatal immune reactions; also used as a laboratory reagent
tachyplesin	*Carcinoscorpius* and *Tachypleus* Southeast Asian horseshoe crab haemolymph – a toll-like receptor protein

3.3 Food

Food additives

Seaweed-derived additives are widely used in foods – agar, carrageenan, alginates are commonplace in a wide range of products. Enzymes are already used for a variety of purposes including removal of membranes and skin, production of liquid proteins and fractionated fish oils, flavour enhancement and fermentation aids. They are also used as components of freshness and toxin-monitoring tests. Enzymes from marine sources could be used for these purposes, utilising their stability under a range of difficult processing environments. Crustacean extracts are also used as flavouring in foods and animal feed.

Fresh and processed foods

Marine products are already well-established in the food sector, particularly gelling and forming agents derived from seaweeds, including agar, alginates and carrageenan. All three materials find their way into food products – one interesting use of alginates is in the ‘pimento’ pieces in stuffed olives, several hundred tonnes a year – but they are also used in healthfoods and for technical uses, such as coating.

The rise in sales of reduced fat, reduced sugar, reduced calorie and health-image foods opens an added-value opportunity in conventional foods and food additives for the products of marine biotechnology. Given the current concerns about plummeting stock of wild finfish and residue levels in farmed fish, there is an opportunity for products from other marine organisms such as microalgae and seaweeds, provided that analysis shows these to be inherently free of pollutants or natural toxins.

Bread baked with fish oil is palatable as long as the oils have been encapsulated, as produced by an EU consortium (FAIR contract No. CT-95-0085) or by researchers at the University of Uppsala Sweden in 1999 and more recently at the University of Guelph, Canada[38], and Food Science Australia, who micro-encapsulated tuna fish oil and won a prize for it in 2003. This has since been commercialised in bread[39], yoghurt drinks, processed meat products and infant formulae[40]. Since fish-origin PUFAs come from marine microbes in the fish diets, such as thraustochytrids, then there should be the potential for using algal oils or fatty acids instead.

There is clearly potential for soya flours to be replaced by marine-origin flours, high in protein and essential fatty acids, provided that controlled and safe production of microalgal biomass and equivalent oxidation stability can be achieved. Food sectors in which the products of marine organisms might be used include fish and fish products; breads, cakes and cereals; and dairy, oils and fats. Marine-origin protein may also provide an alternative to meat. New colorants, anti-oxidants, preservatives and novel flavours from marine sources are possibilities. In many ways, the potential added-value applications of marine products in food come close to the functional food and nutraceutical categories, but we believe there is still a market for marine products as food ingredients.

Other current trends in food and eating include more snacking and grazing, more convenience foods, organic foods, healthy and vitamin-enriched food for the elderly, added value presentations and character merchandising. In UK, breakfast cereals and in particular cereal bars are seen as high-growth areas, together estimated at £3.14 billion in 2001 rising to £4.59 billion by 2006, 9% of the total estimated £51 billion market. There should be some potential for use of marine organisms and their extracts as ‘healthy lifestyle’ and ‘natural’ ingredients for such foods. These developments seem likelier to be higher-valued, and to move towards functional food and nutraceutical sectors.

[38] see http://www.uoguelph.ca/mediarel/archives/003925.html

[39] for example, in a collaboration between the British bakery Warburtons and Australian company Nu-Mega Ingredients, a loaf enriched with microencapsulated docosahexenoic acid from tuna oil was launched in 2003

[40] see http://www.dfst.csiro.au/foodfacts11.pdf

TABLE 21: MARKET SECTORS FOOD UK, RELEVANT TO PRODUCTS OF MARINE BIOTECHNOLOGY[41]

CATEGORY	YEAR & SALES IN £ BILLION (10^9)					COMMENTS
	1997	2001	2002	2005 est.	2006 est.	
FISH AND FISH PRODUCTS	1.95	2.26	2.33	2.48	2.57	marine products easiest to establish in processed fish sector – as feed additives or as novel foods
BREADS, CAKES, CEREALS	7.71	8.96	9.33	9.97	10.18	marine products as humectants, protein and oil ingredients, whole organisms
DAIRY, EGGS, OILS, FATS	8.03	9.89	9.14	9.66	9.76	marine organisms as probiotics, sources of EFAs

Health Foods, Diet Foods and Nutraceuticals

Products in the first category are sold mainly through pharmacies and healthfood shops, occasionally through food retailers. Products in the second and third categories are expanding, driven by their availability through supermarkets as well as in more specialist stores.

There is an increasingly blurred distinction between nutraceuticals and functional foods, indeed it is difficult to compare market reports from different sources because of this (see tables below). This is one of the most exciting 'clusters' in the food sector, including probiotic products, sports drinks and foods, cholesterol-reducing foods and drinks such as fortified milks, fortified fruit drinks and plant-extract preparations.

Vitamin and mineral supplements, which are regarded more as 'health' products than functional or nutraceutical, include products containing ω-3 fatty acids, enzymes, fibre-enriched products and concentrated plant and animal-source products, including algae and fish oils. One successful export from Ireland is calcined seaweed, which is sold by Marigot as an aid in prevention and treatment of osteoporosis.

In the UK, the most promising sectors include functional drinks, probiotic drinks and foods, sports products and organic baked goods and multi-ingredient products. The prominent companies in this market in UK are Holland and Barrett (owned by the US company NBTY) and Seven Seas (owned by Merck GmbH).

These sectors are now affected by the EU's Food Supplements Directive, with a grace period until July 2005 for submission of information dossiers, and a draft Directive on Sports Nutritional Products ('foods intended to meet the expenditure of intense muscular effort').

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41 Source: *The UK Industry Food Market Review*, ed. D Fenn, Key Note Ltd (2002), ISBN 1-84168-394-9

TABLE 22: MARKET SECTORS HEALTHFOODS & DIET FOODS UK, RELEVANT TO PRODUCTS OF MARINE BIOTECH

CATEGORY	DATE	ESTIMATE	SOURCE
Overall market for healthfoods of which:	2002 2006	£2.08 billion £3.37 billion	Key Note[42]
Organic food	2002 2006	£0.92 billion £1.96 billion	
Functional foods	2002 2006	£0.58 billion £0.71 billion	
Vitamin and mineral supplements	2002 2006	£0.39 billion £0.42 billion	
Overall market for diet foods	2000	£5.39 billion	Key Note[43]

The single most interesting development in conventional foods is the rise of the functional drink, especially that built on dairy and/or probiotic organisms. The major players in this sector are the French company Danone, whose Actimel® sold $509 million world-wide in 2002, from group total sales of $14.4 billion, a good result considering that 90% of the company's turnover in the Asian markets comes from bottled water, and the Japanese company Yakult, 86% of whose $1.7 billion sales come from foods and drinks[44] and whose main Yakult® probiotic drink sells over 600,000 bottles a day in Europe[45].

TABLE 23: MARKET SECTORS GLOBAL NUTRACEUTICALS[46]

CATEGORY	DATE	ESTIMATE
Overall market for nutraceuticals of which:	2001 2002 2007	$9.82 billion $10.87 billion $17.35 billion
Dairy	2001	$4.2 billion (40%)
Soft drinks	2001	$2.7 billion
Bakery/cereals	2001	$2.7 billion
Confectionery	2001	$1.0 billion
Snacks	2001	$0.3 billion
regional split of total Japan	2002	$4.1 billion
Europe	2002	$2.83 billion
USA	2002	$2.55 billion
rest of Asia-Pacific	2002	$0.9 billion

42 *The Key Note Market Report 2003: Healthfoods Plus*, ed. R Tambe, Key Note Ltd (2003), ISBN 1-84168-534-8

43 *Diet and Fat-free foods market assessment 2001*, ed. S Taylor, Key Note (2001), ISBN 1-86111-379-9

44 *Global Nutraceuticals*, Datamonitor August 2003, Report No 0199-0759

45 *Europe Nutraceuticals*, Datamonitor 2002

46 *Global Nutraceuticals*, Datamonitor 2003

These products are intended to have a direct impact on health, through a specific mechanism. The Japanese market is the most advanced, with three health targets for functional foods and nutraceuticals in Japan, cardiovascular, with 60% of the $4.1 billion country market, and gastrointestinal health and lipoprotein management, with just over 7.5% each. In Europe, with a total market of about $2.8 billion, dairy and baked goods are the most important sectors overall, with 46% and 27% of the market respectively[11].

It seems quite realistic to explore the use of UK marine algae and other organisms and marine extracts as ingredients of such functional foods and drinks.

Health foods, health supplements and nutraceuticals from marine sources; 'healthy image' food products

Algae are already available as health foods, including *Dunaliella* as a source of carotenoids and *Spirulina*. The US company Martek sells algal fatty acids/oils in baby food formulae.

Products from the sea may be able to capitalise on an image of 'organic' and 'natural'. Current concerns may make this task a little less easy: the UK Food Standards Agency suspects that high levels of β-carotene in the diet may increase the risk of cancer in smokers and those exposed to asbestos, there are general concerns about trace elements such as zinc and manganese[47], and there have been scares in 1999 and in 2003/4 about dioxin and PCB levels in wild-caught oily fish and in farmed salmon that may also raise doubts about the levels of undesirable materials in algae (in addition to toxins).

There may be a rôle for marine-sourced foods and food ingredients in the sectors of fat-reduced and calorie-reduced foods. There is tremendous growth in this market, driven by the realisation that western populations are becoming more obese and developing disorders such as heart disease, arthritis and Type II Diabetes at an earlier age and with greater frequency. Use of marine-origin ingredients can capitalise on existing uses in health and nutritional supplements. The commonest health supplements from marine sources are glucosamine from crustacean-shell chitosan, extract of green-lipped mussels from New Zealand and carotenoids such as astaxanthin from microalgal culture.

As noted before, sales of products containing chondroitin, glucosamine or chitosan in US alone were $250 million in 1996. The US market for human and pet supplements containing glucosamine, chondroitin or methylsulfonylmethane had reached $790 million in 2002. Chondroitin is mainly derived from bovine cartilage, with some from sea cucumber, and MSM is wholly-synthetic. However, chitosan and glucosamine are all of marine origin and represent a significant added-value use of what would otherwise be waste.

Astaxanthin from marine sources is being marketed as an anti-inflammatory and anti-oxidant, potentially protective against retinal deterioration, diseases caused by inflammation-mediated vascular problems such as heart attacks, providing general support of the immune system and protecting against cancer, all effects apparently observed *in vitro* and in laboratory animals. Mera Pharmaceuticals and Cyanotech

[47] Report by the FSA's Expert group on Vitamins and Minerals in May 2003

of Hawai'i are two of the largest producers of microalgal astaxanthin from *Haematococcus*, a freshwater alga, taking advantage of Hawai'i's sunshine and warmth to grow the algae in photobioreactors. Microalgal astaxanthin, in pure form for health supplement use, is priced at more than $100,000 per kilogram at retail. It is easy to see why this market could be attractive for UK marine produce.

The animal health market is also of increasing interest, partly driven by the over-regulation of conventional therapeutic products. A standardised extract of green-lipped mussels, *Perna canaliculata* from New Zealand, is sold by Pfizer Animal Health as 'VMP Mobil' into the pet and horse markets in Germany. This consists of freeze-dried mussels containing 12% glycosaminoglycans plus marine-origin PUFAs, for musculo-skeletal problems. Green-lipped mussel material is also sold in Brazil by the French pet-food company Royal Canin in their 'Mobility Support' supplement. Glucosamine and glycosaminoglycans are available over-the-counter as food supplements for pets, to aid arthritis.

Food safety and remediation, Food packaging and preservation

There is a market for rapid assays for detection of toxins in fish and shellfish, e.g. saxitoxin, as have been developed by the Australian company ToxiTech, a spin-out from AIMS, or okadaic acid, the cause of shellfish vomiting and weakness, as developed by the Scottish company Integrin, which also tests seafood for other algal toxins.

There is also an increasing need for biodegradable packaging, which marine-origin materials can fulfil. Chitin and chitosans are already used in food packaging when gas and moisture barriers are required. However, they have to compete with plant-origin materials such as starches and celluloses, into which government and EU support has already gone in attempts to develop new products for traditional agriculture.

Chitosan-cellulose and polycaprolactone are combined as a bilaminate to produce a modified-atmosphere packaging for fresh produce such as lettuce, broccoli, cabbage, tomatoes and berries. Alginates and carrageenan are used as edible coatings on meats, frozen fish and prawns and cooked pizza bases as moisture barriers and retainers, antioxidants, antimicrobial agents, oil barriers, mechanical protectors and component adhesives, and alginates are used as edible coatings on mushrooms to prevent drying out and shrinkage[48].

3.4 Cosmetics and Cosmeceuticals

The cosmetics market is an important one. Although skin care is not the largest sector of this, the growing interest in cosmetic-based skin protectants and repairing agents and concerns about the impact of sunshine on skin cancers mean that companies active in this sector are looking for new functional ingredients. The cosmetics market is worth more than £110 billion per year, about 21% in USA,

48 *Biobased Packaging Materials for the Food Industry, Status and Perspectives* Report of an EU Concerted Action project, Ed. Weber CJ Dept of Dairy and Food Science, Royal Veterinary and Agricultural University Copenhagen, November 2000 ISBN 87-90504-07-0

30% in Europe, 10% in Japan. The major segments are hair care, skin care and colour cosmetics, accounting for about 54% of the total.[49]

Seaweeds already provide many ingredients used in cosmetics formulation:

TABLE 24: UTILISATION OF MACROALGAL MATERIALS IN COSMETICS

INGREDIENT	USE
agar	thickener and emollient
algal polysaccharides	humectants
alginates	skin moisturiser for elasticity, thickener, emulsifier, stabiliser
alginic acid	gelatiniser
algisium complex	anti-inflammatory agent
fucoidans	stimulate circulation
fucosterol	emollient, blood stimulant, diuretic and moisturiser
kelp	health tonic, skin soother, source of iodine
polyphenols	anti septic, anti-inflammatory and anti-oxidant
seaweed	face-masks and body wraps, thickening agent for lotions, nutritional supplement for skin health

Marine-origin sodium alginates and chitosans can be used as micro-encapsulators for active ingredients (including pharmaceutical products) and, in the case of chitosan, provide some stabilising and anti-oxidant activities that are of interest in new-wave cosmeceuticals.

The prospects are also very interesting, in the context of this project, for bioactives as cosmetic and cosmeceutical ingredients. In addition to novel bioactives from marine invertebrates and their associated microbes, there are anti-oxidants and other compounds from seaweeds including fucoidans and carrageenan.

Examples of commercialised products include a liposome-based product from the US company AGI Dermatics, containing a photolyase from the blue-green alga *Anacystis nidulans*. Pseudopterosin, the anti-inflammatory extracted from the sea-fan *Pseudopterogorgia elisabethae*, has already been mentioned as the active ingredient in Estée Lauder skin lotions. By 1995, the licensing of pseudopterosin for use in cosmetics had brought cumulative royalties of more than $1.2 million to the University of California. Further significant income will accrue if prescription anti-inflammatories and dermatological products containing methopterosin, an analogue of pseudopterosin, are successfully launched. Laboratoires Codif, based in St Malo France, makes algal extracts from microalgae and from seaweeds, including Dermochlorella®, an extract of *Chlorella vulgaris*, which is described as 'protein-rich', high in alanine, glycine and proline, stimulating collagen synthesis by 250% and inhibiting enzymic destruction of collagen and elastin. Another product, Phycosaccharides® from *Laminaria digitata*, is a skin penetrant and is used to treat acne and ageing skin.

[49] source www.elke.gr, the Hellenic Centre for Investment

AIMS in Australia has been investigating the Coenzyme-Q cycling in marine bacteria that are exposed to high levels of UV light due to the sun. By understanding the regulation of the process, they hope to develop products that could be useful in fighting the adverse effects of sun exposure and of ageing on human skin. A number of candidates have been isolated, several of which belong to the family of mycosporine-like amino-acids (MAAs). AIMS has had, or is still working with, a number of collaborators to commercialise this, including ICI Australia (until 1992), the Japanese companies Shiseido and Toyo Suisan Kaisha, and Pan Australia Labs and the Heart Research Institute of Australia.

3.5 Pharmaceuticals

In 1999, 20 of the best-selling non-protein human medicines were natural products, natural product-derived (synthetic or semi-synthetic analogues). Combined sales of these products exceeded $16 billion[50]. According to the authors of the report on Antarctic bioprospecting[51], annual sales derived from traditional knowledge using genetic resources are $3 billion for the cosmetics and personal care industry, $20 billion for the botanical medicine sector and $75 billion for the pharmaceutical industry. More than 60 percent of the cancer drugs approved by the US Food and Drug Administration are of natural origin or are modelled on natural products. Accordingly this sector would seem a naturally-attractive target for marine biotechnology.

The pharmaceuticals and biotechnology sectors

The human pharmaceutical products market is enormous, which is what makes it so attractive. The Top 20 companies sold over £160 billion-worth of products in 2001[52]. The single largest sector of medicines is antibacterials, estimated at $25 billion, projected to grow to $32 billion by 2010[53]. The market for non-antibiotic prescription medicines is dominated by four sectors – autoimmune-inflammatory conditions, depression, hypertension and cancer. The world market for autoimmune and inflammatory conditions is estimated at over $17 billion (2004); that for antidepressants about the same ($17 billion in 2002), with five products each contributing more than $1 billion in sales[54]. The anti-cancer sector, estimated at $15 billion, includes several products that are, in fact, 'blockbusters' – Taxol® is one such, with sales of more than $1 billion a year. In the cancer sector, almost half of the products are cytotoxic agents, the class into which almost all anti-cancer marine bioactives fall. The value of the active ingredients used in all medicines is estimated at $50 billion, 15-16% of the total price of the product.

Because of the issues of low yield and unsustainable harvesting, it is vital to develop alternative methods of production of marine bioactives, either by synthesising them or their analogues, totally or semi-synthetically, in which case

50 A Harvey, *Drug Discovery Today*, Vol 5 No 7 July 2000

51 *The International Regime for Bioprospecting, Existing Policies and Emerging Issues for Antarctica* UNU/IAS Report August 2003

52 see http://www.abpi.org.uk/statistics

53 figure extracted from Quorex web-site www.quorex.com

54 *Antidepressants world prescription drug markets*, Theta Report #1234 December 2003, PJB Publications

the output enters the conventional pharmaceuticals channels, or by cloning and transferring the relevant genes to bioreactor-tolerant organisms, in which case the products are biopharmaceuticals and would tend to be handled by biotechnology companies.

US Biotechnology company sales in 2001 reached about US$21 billion, approx 15% of the total prescription medicines market of $141 billion[55]. Revenues of European biotechnology companies exceeded €13 billion in 2002[56], including approx €8 billion for human biopharmaceuticals, €4.5 billion for service providers and €1 billion for diagnostics[57]. In Japan, an overall biotechnology market worth 1.33 trillion ¥ (appr. €10 billion) can be compared with a pharmaceuticals market worth 6.7 trillion ¥ (approx. €50 billion) in 2001.

There are many sectors of the pharmaceutical and biopharmaceutical markets that could be targets for marine-derived products:

The management of neuropathic pain is an important and growing sector to which a marine-origin bioactive is already contributing. Ziconotide, derived from the cone shell venom, is regarded as particularly exciting in this sector, which in the US alone is expected to grow from $430m in 2002 to $800m by 2007 and $1.25b by 2012). This is because an increasing number of acute and chronic syndromes are now recognised as caused by aberrant nervous activity, including back pain, complex regional pain syndrome, phantom limb syndrome, post-herpetic neuralgia, trigeminal neuralgia and the neuropathies of diabetes and AIDS.

Approx 5-8%, of the $20b market for management of urinary incontinence is contributed by drugs for prevention and management; the remainder is internal and external devices and other products. With newer agents acting on the smooth muscle and on the nervous control of urination, the projection for drug-related management is >$11 billion by 2008.

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[55] *Healthcare Industry Market Update, Pharmaceuticals*, Centers for Medicare and Medicaid Services Jan 2003

[56] *Endurance: The European Biotechnology Report 2003*, Ernst & Young 2003

[57] *Surviving Uncertainty: The Pan European Mediscience Review 2002*, Deloitte & Touche 2002

TABLE 25: ESTIMATES FOR SOME MEDICAL SECTORS

CONDITION	MARKET	COMMENTS
Sepsis	$5 billion worth of healthcare costs per annum in the US alone[58]	products that can more effectively disarm the organisms causing this, or reduce and reverse the effects of endotoxic shock and multiple organ failure, will be very attractive
Neuropathic pain	in US alone, $430m in 2002 to $800m by 2007 and $1.25b by 2012)[59]	ziconotide, derived from the cone shell venom, is already being developed
NSAID market	world-wide of about $10 billion	anti-inflammatories and mild-to-moderate pain
Urinary incontinence	$1.0b, 5-8%, of a total $20b market	projection for drug-related management is >$11 billion by 2008; marine-origin products could be active in both these sectors, as bioactives with neuromuscular effect or as biomaterials for implantable devices
Gout	over US$2 billion each year	Lytone Enterprise, a Taiwanese company launching a product made from deep-sea fish peptides
Erectile dysfunction	estimated at >$2 billion for 2003, projected to $6-7 billion by 2009	vasoactive compounds, nitrogen oxide producers and other molecules appear effective

Marine-origin products could be active in both these sectors, as bioactives with neuromuscular effect or as biomaterials for implantable devices. Even the management of a disease as apparently trivial as gout has a large market, estimated at over US$2 billion each year by Lytone Enterprise, a Taiwanese company launching a product into this sector made from deep-sea fish peptides.

On the research front, and underlying the pathogenesis of several important groups of human and animal diseases, are two fundamental cellular and cell-cell signalling processes – apoptosis and angiogenesis. Molecules that control these processes have tremendous potential in the management of cancers, chronic inflammatory diseases, and our responses to body damage and acute infections. It is clear already that many bioactives obtained from marine invertebrates and/or symbiotic or free-living microbes have a strong effect on cells and, doubtless, they will also have effects on apoptosis and angiogenesis. Extracts of shark cartilage are known to be anti-angiogenic and are being explored by a number of companies for their medical applications.

Because of the strongly cytotoxic activities of many bioactives, cancer treatment is a very strong focus for much development. Although most bioactives appear to be produced by symbionts and other microbes, the Universities of Oxford and Newcastle were working some years ago on cyclin dependent kinases from starfish eggs, which interfere with cell division in humans.

[58] see www.theratase.com web-site

[59] *Neuropathic Pain*, EP Publications, WWMR Inc, www.WWMR.com

TABLE 26: ESTIMATE OF WORLD MARKET FOR APOPTOSIS-RELATED PRODUCTS, 1999-2005[60]

PRODUCT TYPE	SALES ($ MILLIONS)	
	1999	2005
Diagnostics and laboratory research materials	11	19
Cancer	0	350
CNS and neurodegenerative	0	80
Cardiovascular	0	80
total	11	529

TABLE 27: MARKET ESTIMATES FOR ANGIOGENESIS MODULATORS[61]

SECTOR	YEAR AND ESTIMATED SALES IN $ MILLION				
	2003	2004	2005	2006	2007
Total of which:	100	115	575	1,225	2,975
anti-cancer (AI)	-	-	120	300	800
dermatology (AI)	-	-	100	240	650
cardiovascular disease (AS)	-	-	100	200	500
diseases of back of the eye (AI)	-	-	60	120	400
arthritis (immune and damage) (AI)	-	-	50	175	375
advanced wound care (AS)	100	115	145	190	250

notes: AI = angiogenesis inhibitors, AS = angiogenesis stimulators

In the anti-cancer field, other chemotherapeutics are the focus of attention, including epothilones, which are fermentation products that are similar to taxol but are easier to administer, have fewer side effects and are effective against taxol-resistant tumours. There may be potential here for novel marine-derived epothilones or new enzymes that can reduce production costs and generate new semi-synthetic analogues.

Bioactives as pharmaceuticals

Marine products have a substantial history of medical use in the 20th century, as alginates and other biopolymers in dressings and devices for wound-healing. Efforts in exploitation of bioactives as pharmaceutical products are more recent, accelerating over the past 40 years since the discovery and application of the adenine arabinosides A and C (Ara-A and Ara-C) as antiviral and anticancer agents, respectively. Ara-A and Ara-C were isolated from *Cryptotethya crypta*, a Caribbean sponge. Ara-A (vidarabine) was synthesised and later produced by fermentation of *Streptomyces griseus*. Ara-A has also been isolated from a

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60 *Apoptosis: New Growth Opportunities*, Business Communications Co Inc July 2000

61 Theta Report '*Angiogenesis inhibitors & Stimulators*' PJB Publications 2002

Mediterranean gorgonian *Eunicella cavolini*. Ara-C (arabinosyl cytosine or Cytosar-U™ - PharmaciaUpjohn) is now synthesised.

In Europe, the most notable company in this area is PharmaMar SA of Spain. Since most bioactives have shown remarkable cytostatic and cytotoxic effects, the main route for commercialisation has been as anti-cancer drugs. However, their effects on angiogenesis and apoptosis have potential for the management of inflammation and long-term degenerative conditions.

One challenge facing marine biologists and chemists is that too many novel compounds can be isolated from marine invertebrates, marine symbionts and free-living micro-organisms. Producing a list of all those mentioned in the literature would be a monumental task and is beyond the scope of this project, though a partial list is given in **Table 28** below. It is, however, a suitable target for a web database, especially if information on sources, activities, commercial developers, development stages and holders of Intellectual Property Rights is included. A number of disparate databases are available, including Harvard's ChemBank[62], the Unesco-IOC Register of Marine Organisms, maintained by the National Museum of Natural History, Leiden, the Netherlands[63] and the European Register of Marine Species ERMS, maintained at the University of Southampton[64].

TABLE 28: SOME MARINE COMPOUNDS UNDER DEVELOPMENT AND IN USE[65]

COMPOUND	SOURCE	TYPE OF SOURCE	TARGET	STATUS	DEVELOPMENT
antibiotics	*Ruegeria*	bacterium – Wadden Sea, Germany	bacteria, algae, nematodes		Universities of Oldenburg and Göttingen
antibiotics	*Cerastoderma, Macoma and Nereis*	Baltic Sea invertebrates	*Micrococcus luteus* as model		University of Greifswald
antioxidants	*Acremonium roseogriseum*	marine fungus	antioxidants		University of Bonn
Aplidin™ aplidine	*Aplidium albicans*	tunicate – Mediterranean	cancer	natural	I/II PharmaMar
aplyronine-A	*Aplysia kurodai*	sea hare – Japan	cancer	natural	pre-clin
Ara-A	*Cryptotethya crypta*	sponge – Caribbean	antiviral	synthetic	
Ara-C	*Cryptotethya crypta*	sponge – Caribbean	anticancer	synthetic	commercial

62 see http://chembank.med.harvard.edu/bioactives/

63 see http://www2.eti.uva.nl/database/urmo/default.html

64 see http://erms.biol.soton.ac.uk/

65 *'The Potential for the Marine Biotechnology Industry'* Shirley Pomponi, Harbor Branch OI see http://www.oceanservice.noaa.gov/websites/retiredsites/natdia_pdf/17pomponi.pdf; *Marine Organisms as a source of new anticancer agents* Gilberto Schwartsmann *et al.* The Lancet Oncology Vol 2 April 2001 pp 221-226; *Natural products in anticancer therapy* AB da Rocha *et al.* Current Opinion in Pharmacology 2001, 1:364-369; *Book of Abstracts natural products from marine micro-organisms* ESMB International Symposium, Greifswald Germany June 19-22 2002; further extensive lists are given in *Blaue Biotechnologie: Stand und Perspektiven der marinen Naturstoffe*, Technologiestiftung Schleswig-Holstein June 2003 pp33-34, 37-38

TABLE 28: CONT

COMPOUND	SOURCE	TYPE OF SOURCE	TARGET	STATUS	DEVELOPMENT
ascosalipyrrolidinones	*Ascochyta salicornia*	*Ulva*-associated fungus	antibiotics		University of Bonn
aurantosides	*Manihinia conferta & Siliquariaspongia japonica*	New Zealand & Japan	antifungals		
avarol, avarone	*Dysidea avara*	sponge – Mediterranean	anti-inflammatory for psoriasis	natural	KliniPharm
bengamide	*Jaspis*	sponge	cancer	synthetic analogue	Novartis clinical trials
bryostatin 1	*Bugula neritina*	bryozoan	cancer	natural	II
collagen	*Chondrosia reniformis*	sponge	replacing animal collagen, drug delivery	natural (farmed)	KliniPharm
contignasterol	*Petrosia contignata*	sponge	inflammation	natural	
cryptophycins	*Nostoc spp*	cyanobacterium land and marine (Hawai'I)	antifungal, anti-cancer	now synthetic	II
depsipeptide (NSC 630176, FR901228)	*Chromobacterium violaceum*	bacterium	cancer		I – Fujisawa Company
didemnin B	*Trididemnum solidum*	tunicate – Caribbean	cancer	natural	II withdrawn
discodermolide	*Discodermia dissoluta*	deep-water sponge – Bahamas	cancer from Harbor Branch	now synthetic	Novartis & Kosan studying
dolastatin 10	*Dolabella auricularia*	sea hare – Indian Ocean	cancer	natural	II
ecteinascidin 743 (ET-743)	*Ecteinascidia turbinata*	tunicate – Caribbean	soft tissue sarcomas	natural	II/III, PharmaMar
ES-285	*Spisula polynyma*	clam – North Atlantic			PharmaMar pre-clin
girolline	*Pseudaxinyssa cantharella*	sponge	cancer		Aventis evaluating
granulatimide	*Didemnum granulatum*	tunicate – Brazil	cancer	now synthetic	
GTS-21	*Amphiporus lactifloreus*	marine worm	CNS diseases	natural	I
halichondrin B	*Halichondria okadai*	sponge – Okinawa	cancer	now synthetic	pre-clin
halomon	*Portieria hornemannii*	red seaweed – Philippines	cancer		
hamacanthin	*Rhaphisia lacazei*	sponge – Mediterranean	cancer	natural	
hemiasterlins A & B	*Cymbastella*	sponge	cancer		Wyeth Ayerst early clin
IPL 576,092	*Petrosia contignata*	sponge	inflammation, skin, eye, asthma	synthetic contignasterol	I Aventis Pharma and Inflazyme

TABLE 28: CONT

COMPOUND	SOURCE	TYPE OF SOURCE	TARGET	STATUS	DEVELOPMENT
isohalochondrin B	*Lissodendoryx* spp	sponge	anti-cancer	synthetic analogue	PharmaMar pre-clin
kahalalide	*Elysia rufescens*	sea slug – Hawai'I	cancer		I PharmaMar
KRN7000	*Agelas mauritianus*	sponge	cancer	synthetic derivative	I Kirin Brewery Co Japan
lomaiviticins	*Micromonospora spp*	symbiont of *Polysyncraton lithostrotum* ascidian	cancer	natural	from Wyeth research
LU103793	*Dolabella auricularia*	sea hare	cancer	synthetic dolastatin	II
makaluvamine	*Smenospongia aurea*	sponge – Jamaica	cancer	natural	
manoalide	*Luffariella variabilis*	sponge – Pacific	research reagent	natural	AG Scientific
methopterosin	*Pseudopterogorgia elisabethae*	soft coral – sea fan	inflammation , woundhealin g	semi-synthetic analogue	I
mycaperoxide B	*Mycale spp*	sponge-Thailand	cancer		
namenamicin	*Micromonospora spp*	symbiont of *Polysyncraton lithostrotum* ascidian	cancer	natural	from Wyeth research
parahigginols	*Parahigginsia*	sponge – Taiwan	cytotoxic	natural	
pseudopterosin	*Pseudopterogorgia elisabethae*	soft coral – sea fan	inflammation , cosmetics	natural	commercial
sesquiterpenoids	*Drechslera dematioidea*	*Liagora*-associated fungus	antimicrobial , antiplasmodi al		University of Bonn
spiroxins	*fungus from soft coral*		cytotoxins		from Wyeth research
squalamine lactate	*Squalus acanthias*	shark	cancer	now synthetic	II
staurosporine	*Eudistoma toealensis*	tunicate – Micronesia	cytotoxic agent, research reagent	natural	pre-I
thiocoraline	Micromonospora marina	actinomycete – Mozambique	cancer		PharmaMar pre-clin
topsentin	Rhaphisia lacazei	sponge – Mediterranean	cancer	natural	
ziconotide (ziconitide, SNX-111)	Conus magus	mollusc – cone snail	pain	synthetic analogue of ω-conotoxin	III+ – élan, Pfizer/WL, Medtronic

More importantly, investigating all these molecules is impossible. AIMS, for example, is screening over 13,000 of the extracts from its Biodiversity Collection against *E. coli*, *Staphylococcus aureus* and *Mycobacterium smegmatis* (a model for other mycobacteria). This challenge is in fact a driver for new developments in isolation, identification, characterisation and biological screening techniques. Biological screening in particular moves away from the chemist's arena of the structure-activity relationship as a predictor of therapeutic potential to actual testing against targets in a high throughput screen. This also drives cross-discipline developments on novel sensors that can be incorporated into autonomous underwater vehicles (AUVs) and other sampling equipment.

Finally, a successful bioactive is one that reaches the patient, not one that has exciting new activity *in vitro*. Although the history of marine biotechnology began with notable successes - Ara-A and Ara-C were discovered in the 1950s and brought to market in the mid- to late-1960s and pseudopterosin has generated over $2 million in royalties for the University of California[66] - other 'flagship' molecules have fallen by the wayside, such as manoalide and bryostatin.

Indeed, PharmaMar was refused approval for ET-743, ecteinascidin, in the EU in late 2003 for use in soft tissue sarcomas; although the company is continuing to develop other uses and other compounds, it has been forced to close down most of its commercial operation to make best use of its funds. Such experiences are not encouraging for the investment and industrial community; those in the conventional pharmaceutical industry are used to many candidates falling by the wayside, they generally have more in the pipeline.

There is increasing evidence that many of these bioactives are produced by marine micro-organisms that are either symbionts or food components of marine invertebrates. Dolastatins, originally found in the aplysid *Dolabella*, are metabolites of *Symploca spp.* Cyanobacteria and are now thought to be of dietary origin. The tropical sponges *Dysidea* and *Theonella* from the Australasian Pacific contain bioactives that are produced by symbionts including the cyanobacterium *Oscillatoria spongeliae* and a new myxobacterial species. *Bugula neritina*, the source of anti-cancer bryostatins, is host to a proteobacterium tentatively named *Endobugula sertula*, which is the real producer of the bioactives.

There is potential for exploitation of signalling molecules, particularly quorum or consensus molecules, which regulate the interaction between micro-organisms in monospecific populations and in the communities that make up biofilms and other assemblages. This is an area of activity in which the UK is especially expert, partly as a result of the NERC's Marine Biofouling Thematic Programme MBTP.

The most notable company investigating this sector is Quorex Pharmaceuticals Inc, of Carlsbad, California. Quorex is developing new antibacterial compounds starting from a furanone found in *Vibrio harveyi*, a signalling molecule for luminescence, which appears to be a virulence factor in other pathogens. Quorex has also developed two screening technologies that are relevant for the study and inhibition of biofilms, one based on paramagnetic beads coated with film-initiating molecules, thus allowing establishment of monospecific or mixed-species populations within a microtitre-plate context, the other a library of *Pseudomonas* clones in which the gene promoters are fused with a luciferase reporter gene.

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[66] see *California Sea Grant Strategic Plan 2001-2005* page 35

Homeopathic medicines

Tincture of Asterias rubens, the common starfish, is used in homeopathy, with a wide range of indications including inflammation, hypertension, tumours (especially breast cancers) and neuralgia. Other common remedies include sepia, from squid ink, and a number shown in the table below.

TABLE 29: SOME EXAMPLES OF HOMEOPATHIC REMEDIES FROM THE SEA[67]

REMEDY	SOURCE
King crab's blood	*Limulus*
red starfish	*Asterias rubens*
jellyfish	*Medusa*
cod bone	*Gadus morhua*
digestive fluid of live lobster	*Homarus*
mother of pearl	*Conchiolinum*
cod liver oil	*Oleum Jecoris aselli*
weaver fish poison	*Trachinus*
red coral	*Corallium rubrum*
whale secretions	*Ambra grisea*

Many of these remedies are little used, do not have full provings, and if practitioners have cured cases, the information hasn't often been put into print[68]. However, it illustrates that extracts from marine sources, even at vanishingly low concentrations, may find interesting market niches.

3.6 Medical Devices and Biomaterials[69]

The medical device market is the most definable of those that use biomaterials and is worth >$40 billion. Geographically, the US is the single largest market in all sectors; in the medical device market, the EU as a region is second, with Germany, France, Italy all larger than UK. A consistent picture on the EU is that 90-95% of the healthcare technology companies are SMEs, 70% have less than 50 employees, and turnover is below €7m per annum, often below €1m[70].

The US sales of medical devices total about US$30 billion of a $74 billion healthcare market. The largest sectors by value are cardiovascular (14% of total, approx $10.5 billion), orthopaedics (6%, approx $4.5 b) and ophthalmology (4%,

67 *see http://www.likecureslike.org/cancer-4.htm*

68 see *Materia Medica: Exploring the link between the homeopathic remedies that come from the sea & cancer* Jo Evans, http://www.likecureslike.org/cancer-4.htm

69 Healthcare in this context means non-medicinal health treatment and support. Medical devices and medical equipment are usually included, surgical instrumentation and healthcare support services may be included in some definitions of the market.

70 source: Association of British Healthcare Industries, 2003

approx $3 b). Other groups contribute 15%, approx $11 b, and non-device healthcare makes up the remaining 61%, approx $44-45 b[71].

Device sales in Europe are estimated at approximately $12 billion, about a third of these sales coming from biomaterials-dependent devices; this proportion probably holds true in US as well. The majority of these are based on biocompatible synthetic polymers but there is an established sector of natural biomaterials. Those of marine origin include chitosans and chitins from crustacean exoskeletons, alginates and other seaweed hydrocolloids and coral-origin bone replacers. There is some potential for marine-origin collagens and gelatins to replace mammalian material, as a result of concerns over disease transmissions and improvements in economy of waste-processing.

TABLE 30: BROAD ESTIMATES FOR MEDICAL DEVICE END-USE SECTORS OF INTEREST, GLOBAL DATA[72]

SECTOR	ESTIMATED ANNUAL SALES $ MILLION					
	1999	2000	2001	2002	2003	GROWTH RATE
Devices	29,000	32,500	36,000	39,600	44,000	8-14%
Medical coatings[73]		10,000			18,000	
Drug delivery	5,400	6,300	7,400	8,900	10,700	>16%
Tissue engineering[74]	18	20	22	28	35	>16%
Approx. total	35,000	39,000	43,500	48,700	55,000	

Biomaterials for wound-care and general surgical use, and devices for cardiovascular and orthopaedic use are the sectors of interest for products from marine bio[techno]logy. Drug delivery can also provide a market for marine-derived ingredients as carriers and formulation components. An added area of opportunity might come from increased understanding of cell-to-cell signalling, to aid integration of devices by the patient.

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71 *Healthcare Industry Market Update, Medical Supplies and Devices*, Centers for Medicare and Medicaid Services

72 PJB *New Developments in Biomaterials 2000*

73 *Advanced Polymers for Medical Applications* Kalorama Information KLI 513 899 2002, ISBN 1-56241-781-9

74 virtually all bioartificial skin products

TABLE 31: GROWTH-RATES FOR DIFFERENT TYPES OF BIOMATERIALS-BASED WOUNDCARE PRODUCTS[75]

PRODUCT TYPE	GROWTH RATE
Foam dressings	15%
Alginate-based products	15%
Polyurethane absorbent woundcare products	13%
Polymer/polyurethane thin film dressings	9%
Hydrocolloid/hydrogel-based products	8.5%

The sales of implantable and injectable biomaterials and biopolymers are forecast to exceed $12 billion by the middle of the decade, some of which will be contributed by natural biopolymers *per se*. The best-established in current use are collagens, hyaluronic acid derivatives, gelatin and other hydrocolloids such as alginates. Growth is expected to be reasonably buoyant as a result of use in wound-care and cosmetic surgery and potential use in tissue engineering scaffolds. When used in this way, these natural biopolymers are regulated as medical devices. The market for bioabsorbable polymers was estimated at $300m in 1995, $500m in 2001, but only 10% of this enters uses other than absorbable sutures, a very mature market.[76]

TABLE 32: ESTIMATES FOR BIOMATERIALS USE IN SURGICAL PROCEDURES[77]

SECTOR	GLOBAL ESTIMATES $ MILLION	SOURCE
Overall surgical use	1,900	*PJB Publications*
Surgical barriers	1,000-1,500	*IMEDEX Biomatériaux* *PJB Publications*
Wound closure products	1,500	*ML Laboratories*
Bioadhesives	750-1,300	*PJB Publications*
Collagen-based drug delivery implants	500	*IMEDEX Biomatériaux*

75 Clinica report *'New Developments in Biomaterials'*
76 *Advanced Polymers for Medical Applications*, Kalorama 2002
77 *Biomaterials Strategy for Scotland*, BioBridge 2003 for SE Edinburgh & Lothian

TABLE 33: NATURAL BIOMATERIALS – FORECASTS FOR USE[78]

SECTOR	GLOBAL ESTIMATES $ MILLION
Hyaluronic acid & collagen (cosmetic use)	300 – USA only
Hyaluronic acid for viscosupplementation (use in joints, eyes)	150 – world, growth 40% pa
Collagen injectable and other device uses (cosmetic and woundcare)	400 – world
Gelatin (cosmetic, device component)	1,600 – world
Hydrocolloids and hydrogels (woundcare)	800 – growth 8% pa US, 12% pa EU

Gelatins are being produced from fish to avoid the stigma attached to mammalian-origin materials. The colloid firm Croda recently announced the launch of such a product[79]. There is a reasonable potential market for marine-origin gelatins, depending on the price that can be achieved. Current average prices for bovine-origin and similar gelatins are shown below, in comparison with fish gelatin. The physical characteristics of gelatins from different sources are very different (some do not gel, for example).

TABLE 34: PRICES FOR GELATINS[80]

SECTOR	PRICE €/KG
food	3-4.5
cosmetics	4-5
pharmaceutical-grade	4.5-8
photographic grade	7-13
fish gelatin – all sectors	12-18

Companies such as FibroGen (South San Francisco & Helsinki) have taken the biotechnology route to collagens and gelatins and produce recombinant human and mammalian products in microbial bioreactors. FibroGen is interested in using these materials in the surgical sealant, wound-healing, cosmetic, drug delivery and medical device sectors. The Dutch Agrotechnological Research Institute ATO has also recently announced the production of native and tailored gelatins in modified *Hansenula* yeasts. If marine-origin collagens and gelatin-equivalents have special performance characteristics that make them attractive, then this route becomes feasible also, once the relevant genes are identified and cloned.

One important and growing sector of medical devices is cardiovascular stents, tubes that can replace blood vessels in the heart, main blood vessel trunks or peripheral blood system when they have been narrowed by disease. The tubes used for repair of narrowed coronary arteries, coronary stents, are bedevilled by re-stenosis – normal myoepithelial cells invade the lumen of the stent and fail to

[78] *Biomaterials Strategy for Scotland*, BioBridge 2003 for SE Edinburgh & Lothian
[79] source, Croda 2004
[80] H van de Vis, Netherlands Institute for Fisheries Research, *pers. comm.* 2004

stop at the monolayer stage. About 25% of operations are to correct re-stenosis. Over the past 3-5 years, the industry has been developing stents carrying their own cytotoxic agents (eg paclitaxel) to stop cell overgrowth. The US sales for conventional stents of US$2.4 billion (2001) are projected to rise to $4-5 billion if drug-eluting and other controlled-cytotoxicity stents are successful, and will also enlarge the $1.6 billion for other angioplasty products used in peripheral blood vessels. In another area of cardiovascular devices, heart valves, failure of natural-materials valves is due partly to calcification and cracking but also to immune responses. The current US market of $0.8 billion will also rise if this can be tackled. Marine-origin bioactives and biomaterials may certainly have a role to play in coating devices and implants with a biocompatible and lubricated surface and in cutting down unwanted cellular reactions.

TABLE 35: BREAKDOWN OF MARKETS FOR DEVICES IN EUROPE, BY SECTOR[81]

END-USE SECTOR	MARKET (EST.) IN $ MILLION			AV. ANNUAL GROWTH RATE
	1999	2001	2003	
Orthopaedics	2,952	3,387	3,946	7.5%
Wound care	1,668	2,116	2,655	12.0%
Cardiovascular	1,528	2,037	2,637	14.5%
Drug delivery	1,459	2,002	2,889	18.5%
Ophthalmological	**177**	231	353	19.0%
Dental	166	199	237	9.0%
Cosmetic	31	37	44	10.0%
Urological	26	48	95	39.0%
Tissue engineering (skin)	2.7	3.3	5.2	18.0%
Total	8,010	10,060	12,861	12.5%

[81] *ibid.*

TABLE 36: BREAKDOWN OF MARKETS FOR DEVICES IN USA, BY SECTOR[82]

END-USE SECTOR	MARKET (EST.) IN $ MILLION			AV. ANNUAL GROWTH RATE
	1999	2001	2003	
Orthopaedics	8,650	9,822	11,443	7.0%
Wound care	1,587	2,013	2,525	12.0%
Cardiovascular	4,764	6,111	7,909	13.5%
Drug delivery	1,783	2,446	3,531	18.0%
Ophthalmological	326	425	649	19.0%
Dental	209	251	299	9.0%
Cosmetic	40	48	58	10.0%
Urological	36	68	135	40.0%
Tissue engineering (skin)	14	17	26	17.0%
Total	17,409	21,201	26,575	10.5%

The existing medical coatings market achieves surface modification of medical devices and other items through use of silicone, PTFE (polytetrafluoroethylene), diamond-like carbon or ionisation processes applied to metal and hard polymer materials. There is potential for better lubricious coatings (slippery and non-stick) that prevent tissue and pathogen attachment e.g. for urethral catheters or vascular stents as well as for bioactive coatings that enhance the interaction with the body or aid implantation. Marine source materials have a very strong potential here.

TABLE 37: BONE MATERIALS REPLACEMENT MARKET – 2003/4[83]

PRODUCT SECTOR	ESTIMATED SALES $M
Vertebral stabilisation	400
Spinal revision	350
Bone surgery support	325
Spinal fusion	300
New joint prosthesis cements	250
Repair of bone-end (metaphyseal) defects	90
Vertebral stabilisation screws (pedicle screws) support	85
Total estimated	1,790
Total 2001	930

In the orthopaedic area, there is research activity to produce usable scaffolds from ordered combinations of chitosan fibres, which can be turned into woven, knitted or non-woven fabrics, and bone-like minerals such as coral-derived

[82] ibid.
[83] Orthovita Inc. 2002

hydroxyapatite[84]. Chitosan-based materials are already used as sutures and wound dressings. The potential here seems, however, to be rather low compared with other applications such as wound-healing, largely because of current reliance on metals for orthopaedic devices and the slow uptake of bone replacers containing bioactives such as bone growth factors. This will change in the next 5 years, so that any marine-origin bioactive that is likely to have a cell- or healing-stimulating effect should be screened for its osteogenic or chondrogenic activity.

Though biomaterials form a small fraction of the content and value of current end-use products (est. 4% for medical devices[85]), about 35% of the devices on the market are biomaterials-dependent. Some European development organisations have set up programmes specifically aimed at generating new biomaterials; for example Tekes, the Finnish state technology development agency, established a Biomedical Materials programme in April 2003, with a budget of € 26 million, to encourage technology transfer and product development in this area[86].

Drug delivery

Drug delivery is more dependent on the pharmaceuticals and biologicals markets and the value of the biomaterial component is generally outweighed by the value of the active. Delivery systems in which marine-derived materials could be used as carriers include quick-dissolve tablets and no-water tablets; mucosal bioadhesives; hydrocolloid osmotic devices; lipid-encapsulation technologies; nasal and pulmonary delivery of microparticles. Rapidly-growing product sectors include inhalable therapies, gene therapy delivery using polymeric carriers (of which chitosan is one) and mucoadhesive products (mouth, gastrointestinal tract, anogenital). Drug-laden stents have already been referred to. In addition, the devices company Medtronic is developing a pain-relief implant using Neurex's ziconotide as the active component.

TABLE 38: MARKET BREAKDOWN FOR DRUG DELIVERY SYSTEMS – US ONLY[87]

SECTOR	MARKET SIZE $ BILLION			GROWTH RATE
	1990	2000	2005	2000-05
Oral administration (prolonged release, delayed release, mucoadhesive)	2.5	22.0	33.3	8.6%
Parenteral (injectables, targeted therapies, liposomes)	5.6	12.6	19.8	9.5%
Inhalation products	2.8	7.4	11.4	9.0%
Transdermal & implantable	0.15	1.4	2.7	13.3%
Total	11.0	43.4	67.2	9.1%

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84 Japanese and European work described in Baran Et, Tuzlakoglu K *et al.*, *Multichannel mould processing of 3D structures from microporous coralline hydroxyapatite granules …* J Mater. Sci.: Mater. Med. 15 (2004) 161-165

85 Association of British Healthcare Industries, 2003

86 EuroBiotechNews No1 Volume 2 2003, p15

87 *Freedonia Reports 2001*

Sometimes rapid availability of the active is wanted, and there is a recent and growing market for fast-dissolve technology, including no-water tablets, that was estimated at $1 billion in 2002. Chitosans might well be adaptable for this purpose.

3.7 Cell Therapies, Tissue Engineering and Regenerative Medicine

Marine biotechnology and marine biological research could make a strong contribution to these areas of frontier medicine, through marine-origin materials – bioactives, adhesives, anti-adhesives, biocompatible colloids, nanostructures, porous materials – as well as increasing knowledge about how cells and substrates interact and cell-cell signalling, including molecules that might, for example, alter the ability of cancer cells to coalesce and multiply, or metastasise. One activity that could enhance opportunities for marine biotechnologists and researchers of marine-origin materials in the UK would be to interact with the increasing numbers of centres for regenerative medicine and tissue engineering in Europe, to explore opportunities for co-developments.

Cell therapies are those in which cells are injected or transplanted directly into the body. The most common procedure is, of course, bone marrow transplant, with some use of cartilage cells that have been harvested from a patient, enriched in culture and replaced into damaged knees, for example.

Tissue engineering implies the creation of scaffolds outside the body and population of these by cells, to produce bioartificial tissues or organs. Some research is also going on into *in situ* scaffold construction, for example with water and heat sensitive derivatised biopolymers. Regenerative medicine is the overarching title for that frontier activity that is looking to stimulate and support the body itself in restoring normal function of tissues and organs that are damaged, diseased or simply worn out with age.

Cell therapies are those in which cells are injected or transplanted directly into the body. The most common procedure is, of course, bone marrow transplant, with some use of cartilage cells that have been harvested from a patient, enriched in culture and replaced into damaged knees, for example.

Other procedures that might become commoner, and which extend into regenerative medicine, include pancreas repair using cells, brain cell transplants, heart muscle transplants and, with much broader scope, the use of stem cell transplants to repair or replace practically any kind of tissue within the body. One estimate for market potential gives sales of $30 billion by 2010[88], table below.

Targets for marine biotechnology might be cell-activating and cell-maintaining agents or biocompatible cell carriers that help to localise cell implants, thus providing opportunities for marine-derived actives as well as biomaterials.

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88 *Cell Therapy, Technologies, Markets & Opportunities*, P Bassett, D&MD Report #9086, D&MD Inc, Westborough Massachusetts, January 2003

TABLE 39: POTENTIAL ROLES FOR MARINE-DERIVED PRODUCTS IN TISSUE ENGINEERING

POTENTIAL ROLES FOR MARINE-DERIVED PRODUCTS
protectants for cells (oils, chitins, polysaccharides)
scaffolds for cells (chitins, diatoms)
stem-cell differentiator (bioactives)

The current sales of products of tissue engineering are low and mainly derive from dermal structures for skin repair, but the potential is very large; the potential contribution of biomaterials to tissue engineered products is also much greater than for most medical devices (perhaps as much as 80% for scaffolds and matrices), though the value share may not be so high.

TABLE 40: ESTIMATES OF END-USE MARKET SIZE[89]

END-USE MARKETS	
cell therapies	$30 billion by 2010
tissue engineering	$375 million by 2007
regenerative medicine	$4.6 billion by 2010

note: figures not additive; source definitions overlap

A recent interesting discovery with relevance for this area is the result of a collaboration between researchers from Rockefeller University, Roscoff Marine Biology Institute and the University of Athens. A constituent of the marine dye, Tyrian Purple, 6-bromoindirubin-3'-oxime, has been found to inhibit glycogen synthase kinase-3 in vertebrate cells. The molecule stabilises and allows differentiation of embryos and stem cells without the need for mouse feeder cell lines as support in *in vitro* culture. This point is of great importance to cell therapies and regenerative medicine using stem cells, since the use of non-human cells even as *in vitro* support immediately causes a regulatory reclassification of cell therapy or tissue engineering processes as xenotransplantation (introduction of living non-human cells or tissues into the human patient), with a much greater regulatory burden.

Because of differences in definition and what is included, estimates of the future global tissue regeneration market vary from $2.07 billion through $4.6 billion[90], even to $80 billion, the latter including wound healing and chronic non-healing ulcers as well as products replacing existing devices for soft and hard tissue repair.

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[89] *Biomaterials Strategy for Scotland*, BioBridge 2003 for SE Edinburgh & Lothian

[90] *New Development in Biomaterials*, a Clinica report, PJB Publications 2000

TABLE 41: MARKET BREAKDOWN FOR POTENTIAL TISSUE ENGINEERED TARGETS[91]

PRODUCT SECTOR	MARKET SIZE ($ BILLION)	YEAR
Venous stasis ulcers	2.9	2002
Pressure ulcers	1.9	2002
Diabetic foot ulcers	1.4	2002
Other soft tissue/surgical	3.8	
of which acute wounds	2.0	
anti-adhesions	1.0	
Heart valves	1.0	2008
	0.7	2000
of which tissue valves	0.25	
pericardial-flap valves	0.10	
mechanical valves	0.35	
Cardiovascular stents	2.2	2001
	3.0	?
of which small-diameter	0.4	
Regeneration of bone, cartilage, tendon, ligaments	15.0	

TABLE 42: TISSUE ENGINEERED PRODUCTS, GLOBAL MARKET 2001-2013[92]

SECTOR	ESTIMATED MARKET SIZE US$ MILLION		
	2001	**2007**	**2013**
Skin	21	273	1,014
Cartilage	26	54	134
Bone	0	23	103
Musculo-skeletal, organ, CNS etc.	0	25	819
totals in $ billions	-	0.375	2.07

3.8 Diagnostics

Recent industry estimates put the global market for diagnostic enzymes at $120 million. Although the global *in vitro* diagnostics market was estimated to reach $23 billion by 2003[93], revenues of European biotechnology-based diagnostics companies reached about € 1 billion in 2002[94].

91 *Biomaterials Strategy for Scotland*, BioBridge 2003 for SE Edinburgh & Lothian

92 *Tissue Engineering and Transplantation: Products, Technologies and Opportunities 2003-2013* MedMarket Diligence Report #S505 August 2003

93 *New Trends in Viral Diagnostics*, Clinica, 2001

94 *Surviving Uncertainty: The Pan European Mediscience Review 2002*, Deloitte & Touche 2002

TABLE 43: ESTIMATES OF SALES OF *IN VITRO* DIAGNOSTICS BY TECHNOLOGY TYPE, 1999-2004[95]

TEST TECHNOLOGY/PURPOSE	SALES IN $ M	
	1998	2004
Immunochemistry	7,151	8,700
Blood glucose detection	2,600	4,000
Microbiology & nucleic acid tests	1,774	2,700
Chemistry	3,120	2,600
Haematology & flow cytometry	1,796	2,400
Coagulopathies	682	800
Blood gases, electrolytes	588	800
Urinalyses	552	700
Others	746	1,100
total	19,000	23,800

Marine-origin products already established in this sector include the fluorescent phycoerythrin from seaweeds and alkaline phosphatase from shrimp, both also used as laboratory research reagents.

3.9 Research Tools

Culture Collections

The advantages of possessing a marine organism Culture Collection include not only recouping costs by charging access fees but also generating income through licence fees, success fees and royalties from the development and exploitation of any effective and safe bioactives produced by microbes in the culture collection. The income from Culture Collections can be substantial – the American Type Culture Collection raised over $14.5 million in fees in 2001 for supplying samples of its cultures, which are maintained under cryopreservation rather than by continuous culture, considerably reducing maintenance costs[96].

The Culture Collection can also be the basis for important and mutually-beneficial international collaborations, which add to the reputation and credentials of an organisation as well as its knowledge. AIMS in Australia has a successful collaboration with the US National Cancer Institute (NCI), in which extracts from AIMS's isolates are tested in the NCI's cancer screens, the most extensive in the world. Currently, at least two leads from the AIMS-NCI programme are in further pre-clinical testing; these were isolated from Australian sponges.

CSIRO's Microalgae Research Centre (CMARC) in Australia has a Collection of Living Microalgae with over 750 strains, mainly marine, with some freshwater

95 D P Kelly in *Medical Device Manufacturing and Technology, World Market Research Centre September 2000 p40*

96 *Marine Science Review, Report of Visit to Maryland & Virginia*, New Park Management June 2001, chapter 4

microalgae and unusual marine fungi. CMARC supplies these for research, teaching, commercial assessment and as aquaculture larval feeds. The costs are approx. A$100 for 20ml, or A$150 for material in a 250 ml flask, including postage[97]. The Marine Biology Station at Roscoff in France maintains the RCC (Roscoff Culture Collection) of 550 picoplankton and picoeukaryotes. This is part of a newly-created Souchothèque de Bretagne, funded by the French State-Region Plan 2000-2006. There is currently no fee. The MBI's Culture Collection (MBIC) in Japan has over 750 bacterial and 300 microalgal strains on its online catalogue, available for research use under agreements.

A very useful web-site[98] provides the contact details, via web links, of 480 collections in 65 countries. Of these, 19 are based in UK and several are relevant to marine biotechnology. Most are supported by the NERC and charge a small amount for access (£25-30, occasionally £50) to other academic or commercial customers.

Collections of extracts can also be of importance and value – Albany Molecular Research Inc maintains three libraries of extracts at its Bothell site near Seattle USA, with 110,000 primary fermentation extracts, 150,000 fractionated extracts and over 1,000 small-molecule bioactives, from marine and terrestrial sources. The extracts include marine invertebrates, algae and other microbes. The MDPI (Molecular Diversity Preservation International, Switzerland) acts as an exchange house for biomolecules and has also published, since 2003, the on-line access journal *Marine Drugs*[99]. The US company Martek maintains a library of more than 3,300 live microalgal species and a related database, which it uses for in-house research. The Wyeth marine micro-organism collection contains over 3000 eubacteria, fungi and actinomycetes. Wyeth produces bioactives by fermentation and runs them through a high throughput screen.

Advances in recovery of nucleic acids from dead material might allow some of the UK's taxonomic museum collections to be used as sources of information and genes for marine biotechnology R&D. The UK Natural History Museum's 'Discovery' collections total over 51,000 specimens, approximately half plankton and half invertebrates, for example[100]. The feasibility has been tested and some positive results have been recorded in using genetic material for identification and assessment of variation over time[101].

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97 contact microalgae@marine.csiro.au

98 see http://wdcm.nig.ac.jp/hpcc.html

99 see http://www.mdpi.net/marinedrugs/

100 *Marine Sample Collections, their value, use and future*, RG Rothwell July 2001, for IACMST

101 *ibid.* pp50-53

TABLE 44: CULTURE AND OTHER COLLECTIONS IN UK

NAME AND SITE	COMMENTS
UK Culture Collection of Algae and Protozoa (CCAP), SAMS Dunstaffnage Marine Laboratory Dr Frithjof Kuepper, frithjof.kuepper@sams.ac.uk T: 01631 559000	CCAP contains over 600 strains of both marine and freshwater algae, the latter as a result of merger of a collection previously held at Windermere. Efforts are being made to increase the amount of cryopreserved material to ensure genetic stability. CCAP is a WIPO depository for patent purposes.
National Collections of Industrial, Marine and Food Bacteria, NCIMB Ltd, the University of Aberdeen	NCIMB took on the Nathan Smith/Ruth Gordon Bacillus Collection from Virginia USA in 2000
Plymouth Culture Collection of algae, Marine Biological Association, Plymouth Pipe, Dr. R.K T: 01752-633215	This NERC-supported collection contains over 475 algae; there is a small fee for commercial and industrial use
PHBL collection, Philip Harris Biological Ltd. Weston-super-Mare	mainly terrestrial, carries approx. 20 algal strains
British Ocean Sediment Core Repository (BOSCOR), Southampton Oceanography Centre, Keith Birch, Keith.Birch@soc.soton.ac.uk T: 02380 596105	NERC-funded. Deep-sea sediment cores are maintained for oceanographic and palaeoceanographic purposes; value for biodiversity or biotechnology purposes needs to be explored; access to the EU-funded EU-SEASED database
Marine Core Collection, British Geological Survey, Murchison House, West Mains Rd, Edinburgh, Colin Graham	NERC-supported; collection built up to approx, 32,000 samples since mid-1960s;

Research tools and reagents

Researchers at the University of California San Diego developed a retroviral expression system that was originally intended for use in creating transgenic fish and shellfish, to enhance growth and disease resistance. The technology was embedded in a start-up founded by the scientists, Pangenix Inc of La Jolla, but it is now used more for human disease research and therapy than in fish or shellfish[102].

Some marine sources for research reagents are well-known: the value of alkaline phosphatase isolated from frozen shrimp melt-water is approximately € 110,000 for Novozymes, for example, and the catalogue price for 1000 U is approx $85. Phycoerythrin, pre-conjugated with streptavidin, sells for approx. $200/100 ml or $500/mg dry-form, and phycocyanin is also available. These seaweed-origin fluorophores are often used unconjugated as the fluorescent vital dye in cell sorting and are generally obtained outside the UK. There might be some potential for import substitution here.

The market for general-purpose biotechnology reagents has been estimated at over $1.3 billion by 2002[103], as shown in the table below.

102 *The Role and Experience of Inventors and Start-ups in Commercializing University research: Case Studies at the University of California*, R Lowe, Center for Studies in Higher Education UCal Berkeley, 2002, paper CSHE6'02, pp22-25

103 Theta Reports 767, *Biotech Research Reagents*, May 1998. Theta Publications Inc (part of PJB Publishing Ltd)

TABLE 45: SALES ESTIMATES FOR BIOTECHNOLOGY REAGENTS[104]

SECTOR	SALES ESTIMATES $ MILLION	
	2000	2002
DNA sequencing reagents	264	380
General purpose biotechnology reagents & materials	215	284
Electrophoresis reagents	181	260
Tissue culture reagents & materials	125	159
Liquid chromatography reagents	117	141

Extremophile and marine organisms have generated three of the most widely-known of modern bioreagents – Taq polymerase, a vital ingredient of the Polymerase Chain Reaction, from *Thermus aquaticus*, a hot-springs organism and the two products from the north-east Pacific coldwater jellyfish *Aequoria victoria* – aequorin, the blue bioluminescent indicator of calcium flux, and Green Fluorescent Protein, which converts aequorin to green light. Following on the heels of Taq polymerase is VENT™, derived from the deep-sea hot vent relative, *Thermus thermophilus*. Sales of PCR enzymes are estimated at up to $100 million annually world-wide, and the market for extremophilic enzymes is projected to grow 15-20% per year[105].

More marine natural substances are likely to have an attractive market as research reagents, once they have undergone total synthesis or a semi-synthetic route has been found for them. Manoalide and staurosporine are being made available by the US company AG Scientific Inc at prices of $360 and $280 per mg for synthetic analogues, which would be excellent if demand was in kilogrammes and the dicoverer of the bioactive had the rights. Where synthetic versions are not yet available, prices are even higher – GPC Biotech Munich and LC Laboratories apparently have put a price on bryostatin I of $3,750 per mg[106].

Researchers at Oregon State University are using the unique modes of action of marine molecules as tools for molecular biochemistry. Antillatoxin, a fish neurotoxin from a cyanobacterium isolated off Curaçao; has an effect on membrane sodium channels through a previously-unknown mechanism and has become a new tool for pharmacological investigations.

Models for mammalian function and disease

The University of Florida is using the lobster as an experimental model for neural responses to smells, jellyfish for nervous system studies and mud minnows as stress indicators. The Scripps Institution of Oceanography uses sperm and egg physiology in sea urchins and abalone to cast light on processes in humans during fertilisation. Zebrafish are fast becoming the fruitfly of the vertebrates, for studies

104 *ibid.*

105 quoted in The International Regime for Bioprospecting, Existing Policies and Emerging Issues for Antarctica UNU/IAS Report August 2003

106 Blaue Biotechnologie: Stand und Perspektiven der marinen Naturstoffe, Technologiestiftung Schleswig-Holstein, June 2003 pp 25-26

of molecular development and the impact of gene mutations. One output of the National Sea Grant Program has been the use of fertilised transgenic fish eggs in place of transgenic mouse embryos, "with considerable savings in cost and handling effort"[107].

These are individual stories that can make good news items, but there are broader benefits from undertaking fundamental marine bio[techno]logical research, including an increased understanding of how cells interact and signal to each other in complex communities, how cells and biomaterials bind to inorganic surfaces, and how micro-organisms keep each other under control. The understanding of cell-to-cell signalling is one area in which there is considerable research strength in the UK.

3.10 Agriculture

Crop protection market

The global crop protection market consists of products applied to plants to kill or repel pests, including fungal diseases and insects, and to control weeds. In 2000, the world market was approx US$30 billion, projected to rise to $40 billion by 2010[108]

TABLE 46: SALES OF CROP PROTECTION PRODUCTS WORLD-WIDE 2000[109]

CROP-PROTECTION PRODUCT TYPE	EST. REGIONAL SALES 2000, US$		
	EUROPE	USA	JAPAN
fungicide	2,700 million	820 million	740 million
post-emergence herbicides	2,850 million	3,880 million	820 million
pre-emergence herbicides		1,520 million	
insecticides	1,200 million	2,070 million	1,005 million
combined insecticide-fungicide	-	-	345 million
growth regulators, others	355 million	360 million	470 million
total	7,000-8,000 million	8,800 million	3,400 million

Crop agriculture

Chitin and chitosans have been used widely in agriculture as soil conditioners, anti-fungal materials and components of seed coatings. Work at Washington State University is capitalising on the abundance of crab-shell chitin to produce fungicidal chitosan for control of potato blight, and lobster-shell waste has been put to practical use in production of organic potatoes on the Prince Edward Island

107 see http://www.nsgo.seagrant.org/research/biotech/initiative/i2a.html

108 *The Global Crop Protection Industry in 2010*, Agrow Reports DS221, PJB Publications 2001

109 *ibid.*

Canada for McCains Potatoes, after drying, grinding and extraction of astaxanthin[110].

More recently, marine biotechnology is yielding bioactives of interest. AIMS has isolated more than 30 potential herbicides in the period since the late 1990s, in collaboration with the Nufarm company, and the AIMS spin-out ToxiTech has succeeded in growing one source, a marine fungus, on large-enough scale to yield enough material for initial trials. The US company AgriQuest is developing biopesticides from marine and other natural sources.

Animal agriculture and feeds

BioZyme Inc. of St Joseph Missouri incorporates Amaferm®, a fermentation product from a terrestrial *Aspergillus oryzae* strain, into animal feeds, producing a stimulation of the animal's normal flora and fauna and increased performance and better feed use. This suggests the possibility that extracts of marine fungi might also have a positive impact. There is increasing pressure against the use of antibiotics and other pharmaceutical-type products in animals, so that such 'natural' extracts are attractive.

Petfoods

The total sales of petfoods are astonishingly high, about $17 billion in the USA, £7.2 billion in the UK and € 2.2 billion in France. Alginates and carrageenan are used as fillers and humectants. One avenue to explore is algal-based foods for pets, with high carotenoids, PUFAs and other components.

Aquaculture

There is a considerable market for microalgae as fresh food for organisms in aquaculture, including larval fish and crustacea, as well as filter-feeders such as clams, oysters and abalone, with at least 50 species or strains being in use or of potential value. In Europe, *Tetraselmis suecica* is possibly the best-known of these. CMARC, the Australian Marine Algae Research Centre, supplies a wide variety of algal strains to the aquaculture industry in Australia and Asia-Pacific, including *Isochrysis*, *Pavlova lutheri, Chaetoceros muelleri, Chaetoceros calcitrans, Nannochloropsis oculata, Skeletonema costatum* and *Tetraselmis suecica*, as well as new Australian strains that are more suited to local environments and nutritional needs, including *Pavlova pinguis, Skeletonema*, *Rhodomonas salina* and *Navicula jeffreyi.*

The most important components of microalgae for nutrition are polyunsaturated fatty acids, sugars, vitamins, and sterols. There is also some interest in components of microbes that might assist in maintaining healthy immune systems, such a beta-glucan derivatives, as well as the potential for chitin derivatives such as chitosans and glycosaminoglycans to have health benefits for young fish and invertebrates. In Australia, AIMS is screening a large number of its extracts of marine organisms for activity against *Mycobacteria*, with a target of finding treatments for ulcerative diseases of prawn and shrimp.

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[110] B Burles *pers. comm.* 2004

TABLE 47: EXAMPLES OF USE OF MICRO-ORGANISMS AS PROBIOTICS IN AQUACULTURE[111]

ORGANISM	USE	REF
Tetraselmis suecica microalgae	inhibited *Aeromonas hydrophila*, *A. salmonicida*, *Serratia liquefaciens*, *Vibrio anguillarum*, *V. salmonicida and Yersinia ruckeri* type I *in vitro*, and *in vivo* in salmon as whole cells or extracts in-feed	Austin et al (1992)
Vibrio alginolyticus	*in vitro* control of *V. ordalii*, *V. anguillarum*, *A. salmonicida* and *Y. ruckeri* and *in vivo* reduction in mortalities from *A. salmonicida* and to a lesser extent *V. anguillarum* and *V. ordalii*, in salmon	Austin et al (1995)
Fluorescent pseudomonad	inhibited *A. salmonicida in vitro* and reduced mortalities from challenge infection – by competition for free iron	Smith and Davey (1993)
Vibrio alginolyticus	increased survival and growth in *Penaeus vannamei* postlarvae, reducing or eliminating antibiotic use in intensive prawn culture	Garriques and Arevalo (1995)
Vibrio alginolyticus	competitive exclusion of *V. harveyi* type E22 responsible for 'Zoea syndrome' of *P. vannamei*	Garriques and Arevalo (1995)
Natural marine assemblages induced from seawater by using nutrients	improved nutrition and growth of crab larvae of *Portunus trituberculatus*, improved yield of prawn larvae *Penaeus japonicus*	Maeda and Nogami et al (1992)
Rhodomonas spp	water cleaner and auxiliary food for hatchery rearing of *P. chinensis*	Cui Jingjin et al (1997)
Vibrio spp from a shrimp hatchery	two natural isolates reduced the number of plaques of shrimp infectious haematopoietic necrosis virus (IHNV) and Oncorhynchus masou virus (OMV) *in vitro*	Direkbusarakom, Yoshimizu et al (1997)
Vibriostatic bacteria	improved the growth and survival rate of prawn and crab larvae, decreased growth of *Vibrio* spp	Maeda and Nagami (1989)
Bacterial isolates from a crustacean culture pond	improved the growth of crab (*Portunus trituberculatus*) larvae; repressed *Vibrio* growth without affecting microalgal growth	Nogami and Maeda (1992)
Lactobacillus spp.	successful treatment of vibriosis and white spot diseases in *Penaeus monodon* (giant tiger shrimp)	Jiravanichpaisal and Chuaychuwong et al (1997)
Soil isolates	increased survival and moult rates of *P monodon* larvae	Maeda and Liao (1992)
Photosynthetic bacteria	improved growth of *P. chinensis* and enhanced water quality	Qiao Zhenguo et al (1992)
Mixed isolates from adult shrimp intestines	two strains in water of larval *P. chinensis* produced improvement in disease resistance, low salinity tolerance and survival rate and increased length and weight; bacteria produce digestive enzymes that may be helpful to larvae	Wang Xianghong et al (1997)
'Probiotic bacteria'	growth improvement of larval oyster *Crassostrea gigas* in culture	Douillet and Langdon (1994)
Mixed isolates from farmed freshwater fish	antibacterial effect against fish and human pathogens *in vitro*	Sugita and Shibuga (1996)

Mixtures of marine and aquatic microbes are being widely used as probiotics in South-East Asia, China, Japan, USA and some EU countries as aids to healthy production in fish and shellfish farming and improvers of water quality in growing

[111] web-site of the Alken-Murray company – for detail of references please see web-site

ponds. The probiotic effect is thought to be achieved by a combination of digestion of waste materials in the water (heterotrophic action), competitive exclusion of pathogens, production of enzymes that help fish and crustacean digestion, and release of nutrients from other aquatic organisms.

A prominent company in this activity is Alken-Murray, New Hyde Park USA, which specialises in combinations of *Bacillus* and other species, collected from crustacean and fish-farming ponds and formulated into easy-to-apply mixtures.

3.11 Enzymes & Industrial Uses

The annual world market for industrial enzymes is estimated at $3.6 billion (£2.3 billion), with less than 30 enzymes contributing more than 90% of volume.[112] The scope for use of marine-origin enzymes will be some fraction of this, but there is attraction in finding, for example, detergent enzymes that work at lower temperatures or process enzymes capable of high efficiency under pressure. These avenues could usefully be followed up with the Pro-Bio Faraday Partnership.

Existing processes using marine materials might benefit from the use of marine-origin enzymes. The extraction of chitosan from shrimp shell waste is an example. Shell plus organic remnants is typically 78% water, 14% inorganic minerals, about 9% is protein and about 5% of the total shell waste is chitin. The conversion efficiency of chitin into chitosan is 60%, resulting in an overall productive efficiency of only 3%, with production costs quoted at $8-10 per kilo[113]. Marine-origin enzymes should be able to make some impact on yield and economic efficiency.

A recent report points to the prospects for better use of biotechnology, especially for nutraceutical and pharmaceutical uses, in dealing with Ireland's 70,000 tonnes of waste a year from landed and farmed fish and shellfish[114]. This waste is high in recoverable protein, collagens, oils, fatty acids, calcium and chitin but current processing systems add too much cost. We believe there is potential in management of fish and shell-fish wastes for appropriate-scale biotechnology approaches that, without needing high-volume ultra-clean and consistent input, can still produce pure, high-quality, toxin-free outputs, ideally in separated streams. An alternative is to use mixed wastes to produce energy on-site, again in appropriate-scale and economically-effective systems. Intuitively, marine-origin enzymes should be better able to achieve this than enzymes from terrestrial sources.

Diatomite, or diatomaceous earth, has wide uses in filtration, purification and removal of microbial contaminants from liquids, including beer, wine, water, oils, greases, public water systems and blood plasma, and in paints as a filler. Most of these more traditional uses are declining. A growing market is use as a filler for polyethylene, which represents about 100,000 tonnes per year. Emerging applications include pharmaceutical processing and non-toxic insecticides. World

[112] see http://www.diversa.com/markprod/mark/induappl.asp

[113] see http://www2.rf.is/taft2003/PPtskjol/Fyrirlestrar/K08%20-%20MMorrissey.pdf, slides 46-47

[114] DK/01/003 – Disposal and re-utilisation of fish and fish processing waste (including aquaculture wastes) June 2003, Nautilus Consultants Ireland Ltd, for the Marine Institute Ireland

production totals 1.6-1.7 million metric tonnes, but there is almost 1 million tonnes in reserve. The US's production of 625,000 tonnes is worth about $159 million. The US also imports diatomite, mainly from France, Italy and Mexico. Although the market is relatively stable for this material, there are increasing concerns about the costs of long-distance transport and environmental impact of mining[115]. One possibility is to farm diatoms and process them into diatomite, using smaller-scale plants that can be built locally according to need.

Over 20 million tonnes of marine sand and gravel are used each year in British building, about 24% of annual consumption, and about 7 million tonnes are exported to the Netherlands and France; most of this is excavated in southern England, especially the south-east and the Bristol channel[116]. Recent reports that the UK Government has granted licences for excavation of sand and sea-bed materials from an ecologically-rich area south of Beachy Head[117] gives some urgency to finding a sustainable answer to the shortage of sand and gravel that impedes building works; at this stage, there is no suggestion that marine microbes or other organisms such as molluscs and crustacea could contribute to this, but a valid question, given the unsustainability of the gravel extraction, is whether solid marine wastes could be used in some way.

Higher-technology development of marine microbes might be forthcoming. Dow Corning and Genencor formed an alliance in 2001 to develop silicon biotechnology, in which Dow Corning paid Genencor $35 million over 2001-2003, to create a new, proprietary Silicon Biotechnology™ platform. Understanding and using the physiology and biochemistry of marine plankton that utilise silicon are fundamental aspects of this. The companies hope to commercialise biologically-mediated silicone based products for the life sciences, personal care, cleaning and fabric care markets, in the short-term, then move on to applications in diagnostics, biosensors, electronics and controlled delivery of active ingredients. The materials may be used in developing new biochip-based devices with acute recognition and superior signal transduction capability. The ability of marine micro-organisms to build protein lattices for deposition of silica and other inorganic material in a nanostructured way holds out potential for bioproduction of silicon chips and other nano-structures.

3.12 Environmental Management and Energy

Monitoring the environment

The global sensor technology market, both for environmental sensors and new forms of monitoring and exploration, is estimated at $5 billion per annum and is growing at 5 per cent per annum[118].

Scripps Institute for Oceanography is researching the possibility of monitoring heavy-metal pollution in coastal areas using luminescent brittlestars as indicators.

[115] see http://www.roskill.com/reports/diatomite and TP Dolley, US Geological Survey, Mineral Commodities Summaries Jan 2004

[116] see http://www.bmapa.org/pdf/ukmarinesand.pdf

[117] see http://www.thisismidsussex.co.uk/mid_sussex/archive/2004/03/16/NEWS200ZM.html

[118] Marine Foresight Panel Ireland 2003

In a collaborative research project with Texas Instruments, Inc., researchers at the University of Washington, Seattle have developed a prototype surface plasmon resonance sensor system to monitor pollution and bioremediation, with the aim of producing portable instruments for marine fieldwork. Other researchers at the Friday Harbor Labs, University of Washington are collaborating with the Photobiology Laboratory of the Institute of Biophysics, Krasnoyarsk, part of the Russian Academy of Sciences in Siberia, to use marine photoproteins to detect calcium ion flux into cells. The work aims at producing genetically-improved photoproteins.

The UK company Remedios is a spin-out from the University of Aberdeen, which is a shareholder and research and development partner. The scientific staff are based at the University, in the Departments of Molecular & Cell Biology and Plant & Soil Science. The products and know-how within the company were developed partly through work at the University and partly through a series of BBSRC-funded projects on immunological and cellular tools for pollutant biosensing, between 1997 and 2001, including the development of a novel eukaryotic biosensor based on a marine microbe. Remedios likens its sensors to the canaries that miners used to take down the mines with them. The basis of the tests is bioluminescence, the intensity of which is directly proportional to the metabolic activity of the marine microbes used as the biosensor. Samples of water, soil, sediment or sludge which might be toxic reduce the bioluminescence in direct proportion to the level of toxicity present, thus giving a rapid real-time screen of overall contamination of the environment. Remedios also uses other biosensor organisms that are representative of the bacterial strains found in the environment as well as those involved in bioremediation.

Environmental remediation

It is estimated that about 3.5 billion gallons (1.2 x 10^{10} litres) of oil are extracted at sea or are in transit across the oceans each day, and spillage is estimated at over 120 million gallons per year. Marine-origin biodegradable dispersants or *in situ* bioremediation by surface spray of oil-degrading microbes or enzymes would be welcome.

Transferring mammalian or avian metallothionein genes to *Synechococcus* and *Chlamydomonas* produces genetically enhanced microalgae that are better at extracting and sequestering heavy metal pollutants from seawater. Research with a modified *Delinococcus radiodurans* has shown an ability to degrade organopollutants in radioactive surroundings. There would be an exciting potential for genetically-enhancing marine organisms so that they are more capable of metabolising and detoxifying pollutants in sea water arising from human activities. However, the current guidelines and Strategy plans for marine management and ecological conservation explicitly state that GMOs should be prevented from entering the sea. UK's strengths in marine bacteriology would play well into this opportunity for development of closed bioremediation systems using microbes that may or may not be genetically-enhanced.

Rita Colwell, a staunch US champion of marine biotechnology, was the first to show that pathogens such as *Vibrio cholerae* survive in surface marine biofilms and infect swimmers and bathers through this route. *Escherichia coli* and hepatitis virus behave similarly and the biofilms act as a source of contamination for filter-feeders such as shell-fish. Indeed, it seems clear that *Vibrio* species are mainly marine or aquatic bacteria, causing problems when ingested by an animal. Ability to attack these organisms in biofilms using some kind of surface water treatment would be welcome; treatment might include the use of a biodegradable marine surfactant, a marine bacteriophage cocktail or swamping with a benign marine organism that out-competes.

Success in this endeavour has to be based on either a better understanding of interactions within biofilms or on knowledge of marine micro-organisms that could act as bioremediators.

A significant source of ecological pollution is ship ballast water. Problems caused by exotic organisms are well-known and there are, as yet, no really effective ways of dealing with this. Forcing ships to flush their ballast-holds while out in open water may help the final dock to avoid contamination, but the action simply shifts the load elsewhere rather than removing it altogether. It seems viable to explore whether a combination of 'probiotic' non-exotic organisms, marine viruses and suitable neutralisers might not eliminate stowaways in ship ballast water.

New sources of energy

CO_2-neutral and renewable energy sources are of increasing importance due to climate change and the increasing global CO_2 concentrations in the atmosphere. One of these alternative energy sources is hydrogen, which can be used to generate electricity and heat in a fuel cell at a high efficiency.

A number of countries have (and have had) significant investment in biological hydrogen production using photosynthetic bacteria and algae. These include USA and Japan, but not UK. In the last few years the same technology has been directed towards CO_2 biofixation, which can also be seen as under the umbrella of Marine Biotechnology.

Hydrogen production from biomass represents a renewable way of producing such energy. The Dutch have established a significant national effort in this field, co-ordinated from the Food and Bioprocess Group in Wageningen University[119].

Some bacteria take up dissolved iron from the surrounding water, generate magnetite microparticles and become magnetotactic. In Japan, these nanoscale magnetic particles have been used to make high-density audio tape. Magnetite-containing bacteria can be used to construct ferromagnetic microstructures, 'bionites', including threads 100µ in diameter and 20-30 cm long, which results in high densities of particles about 100 nm in size and extremely high tensile strengths. Biomaterials-engineering techniques, such as bacterial templating, could provide such ordered arrangements of microscopic particles over macroscopic length scales[120]. Marine microbes with similar properties might also be useful.

[119] see http://www.biohydrogen.nl for information

[120] see http://www-als.lbl.gov/als/workshops/scidirecthtml/4Magnetic/magnetic.html

3.13 Bioengineering and New Production Techniques

There is considerable work going on to devise bioreactors for algae. Workers at the University of Wageningen in the Netherlands, in Germany and in Italy at the University of Firenze, are looking to create new photobioreactors and economical plate or cylindrical algal fermenters, to take advantage of natural light. The work at the University of Firenze is to develop mass cultivation methods for *Tetraselmis suecica*, a green microalga, which has a high amino-acid and lipid content and is a good food source for other marine organisms in culture or farming. An extract of *Tetraselmis* is also reported to inhibit *Vibrio* infections in prawns and shrimp and addition of the microalga to feed at 0.5-1.0% protects salmon against bacterial pathogens. The new method is based on upright hollow cylinders (annular columns) rather than the existing types of flat-panel or tubular bioreactors. Both Mera and Cyanotech in Hawai'i depend on their bioreactor technology for economic production of their microalgae.

The University of Wageningen, PharmaMar and the Croatian maricultural company MariMirna have been able to develop sponge production. Wageningen is doing this in closed reactors using clusters of cells that form small sponge colonies, primmorphs; and PharmaMar is cultivating them in semi-closed warm Mediterranean waters.

4. BARRIERS TO GROWTH – FINANCIAL AND OPERATIONAL

4.1 Bridging the Gap

A UK-based respondent has pointed out that

> *"there's a kind of institutional or cultural void between the people with relevant academic competencies and the ultimate end users (oil companies, pharmaceuticals, etc). Other sectors have a fertile middle ground of "appliers" – IT, for instance. Academics who are good at being academics are not always the risk-coping entrepreneurs that these high-investment high-tech outputs demand, and experience seems to suggest that the market for one brilliant idea is more finite than university researchers expect."*

If accepted as true, then the primary efforts should address bridging that gap. Tools for achieving togetherness might include:

- Establishing internet-based communities, often *ad hoc* but sometimes based on a specific establishment, with suitable funding from institutional, regional or national sources.
- Stimulating the establishment of networks with cross-cultural meetings, seminars, issue workshops, usually achieved by suitable pump-priming funding and having an identifiable focus, whether a new organisation or built onto a well-recognised existing one.
- Establishing more formal communities with substantial funding to facilitate targeted R&D proposals, sector development, practical collaborations, within the newly-established Knowledge Transfer Network and Knowledge Transfer Partnership programmes.
- Creating Centres of Excellence, perhaps in a process of competitive tendering.
- Creating Virtual Institutes, perhaps by directed funding at national development level.

But the question remains of how to build a head of steam rapidly. The answer is not certain but at least includes identifying enthusiasts, bringing them together and using public funding to make things happen sufficiently well that private funding is then attracted.

The products of marine biotechnology can enter many different markets. This may be the source of some of the problems perceived in making full use of the output of current UK marine sciences. Conventional technology transfer processes may not be appropriate for such diversity, because there is a combination of individual and largely uncoordinated contacts between researchers and industry, and the efforts of institutionalised technology transfer offices, which often lack the resources to map and broadly-place all the intellectual property arising in their institutions.

At the moment, except for the direct output of marine aquaculture, the major marine products are hydrocolloids and polymers that enter the food, health, laboratory and chemicals sectors. Although the pharmaceutical sector is seen as the significant high-value outlet for new products from marine organisms, it will still be useful to put some effort into analysing specific high-value opportunities in the more-conventional channels.

One route for creating a stronger link between a diversity of research and a diversity of user groups, in the UK context, would be the establishment of a network that focuses on new products and processes from Marine Bio[techno]logy. The new Knowledge Transfer programmes are likely to be appropriate for a marine biotechnology network or collaborative development project and this possibility can be explored with DTI.

Four relevant Faraday Partnerships exist: FIRST, which focuses on environmental remediation; Pro-Bio, which has biocatalysis as its theme; the Medical Devices FP (with reference to biomaterials of marine origin); and TechniTex, technical textiles, which has a healthcare component relevant to biomaterials.

In land-based agriculture, experience has been that building closer links between research and potential markets is possible, using four different and complementary routes:

- Pre-competitive R&D platforms.
- Technology transfer groups dedicated to a specific source sector, rather than use sector, an example being PBL[121] and the John Innes Centre.
- Use-sector organisations, usually funded by industry levy or subscription, with one specific remit as the introduction of new technologies for the benefit of the industry, examples being the Meat and Livestock Commission and the Potato Marketing Board.
- Producer co-operatives with a strong belief in science, of which the most successful in Europe is probably Limagrain SA of France.

The feasibility of establishing something similar for marine bio[techno]logy needs to be evaluated.

4.2 Financial Barriers and Challenges

Financial barriers and challenges to exploiting marine resources are manifold:

- The cost of carrying out marine research and bioprospecting, maintaining appropriate facilities and research vessels.
- The cost of establishing appropriate analytical, purification and manufacturing facilities for bioactives and other exploitable marine produce.
- The amount of grant funding for exploitation development, proof-of-principle and commercial prototyping..
- The availability of funds to market effectively the UK's activities in marine biotechnology and the outputs from marine resources
- The amount of seed-corn funds, venture capital funds and more serious investment funding for commercial start-ups based on marine resources and services.
- The presence or absence of fiscal stimulus for sustainable exploitation and business establishment in this sector.

121 indeed, PBL is expanding its services to offer IP consultancy and assistance to organisations outside plant breeding (S Armfield *pers. comm.* 2004)

The challenges of securing technology transfer and exploitation encompass most of these issues.

Technology transfer and exploitation

Of course the scale and scope of technology transfer activities go hand-in-hand with how well-established an institution is. **Table 48** shows a list of the innovations from Australian marine science research highlighted in the Australian organisation AIMS's 2002-2003 report[122].

TABLE 48: AIMS INNOVATIONS COMMERCIALISED OR USED IN 2002-2003

TECHNOLOGY	PURPOSE
Handheld corers	assessment of reef damage (used in Saudi Arabia)
Video-capture tools	non-intrusive assessment of fish abundance and diversity
Interactive computer tools	identification of corals world-wide
Rapid Web Report for monitoring data on Great Barrier Reef biodiversity	general public information
Data-mining and Bayesian decision tools	Causality attribution in analysis for research and management decisions
Prototype simulation models for reef biota	used in discussing reef futures and policies
Manual for coral reef management	socio-economic focus for practical management, aimed especially at developing countries
Automatic weather stations	monitoring weather conditions on Great Barrier Reef and making results available in real-time via AIMS Web (used by recreational fishers)
Atlas of surface temperatures	mapping sea around Great Barrier Reef to correlate with bleaching of corals
Baseline data on nitrogen cycling	greater understanding of nutrient cycling within Great Barrier Reef
Global model for water recycling	application in agricultural communities
River logger system	measures levels of sediment and water quality
Tidal prediction data	used by cargo loaders-unloaders
Web-based tools for database access	for water quality and chlorophyll levels
New aquaculture technologies and breeding protocols	for prawn culture
Tests for detection of saxitoxin	use in seafood and drinking water
Herbicidal bioactives	under development for problem weed control
Assay for symbionts	real-time assay gauges abundance of different zooxanthellae within host tissues

It can be seen that, in addition to practical 'bits of kit' and potential bioactive products, there is a focus on the intelligent use of IT, including computer-based and web-based systems or tools.

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122 *Annual Report 2002-2003* Australian Institute of Marine Sciences, available as a .pdf file from www.aims.gov.au

However, an important point for UK is that, as one respondent to our project survey expressed it:

> *"The tricky bit is not to have ideas, but to keep a flow of them going into the market, so as to capture the necessary scale-economies."*

To do this requires optimism and adequate funding, not only for prototyping, proof-of-concept and product development work, but also for commercial activities such as start-up establishment, licensing-out activities and business consolidation.

Investment climate

There are some apparent success stories to cheer the investment community. The support of Nereus Pharmaceuticals in the USA by the Novartis Foundation is one such; but this company has a very strong scientific founder in Bill Fenical, whose reputation adds gravitas to the investment opportunity. More obvious are the difficulties and the eventual failures of what look like very encouraging enterprises.

CalBioMarine Technologies Inc, previously mentioned in the USA section, is one such. By 2003 CBM had raised $4.7 million through SBIR grants and contracts, and supply arrangements with private companies. The SBIR grants were with important marine biotechnology institutes such as the Scripps Institution of Oceanography and Florida Atlantic University. CBM sought $6 million further funding to maintain its operations, failed to do this and closed down its laboratories and collaborations. The founder, Dominick Mendola, has continued the business at a very much reduced level in order to keep the IP in play.

The problems with this company appear to us to be three-fold and to have lessons for UK companies:

- over-reliance on government grants for process development;
- insufficient private and institutional investment from early milestones onwards;
- lack of clarity in whether CBM had a monopoly or even favoured position on the supply of bryostatin and ET-743 (the Spanish company PharmaMar appears to be developing these independent of CBM).

4.3 Operational Barriers and Challenges

Some of the operational barriers and challenges come from the characteristics of marine bio[techno]logy itself, and the way that knowledge has evolved – for example:

Getting to the sites

Although there is some interesting work that has investigated organisms and environmental cycling in coastal sediments and in salt-laden soils in bays, most marine biotechnological and biodiversity research depends on getting out to sea and then into extremophile territory. This implies use of research vessels, submersibles and extreme-conditions remote-access vehicles. The NERC has recognised some of the difficulties by funding the development of Professor Adam Schultz's collection robot for deep-sea samples.

Commercial and scientific intelligence

There have been very few formal UK Trade or Scientific Missions on marine biotechnology (or exploitation of marine resources). There are clearly many opportunities for dedicated scientists to interact informally and exchange or gather useful information, at the regional and international conferences that take place. However, the most recent DTI-supported mission concerning marine biotechnology [for which I have found a report] was to Canada in 1998 and in the event was not about biotechnology at all, but about advanced aquaculture management and farmed and wild-caught fish and shell-fish processing.

There is clearly a gap here that needs to be addressed and it is encouraging that there may be a mission to China later in 2004 to examine marine biotechnology activities there.

Bioprospecting and environmental issues

Sustainability of marine resources is a topic that is of growing and unavoidable importance. In the USA, three challenges are seen in making use of marine resources[123]:

- access to resources and organisms
- biosafety aspects
- intellectual property rights

The Convention on Biological Diversity (1993), with its requirements for sustainable development of natural resources and sharing the value of benefits of exploited discoveries with the owners of the originating material, has taken over from the Law of the Sea Convention (1982), which required only exchange of scientific information and inclusion of local scientists in bioprospecting missions.

There are also areas of uncertainty created by different laws governing different compartments of marine biotechnology activity, from inland waters, through coasts, intertidal land, shallow coastal waters, shelf waters to economic exclusion zone areas, not to mention the aspects of seabed-surface versus below-seabed-surface. Added to this is the natural uncertainty caused by marine organisms not respecting such boundaries, which has led to definitions in UK law circumscribed by the word ‘sessile’, since only if organisms are fixed in place can the correct compartmentalised law be applied to them.

More recently, as a result of a legal case in 1999 brought by Greenpeace against the UK Government, the EU Birds and Habitats Directives were required to be extended to cover the entire ‘200 mile limit’ and not just the UK’s territorial waters, as the government had previously interpreted them. Consequently, the identification and selection of marine Special Areas of Conservation (SACs) and Special Protection Areas (SPAs) was required, as part of the Offshore Natura Project[124]. WWF-UK has been prominent in campaigning for the Darwin Mounds to be better-protected. These are a collection of sandy and cold-water *Lophelia pertusa* coral mounds 185 km off Cape Wrath, north-west Scotland, about 1000m

[123] see http://www.oceanservice.noaa.gov/websites/retiredsites/natdia_pdf/18udel.pdf

[124] *Nature 2000 in UK Offshore Waters*, Joint Nature Conservation Committee

down, with some extremely interesting marine biota including giant foraminifera. The area was originally surveyed as part of the activities of the Atlantic Frontier Environmental Network (AFEN). AFEN is a consortium of offshore industries and the environmental survey programme is an essential part of risk assessment for new drilling, platform and pipe- or cable-laying activities. During the course of AFEN's work in 1996-1998, about 120,000 zoological specimens were retrieved and presented to the National Museums of Scotland[125].

The George Deacon Division at University of Southampton, with funding from UK DTI, carried out deepwater surveying that demonstrated trawler damage to this area[126]. Stoppage of trawling in this area has been secured under UK Fisheries action. However, the situation does raise the question of how access can be managed for bioprospecting and 'valorisation' purposes to such unique sites, where one may also suppose unique bioactives, enzymes, peptides etc. might be found. As it happens, there may well be many more of these sites to be found in the north east Atlantic – Norway also possesses similar *Lophelia* reefs.

A recent report from the United Nations University in Tokyo Japan highlights concerns that there are no controls on bioprospecting in areas such as the Antarctic[127]. The writers, opponents of uncontrolled exploitation, point to 92 patent filings in USA and 62 filings in Europe relating to Antarctic organisms and the difficulty of reconciling the Antarctic Treaty System (ATS) and commercialisation activities.

Among the key issues not addressed by current treaties, according to the writers, are:

- Who owns the Antarctic genetic resources?
- How can scientists working in the Antarctic Treaty area legitimately acquire these resources?
- What measures do scientists have to take to protect these resources?
- Is benefit sharing feasible and, if so, with whom?
- Who owns the commercial products resulting from these resources?
- What is the relationship between the ATS and other international agreements e.g. the Convention on Biological Diversity (CBD) and the UN Convention on the Law of the Sea (UNCLOS)?
- Does bio-prospecting contravene Article III of the ATS which stipulates that:
    - Information regarding plans for scientific programs in Antarctica should be exchanged.
    - Scientific personnel should be exchanged between expeditions and stations.
    - Scientific observations and results should be exchanged and made freely available.

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[125] see *Marine Sample Collections, their value, use and future*, IACMST July 2001, pp 20-21

[126] see http://www.externalrelations.soton.ac.uk/publications/resrep00/deansreportscisoc.htm

[127] *Biotech 'cold rush' threatens pristine Antarctic*, Ian Sample, *Guardian Weekly* February 5-11 2004, p2; also see http://www.ias.unu.edu/binaries/UNUIAS_AntarcticaReport.pdf

Key recommendations from this report include availability of information on bioprospecting and commercialisation plans involving Antarctic biota, laying down a definition of bioprospecting and deciding on benefit-sharing schemes. Any action taken as a result of this report will undoubtedly have an impact on other kinds of collaborative bioprospecting efforts.

The *Study into the Legal Framework for Marine Biotechnology Development in the UK*[128], commissioned by Defra and the Foresight Marine Panel's Marine Biotechnology Group as a companion to this one commissioned by DTI and SWRDA, discusses some of the issues that will need to be considered as a matter of UK marine rights in the near future. It highlights the uncertainties in moving forward with assertion of UK rights in the Economic Exclusion Zone (the '200 mile zone').

One major consideration is that asserting rights to marine bioprospecting, and therefore instituting a system of controls on bioprospecting, may also bring into play the need for exploitation to confirm to the Biodiversity Convention, so that there is profit-sharing in some way with the 'owners' of the original material. Defra, in its press release[129], set out what might be interpreted as its policy, or approach, in this area:

> *"A major factor in developing marine biotechnology is the issue of the sustainable use of natural resources. It is vital that an industry is created that has a primary obligation to only develop bioproducts that can be supplied or manufactured in such a way as to prevent perturbation of the marine ecosystem or deplete living resources."*

Without investment in making the move from wild harvesting to managed exploitation in a clear and consistent way, there will be a severe brake on the exploration and utilisation of marine resources of any sort. When organisms can be farmed, this is not so much of a problem, although there are necessarily considerations of impact on the unfarmed environment. However, wild harvesting would undoubtedly have an appalling effect on natural communities of marine invertebrates and associated symbionts. Estimates, based on the actual tissue content of bioactives in sponges and tunicates, suggest that 1 tonne of *Ecteinascidia* sponges would be needed to extract 1 gram of ET-743[130]. Total synthesis is now possible and, indeed, is the only way PharmaMar SA would have been able to consider embarking on clinical development.

In the context of understanding what might happen with respect to bioactives, products from shark cartilage might make a good case study. There is certainly evidence for ever-increasing market demand and supply that appears to be rising to meet this, but very patchy estimates for the result on shark populations. Widely promoted through healthfood stores and other outlets for unlicensed medicinal 'food supplements', this material is claimed to prevent cancers and musculoskeletal disorders such as arthritis and rheumatoid arthritis. There is indeed scientific data showing that components of different cartilages, including shark, are anti-angiogenic *in vitro*, that is they suppress the growth of new blood

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[128] D Owen, 2004, for Marine Fore*sight* Panel, Marine Biotechnology Group, and Defra

[129] see http://www.defra.gov.uk/news/2004/040305b.htm

[130] see M Vatalaro http://www.nih.gov/news/NIH-Record/09_19_2000/story04.htm

vessels, and several pharmaceutical companies are developing products based on this concept, including the Canadian company Aeterna. It is still not clear if the *in vitro* activity will be translated into a definite *in vivo* efficacy. In the meantime, large numbers of sharks are caught, purposefully or as a by-catch[131], their cartilage is harvested and sold as a health supplement. The exact numbers are unknown but one estimate suggests over 200,000 were being caught annually in the 1990s in US waters and UMN data suggests that millions of sharks are killed annually as by-catch. Sustainable use of any potential medical benefits demands an approach such as the culture of shark cartilage cells in bioreactors or creation of nature-identical molecules or analogues by chemical synthesis, as can be done for squalamine, another potential anti-cancer and anti-angiogenic agent derived from shark liver.

Some approaches to consistent and clear bioprospecting policies have already been made in New Zealand[132]. The paper defines bioprospecting to include a deliberately broad range of activities:

- The examination of biological resources for features that may be of value for commercial developments.
- A targeted search for such features.
- The downstream testing and development activities following discovery of a useful substance (for the purposes of the discussion paper, and because the greatest benefit from the initial discovery is obtained at these stages).
- Manufacturing and marketing results of bioprospection.

Finally, some of the stakeholders in the UK concerned with the sustainable management of the environment and the conservation of wild resources are shown below.

Any proposals to make use of the UK's marine resources for gain, even if carried out by UK entities and not international bioprospectors or companies, licensed or otherwise, would require some approval, explicit or implicit, from such bodies, or an understanding that exploitation activities would not be impeded.

The European Commission's white paper on a strategy for the marine environment[133] may be a brake on bioprospecting and on applications of marine biotechnology or may encourage cautious and well-controlled development. This paper proposes a number of objectives and actions to tackle the range of issues facing Europe's marine environments and the plethora of existing legislation and marine conventions that in some cases are confusing or duplicative. Relevant overarching objectives are to halt biodiversity decline by 2010, ensure a sustainable use of biodiversity and approach concentrations of hazardous substances that are near background for naturally-occurring and almost zero for man-made synthetic compounds.

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131 the FAO estimates the shark catch to have reached 760,000 tonnes by 1996 – see http://www.fao.org/WAICENT/OIS/PRESS_NE/PRESSENG/1998/pren9861.htm

132 *Bioprospecting in New Zealand, discussing the options*, Ministry of Economic Development November 2002

133 *Towards a strategy to protect and conserve the marine environment*, COM(2002) 539 final, 2nd October 2002, Commission of the European Communities

TABLE 49: SOME UK STAKEHOLDERS IN THE ENVIRONMENTAL SECTOR

Advisory Committee on the protection of the sea
The Crown Estates Commissioners
Defra
English Nature
Friends of the Earth
Greenpeace
The Invertebrate Conservation Trust
The Joint Nature Conservation Committee
Marine Conservation Society
The OSPAR Commission
Royal Society for the Protection of Birds
Scottish Natural Heritage
The Wildlife Trusts
WWF-UK

However, as previously noted, objective 2 also calls for preventing the introduction of genetically-modified organisms, which removes one of the more powerful tools that the marine biotechnologist might be able to apply to questions of marine environmental pollution and bioremediation. This underlies our suggestion that closed bioremediation systems might be one answer; selection of appropriate marine organisms, improvement of their remediation capabilities and use of enzymes of marine origin are all potential responses to the challenge of enhancing and protecting the marine environment.

Invertebrates or microbes

There is increasing evidence that the bioactives of medical interest that have been found in marine invertebrates such as sponges, tunicates, molluscs or bryozoa have most likely are produced by symbiotic microbes or have accumulated as a result of eating marine micro-organisms. Although this raises a more promising possibility as far as mass-production of such bioactives is concerned, it also means that more investigative effort is needed to pin down precisely which organism is the source of a potential therapeutic.

A perceptive comment[134] underpins the need to go beyond the obvious:

> *"Since 1995, there are signals of decreased interest in the search of new metabolites from traditional sources such as macroalgae and octocorals, and [stabilisation for] marine sponges. On the contrary, metabolites from micro-organisms is a rapidly growing field, due, at least in part, to the suspicion that a number of metabolites obtained from algae and invertebrates may be produced by associated micro-organisms."*

This issue of symbionts versus hosts is illuminated by work carried out at the Center for Marine Biotechnology and Biomedicine (CMBB), Scripps Institution of

[134] Alphonse Kelecom in Anais da Academia Brasileira de Ciências 2002 74 (1) 151-170

Oceanography, University of California San Diego. They have studied sponges containing cyanobacteria, filamentous bacteria and heterotrophs. The cyanobacterium *Oscillatoria spongeliae* can contribute up to 50% of the weight of the sponge *Dysidea herbaria*. In a sample from the Great Barrier Reef, the cyanobacteria produced chlorinated amino acid-derived metabolites and the sponge produced terpenes. In samples from Palau, Micronesia, the cyanobacteria produced polybrominated biphenyl ethers.

The ascidian *Polysyncraton lithostrotum* produces namenamicin, a highly potent cytotoxic antibiotic that could be a cancer blockbuster. This is clearly produced by a symbiont, but over 50 different types of organism have been recovered or detected in the invertebrate host, including 16 different *Micromonospora* isolates. Wyeth Ayerst did not find the namenamicin-producer; however, it was discovered that one of the *Micromonospora* produced lomaiviticins, equally cytotoxic.

In the sponge *Theonella swinhoei*, complex bicyclic peptides are produced by filamentous bacteria and swinholide A, a potent cytotoxic agent, was found in a fraction containing many unicellular heterotrophic bacteria: the sponge itself appears to produce no useful bioactives. However, some invertebrates may be sources of bioactives themselves – the sponge *Oceanapia sagittaria*, which is relatively symbiont-poor, produces the pyridoacridine alkaloid dercitamide in high yield. Making further use of bioactives from marine invertebrates clearly requires some stringent work-up on the source of the interesting molecules before serious managed industrialisation can take place.[135]

Isolation and identification

There continue to be problems with the isolation of marine microbes and their culture under laboratory conditions in order to identify them accurately and study their metabolism. This is mainly because of the extreme difficulty of reproducing the correct conditions for growth, whether it be temperature, pressure, nutrient sources or the presence of other necessary microbes. The use of gene probes and advanced analytical techniques has revolutionised the ability to detect and identify microbes in marine samples and is allowing the complex mixtures of microbial symbionts in marine surface or extremophile films and invertebrate hosts to be characterised. Whether it is therefore worth the effort to spend time and money on trying to culture the 'unculturables' is to be questioned.

Dereplication is an important aspect of making the isolation and selection process more efficient, and some effort should be spent on ensuring that the right equipment and techniques are available to do this effectively and cheaply and, if there are barriers to achieving these at the moment, funding should be provided to ensure that new techniques can be developed.

Manufacturing and process

One of the greatest challenges to exploitation of marine resources is the development of reliable and inexpensive cultivation systems. It is certainly possible to farm microalgae such as *Dunaliella* under extensive conditions in tropical or sub-tropical areas and yield enough microalgal carotenoids to be profitable.

[135] see http://www.mrd.ucsd.edu/jf/

Marine seaweeds are to a large extent farmed. The question is how we can achieve similar economies of scale and cultivation in coastal or land-based mariculture under UK conditions. In warmer waters there is some progress in cultivation of tunicates and bryozoa (*Ecteinascidia* and *Bugula* respectively), and AIMS is supporting the aquaculture of bath sponges for Aboriginal communities in northern Australia, but controlled and consistent mass-production is still far away.

More promising are two avenues:

- To develop bioreactors that can be used to mass-produce the microbes that are increasingly believed to be the source of bioactives originally isolated from larger marine organisms.
- To identify the genes responsible for the bioactives of interest and transfer them to a suitable, well-established host such as *E. coli* or yeasts, and produce the bioactives under more conventional bioreactor conditions.

Implicit in the above is the need for advances in bioreactor and fermentation knowledge, and a tremendous increase in genomic and proteomic research activity related to marine organisms. Specifically, in the case of marine biotechnology, there is a need to establish and stabilise methods of isolation for organisms, genes and bioactives, identification and structure-elucidation techniques, processing and purification procedures, reliable and robust assay methods for bioactives and a manufacturing method that yields consistent products.

In addition to adequate facilities at each centre carrying out research into marine organisms as sources of useful products, it is essential to have at least one site with pilot production facilities, skilled bioengineering staff and practices that add value to research, produce materials for proof-of-concept work, identify specific issues in scale-up and devise ways of dealing with these. The addition of GMP capabilities immediately makes such a facility ideal for the production of new biopharmaceuticals for clinical use. This would, potentially, be a Centre of Excellence for Marine Bioengineering.

But this is clearly not enough. The marine micro-organisms that we need to deal with range from elusive endosymbionts to free-living marine moulds and actinomycetes. Over 98% of the known microbes cannot yet be grown successfully in the lab. There remain hundreds of thousands more microbes to be found. Although it is vital, in our view, to have a centre that can tackle the problems of culture, to rely on establishing the right conditions for managed mass-production of marine microbes creates a critical bottleneck in exploiting marine bioactives.

The other essential route, which has the potential to bring more products to market more quickly, is to make use of modern gene technology. At this stage, it is not possible routinely to isolate relevant genes from potentially-useful marine micro-organisms, transfer them to *E coli* or a yeast, and institute conventional bioreactor processing. Significant additional investment is needed in identifying and extracting candidate genes without the need to culture the organisms concerned.

4.4 Other Barriers and Challenges

Warm-water versus cold-water

Most of the current high-value applications of products from marine sources have been generated from warm waters of the Pacific, the Caribbean or, in some cases, the Mediterranean. Proksch *et al*[136] suggest that this is because the grazing pressure from predators such as fishes is higher in tropical and subtropical seas than in any other ecosystem, leading marine organisms to develop many more of the defensive molecules that are of interest as bioactives. This clearly raises a question of how rich a source of bioactives the Atlantic and Arctic waters, only somewhat warmed by the Gulf Stream, might be. The success of the German Federal programme on natural products from the colder seas disproves this rather limited view.

Competition or Substitution?

Marine biotechnology is competing with other areas of scientific endeavour for the attention of funders and exploiters. How can marine biotechnology hope to compete with funding for the human genome and its outputs, for example?

In some areas, the outputs of marine biotechnology might be seen as too remote for end-users, either in application or in time-to-market. In the EU and UK, for example, scientists and industry have been encouraged to work with non-food crops in substantial knowledge and technology transfer programmes over the past 5-10 years. The UK's National Non-Food Crops Centre (NNFCC)[137], based in York, indeed aims at those industrial end-use sectors that marine biotechnology is trying to reach – chemicals, enzymes, process, pharmaceuticals, healthcare. In some cases, lack of response from these to approaches from the marine biotechnology sector may simply signify an overload of the systems in place for assessing potential in-licensing or co-development opportunities.

Another question that faces marine biotechnologists is whether they are looking to replace existing products and/or processes, or introduce something completely new. In the first case, there is the plus that end-users are being offered a step-wise improvement that they can easily grasp, in the second case, a leap of imagination has to be undertaken, sometimes difficult in the corporate context. In both cases, there is the minus that existing methods and mind-sets have to be changed.

Developing and energising a science-industry network or platform would enable dialogue between marine biotechnologists and potential end-users that would, if successful, evoke real needs and collaborative projects.

Another question is whether to go for the big target, the cancer therapeutic market, say, where both barriers to market and potential returns are high, or a definable small niche where a demonstration project might be more easily achieved. Examples here might be:

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[136] Proksch P, Edrada RA and Ebel R (2002) *Drugs from the seas – current status and microbiological implications*. Appl. Microbiol. Biotechnol. 59.125-134

[137] see http://www.nnfcc.co.uk/

- Replacement in the food glucomannan market of konjac flour, imported from Asia, by a marine source. Konjac sales in the EU are estimated at € 12 million (4000 tonnes at € 3000 per tonne), imported in high grade from Japan and in lower grades from Japan, China, Thailand and Indonesia.
- Using PUFAs extracted directly from marine microalgae as food additives, nutraceuticals and nutritional supplements for humans, animals and fish, rather than using fractionated fish oils; an additional benefit is that the microalgae provide their constituents already microencapsulated in their cell wall.

Global Warming and a new Ice Age

Models of climate change and ocean cycle dynamics suggest that Britain may experience not a general rise in temperatures but the opposite, as Arctic currents change and the Gulf Stream is deflected further south. Although this topic may well be a 'red herring', marine biotechnologists and those who are involved in exploiting marine resources might wish to consider what impacts there might be, the timescales and whether any realistic actions can or should be taken in the next 15 years.

4.5 Positive Aspects

Systems for technology streaming

BioBridge uses the term "Technology Streaming"[138] to describe the supply chain from creation of a scientific concept to the end-user in the market, as a combination of knowledge transfer, demonstration of application, technology transfer and successful embedding of new technology in a product. The concept is valuable because it encourages researchers at the start of the supply chain to think about other staging posts than the final output, the end-user who industrialises the research outputs. Effectively, a scientific researcher has to market the idea to everyone down that chain, not just the industrialist, or at least present the idea and its potential for application in such a way that others are persuaded to take it up. Tools in this process include technology mapping, feasibility prioritisation, pipeline risk analysis and other ways of trying to decide where to invest resources when the overall budget is somewhat inflexible.

The Technology Translator post attached to the NERC's M&FMB programme is a welcome example of a new approach to making use of scientific output and building links with end-user groups. Subject to post-programme evaluation, this activity could well become a model for other programmes of research funding.

UK's geographic and oceanographic situation

The UK has access to some very interesting coldwater and deepwater habitats. The Darwin Mounds have come to prominence recently, but are not the only areas of potential interest to marine biotechnology. Advantage could be taken of the environmental surveys undertaken by offshore operators, to set up ways of conserving living material that is retrieved, via the Atlantic Frontier Environmental

[138] ©BioBridge 2003

Network, and also to work with curatorial museums and the UK Offshore Operators' Association to gain access to the benthic materials that the latter retrieve during other types of operation. This is partly a contribution to taxonomic studies and to the Marine Life Information Network, and partly in order to get samples for further study without having to send research vessels out to get them.

Research vessels

Of the UK's 33 RVs and survey vessels, Charles Darwin, Discovery, Ernest Shackleton and James Clark Ross are world-class. Given the cost of maintaining research vessels and undertaking research cruises[139], the UK science community could try to make more use of MoD vessels and technology. It must be possible to design tools and protocols for sampling, storing samples, recording accurately the depth and position of collection and transmitting samples safely back to UK, either using appropriately-qualified scientific officers or through secondment of staff from marine organisations on specific voyages, depending on the perceived level of security risk.

Undersea vehicles are rather limited in Europe. The UK has the most advanced remote operating vehicle (ROV), based at the Southampton Oceanographic Centre, operating to 6500m. This does not require a large support vessel, making it more flexible than others in the EU. NERC has one autonomous underwater vehicle (AUV), capable of operating at 1500m, and the UK has strengths in sea-bed Observatories, which are widely regarded as being a constructive way forward in mapping and understanding the physical and biological environment around Europe.

National and International collaborations

The NERC's M&FMB programme appears to have been extremely successful at national level in creating a community of marine biologists and scientists who have begun to focus on two benefits: first, the additive power of effective networks, second, the validity of a drive to commercialisation. At a regional level, the most effective types of collaboration for UK researchers have been achieved through involvement in the European Union's Research and Technology Development Framework Programmes, such as the Marine Science and Technology programme MAST-III (FP4 1994-1998) and 'Supporting Marine Ecosystems' in FP5.

International collaboration is certainly helpful in increasing the chances of successfully exploiting a marine resource. Possible projects that positively encourage such collaboration might include making better and more strategic use of UK culture collections by sharing and screening arrangements, or managed prospecting of interesting habitats in concert with countries with complementary habitats[140]. During the survey of activities carried out in this project, however, it

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139 the report on *Marine Sample Collections*, IACMST July 2001, gives a figure of £150,000 for a 3-week cruise to collect 20 marine cores; this figure must be the minimum for a similar cruise for marine biotechnology and biodiversity purposes.

140 Dr J Oliver suggests, in *Marine Science Review, Report of Visit to Maryland & Virginia*, New Park Management June 2001, a possible collaboration between the Coral Reef Research Foundation and SAMS to "take advantage of the deep ocean sampling ability of Scottish marine establishments and their unique access to North Atlantic deep water sites".

seemed that the UK is comparatively poor at constructing international collaborations over greater distances; the Germans and the French appear to have more collaborations in place with the US, Australia, the Philippines, Thailand, Malaysia and so on, thus giving them access to a rich source of marine biodiversity. One exception would be the UK's involvement in the Antarctic programme MICROMAT.

In the context of pan-European projects, the network of European Marine Research Stations MARS is a very important and effective resource. Established in 1996, it includes over 40 stations from Svalbård within the Arctic Circle to the warm waters off Israel, Turkey and the Canary Islands. Co-ordinated from NIOO-KNAW Centre for Estuarine and Marine Ecology at Yerseke in the Netherlands, the UK members are Plymouth Marine Laboratory, Marine Biological Association of the UK, Plymouth, School of Ocean Sciences, Bangor, University of Glasgow Marine Biological Station Millport, Southampton Oceanography Centre and Dunstaffnage Marine Laboratory, SAMS. The MARS network has been successfully involved in three large-scale EU-funded projects, BIOMARE, M@RBLE and MARBENA.

The European fleet of research vessels, 181 including the UK's, is listed on the EurOcean web-site[141], as is an international schedule of research vessel sailings. One unexplored possibility is whether there is sufficient access to other vessels to allow them to be 'hired' to supplement UK activities.

Knowledge of what is actually in the sea and where, is fundamental to planning marine biotechnology activities and avoiding environmental and ecological damage. The Census of Marine Life (CoML)[142] is an unprecedented research programme with several components, that is assessing and describing the diversity, distribution and abundance of ocean life. The Ocean Biogeographic Information System (OBIS) is an internet-accessible database, the History of Marine Animal Populations project (HMAP) assembles comparative historical views of ocean life, providing time-series for projections from a current global census to the Future of Marine Animal Populations (FMAP), which integrates new biological knowledge with rapidly improving knowledge of continuous ocean movements. It is chaired by Professor Fred Grassle, of Rutgers University.

COML's sponsors are headed by the Alfred P Sloan Foundation, with funding from 7 other non-governmental foundations or organisations and support from 15 organisations in USA, Canada, Australia, Japan, Germany, Denmark, Sweden, Norway and the UNESCO IOC (Intergovernmental Oceanographic Commission).

HMAP is co-ordinated by the Centre for Maritime and Regional Studies in the University of Southern Denmark, Esbjerg. FMAP is co-ordinated from the Department of Biological Sciences, Dalhousie University, Halifax, Nova Scotia. OBIS itself is run from Rutgers University. There is also a DNA Barcoding Protocol, to attempt to classify all species.

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141 see http://ioc.unesco.org/eurocean/categories.php?category_no=23

142 see http://www.coml.org/coml.htm

The UK and Ireland are collaborating on a similar project for sharing of marine information, MarLIN[143], the Marine Life Information Network for Britain and Ireland, co-ordinated by the Marine Biological Association in Plymouth.

Sources of support – societies and associations

TABLE 50: SOME SOCIETIES INVOLVED IN MARINE BIO[TECHNO]LOGY

SOCIETY	COMMENTS
The European Society for Marine Biotechnology	founded in 1995
The Japanese Society for Marine Biotechnology	founded in 1989
The American Society for Molecular Marine Biology and Biotechnology	proprietor of the journal Molecular Marine Biology and Biotechnology, renamed Marine Biotechnology in 1999, published by Springer Verlag
The Pan-American Marine Biotechnology Association	founded in 1999
The Asia-Pacific Society for Marine Biotechnology (APSMB)	founded in 1995. Its object is to promote marine biotechnology for the scientists, industries and governments in the Asia-Pacific region. The APSMB has organised four international meetings, in Japan 1995, Thailand 1997, Philippines 1999 and at the University of Hawaii at Manoa, Honolulu in 2002.
The National Association of Marine Laboratories, USA	over 120 marine and Great Lakes laboratories from the US's islands of Guam, Bermuda and Puerto Rico to the arctic waters of Alaska, based in Solomons, Maryland
The European Network of Marine Laboratories	the MARS network covers marine stations from external and internal waters, including the cold and temperate waters of the Atlantic Ocean, North, Irish and Baltic Seas, and the warmer waters of the Mediterranean, Adriatic and Black. www.marsnetwork.org
The Marine Biological Association of the United Kingdom	premier organisation for marine biologists, with over 1200 international members, based in Plymouth UK
The International Society for Applied Phycology	Currently managed from the Università degli Studi di Firenze Italy, but due to shift Presidentship to Murdoch University, Australia, this society focuses on algae and is a good source of information on world-wide research in this area, as well as forthcoming meetings

EurOcean and the European Centre for Information on Marine Science and Technology appear to be promising fora or foundations for cross-European activity in marine biotechnology. However, a search on EurOcean's web-site for

143 see http://www.marlin.ac.uk/

"biotechnology" yields only one 'hit'[144] and it is clear that, at this stage, EurOcean is focused on the practicalities of marine research and its infrastructure.

Conferences

These are potent sources of networking opportunities and also for marketing the science and development going on in a country. In some cases, where conferences also include a well-attended trade show such as the US BIO's annual conference or the 4-yearly BioJapan conference, there is also an opportunity for group exhibition stands that bring together research, commercial and support activities. The UK biotechnology industry, Irish medical devices, Scottish biosector, Australian biotech and German BioRegio initiatives have done this very successfully in the past.

TABLE 51: SOME RECENT AND FORTHCOMING CONFERENCES WITH MARINE BIOTECHNOLOGY OR BIOACTIVE FOCUS

CONFERENCE	SITE	DATES
Marine Microbes – picophytoplankton taxonomy, diversity, ecology, genomics, physiology and molecular approaches	Gordon Research Conference, Roscoff France	6-11 June 2004
37th CIESM Congress	Barcelona, Spain	7-11 June 2004
2nd Symposium on Microalgae and seaweed products in plant/soil-systems	Mosonmagyarovar, Hungary	30 June-2 July 2004
39th European Marine Biology Symposium	Genoa, Italy	21-24 July 2004
10th International Symposium on Microbial Ecology	Cancun, Mexico	22-27 August 2004
First International Symposium on Marine Drugs	Ocean University of China, Qingdao	18-22 October 2004
1st Latin-American Conference on Algal Biotechnology	Buenos Aires, Argentina	25-29 October 2004
International Marine Biotechnology Conference	St John's, Newfoundland Canada	7-12 June 2005
2nd Congress of the International Society for Applied Phycology	Kunming, China	17-23 July 2005

Cross-discipline activities, networks and government-funded programmes within the UK

In order to maximise the potential of the marine biotechnology sector, links can be built with existing cross-discipline activities, networks and development programmes, many of which are government-funded or supported. In addition, the new support programmes operated by DTI should be evaluated for their relevance to the development and exploitation of the outputs of marine bio[techno]logy.

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[144] www.eurocean.org – *Marine biotechnology : an overview of leading fields*, the proceedings of the ESMB IXth meeting 12-14.5.02

Knowledge Transfer Networks and Partnerships

Knowledge Transfer Networks[145] are new DTI-supported mechanisms for encouraging and supporting effective information capture and flow across a sector, in order to bring research and application, academics and industry together. A KTN in Fuel cells has been established. Currently-open calls that have elements of potential interest for marine bio[techno]logy and resource utilisation are Bioprocessing, Advanced Composite Materials and Structures, Renewable Technologies, Disruptive Technologies in Electronics and Displays and Sensor and Control Systems.

The Knowledge Transfer Partnership[146] programme has been set up by Government to assist the development of links between academic research and companies and encourage the application of science and management studies in the commercial context. Funding is available to establish networks that will exchange ideas and information, work together on concept development, product development and problem-solving, and build pipelines for the easier translation of UK scientific innovation into the market. There are 11 sponsors of the programme including the research councils (BBSRC, PPARC, NERC, EPSRC, ESRC), government departments (DEFRA, DH, DTI) and national development bodies (Invest Northern Ireland, Scottish Executive, Welsh Assembly Government). The Knowledge Transfer Partnership (KTP) programme also allows graduates to become KTP Associates, continuing their doctoral or post-doctoral work on extension at a suitable company. The scheme brings together a number of previous programmes under one umbrella. Currently there are 185 projects in place, of which four have some resonance with marine bio[techno]logy activities, see **Table 52** below.

TABLE 52: UK KNOWLEDGE TRANSFER PARTNERSHIPS POTENTIALLY RELEVANT TO MARINE BIOSCIENCE

ACADEMIC PARTNER	COMMERCIAL PARTNER	TOPIC
Napier University	DB Projects	a new biocide
Hull University	EV Offshore Ltd	a real-time video camera for offshore monitoring
Queen's University Belfast	NA & SA McGarry	innovative high-performance pet foods
Manchester Metropolitan University	Micap Ltd	new micro-encapsulation materials and technologies

Faraday Partnerships

Faraday Partnerships were created under the aegis of the EPSRC and DTI. Review of best practice in the Faraday Partnerships (FPs) would benefit marine biotechnology activity from two perspectives – models for technology or knowledge transfer, and cross-institutional modular training. Informal approaches or linkages could be explored, to assess the potential of knowledge and

145 see http://www.dti.gov.uk/ktn/

146 see http://www.ktponline.org.uk/

technology transfer into marine biotechnology and use of FPs as conduits for outputs of marine biotechnology.

TABLE 53: FARADAY PARTNERSHIPS POTENTIALLY RELEVANT TO MARINE BIOTECHNOLOGY

NAME	THEME	WEB-SITE	COMMENT
FIRST	Innovative Remediation Science and Technology	www.firstfaraday.com	bioremediation, novel organisms, enzymes, sensors
FOOD PROCESSING	Developing the underpinning Materials, equipment and Process knowledge applicable to food processing	www.pera.com/foodfaraday/index.asp	marine products and food safety, processing
IMPACT	Innovative Materials Development and Product Formulation by the application of Colloid Technology	www.impactfp.org	marine colloids
INSIGHT	High throughput technologies for new product and process development	www.insightfaraday.org	screen or reactor processes
INTERSECT	Intelligent sensors for control technologies	www.intersect.org.uk	sensor technology, robotics
MEDICAL DEVICES	Medical Devices	www.medical-devices-faraday.com	biomaterials, scaffolds, tissue engineering
IMAGING	Digital Imaging	www.imagingfp.org.uk	virtuality, deep-sea imaging
GENESIS	Farm Animal Genetics and Genomics	www.genesis-faraday.org	genomics in aquaculture – parallels
IMSE	Industrial Mathematics and System Engineering	www.smithinst.ac.uk	modelling, algorithmic profiling
INREB	Integration of new and renewable energy in buildings	www.inreb.org	maybe H2 or renewable energy units
MINI-WASTE	Novel Technologies and processes for the minimisation of industrial waste	www.mini-waste.com	marine-origin materials
PACKAGING	Practical Innovation for fast-moving consumer goods (fmcg) packaging, its manufacture and supply	www.faradaypackaging.com	marine-origin materials
PINPOINT	Global navigation satellite systems (GNSS) applications	www.pinpoint-faraday.org.uk	biodiversity mapping
PLASTICS	Enabling research to meet the critical technological challenges of the plastics sector	www.faraday-plastics.com	new materials, biocatalysts, remediation
PRIME	Smart Products (products with inter-dependent mechanical and electronic parts)	www.primefaraday.org.uk	nanostructures, novel biocatalysts, piezophile molecules
PRO-BIO	Bio-catalytic processes for manufacturing	www.pro-bio-faraday.com	novel enzymes
SMART OPTICS	Smart Optics	www.smartoptics.org	advanced marine materials, nanostructures
TECHNITEX	Technical textiles	www.technitex.hw.ac.uk	marine-origin fibres, materials

LINK programmes

These are under the aegis of the Office of Science and Technology at DTI, with funding from other Government departments, research councils and organisations, who may then act as programme co-ordinators. LINK programmes that are still open and that may be relevant to researchers and companies working in marine biotechnology include:

TABLE 54: LINK PROGRAMMES OF INTEREST

PROGRAMME	CO-ORDINATOR	RELEVANT TOPICS
Advanced Food Manufacturing Programme	Dr Christina Goodacre DEFRA T: 020 7238 1517	sensors, control of contamination, manufacturing that translates good nutritional science into nutritionally-enhanced products, sustainable manufacturing technologies (decreasing waste, energy use, impact etc) Jointly funded by DEFRA, SEERAD, BBSRC and EPSRC
Food Quality and Safety	Dr Christina Goodacre DEFRA T: 020 7238 1517	Raw Materials Quality, Food ingredients, food safety and materials science, Quality and safety measurement Jointly funded by DEFRA, SEERAD and BBSRC
Earth Observation	Earth Observation Team, NERC/BNSC T:01793 411752	integrated ecosystem management, coastal zone management, improved systems for aquaculture, non-renewable resource management Jointly funded by DTI, NERC and Dept of Environment
Health Technology Devices Programme	Department of Health T: 020 7972 5645	new biomaterials, new devices to reduce NHS costs or enhance patient care, non-pharmaceutical approaches to improved patient care Jointly funded by Dept of Health with other appropriate funding

Environmental initiatives – BIO-WISE

The widespread belief that marine micro-organisms may be able to provide novel tools for environmental monitoring and clean-up suggests that use might be made of the DTI-supported BIO-WISE initiative, which has very successfully brought practical experience of bioremediation into the UK's industries and embedded biotechnology in many places where it would otherwise not have gone. Marine microbes and potentially-useful bioactives, enzymes or other materials could be eligible for similar applied projects. Although drawing to a close in its present form in December 2004, a Bio-club electronic forum has been set up at www.dti.gov.uk/biowise to help grow networks. An Industrial Biotechnology Task Force has been set up and has been invited by DTI's Bioscience Unit to suggest areas and actions for DTI's Technology Strategy and its support Programmes. Access to information and to contribute to the discussion is via the Bio-Wise and Bio-club sites, which require registration.

DTI Grants for Research and Development

These have replaced the SMART scheme and include funding for individuals and SMEs to research and develop technologically innovative products and processes, the 'Grant for Research and Development', and support for businesses with concepts for innovative products, processes or services who need help with taking it forward successfully, the 'Grant for Investigating an Innovative Idea'[147].

The above DTI-supported programmes seem eminently suitable for building the UK's marine biotechnology sector and making best use of its outputs.

Proof-of-Concept Fund (PoCF)

This is a specifically Scottish funding programme[148]. Marine biotechnology is not a specific target but there are at least 8 projects in which marine bioactives could have been used as research materials. These include biocompatible coatings at Aberdeen, biocides at SAMS, osteoclast inhibitors at Aberdeen, new high-throughput screens at Dundee, new high-throughput screens for cancer at the Beatson Institute Glasgow, study of extracts from natural sources at Glasgow, anti-E coli materials from natural sources, and oral immunisation at Strathclyde. Of these, the 'Shinkanco' project on extracts from natural sources at Glasgow has a collection of about 6,500, of which a few dozen are marine from overseas[149]. By promoting the marine biotechnology research sector and encouraging additive networking, it might be possible to embed some aspects of marine bio[techno]logy into other projects within the PoCF programme.

Practical networking

There is a need to identify the technology gaps that are present and use existing achievements from other areas to benefit marine biotechnology. These might include supercritical carbon dioxide for extraction of bioactives and other materials from organisms, as is already routine in the plant extract and food industries (instant coffee, for example) and as has already been developed by the US company Aphios for marine and other nature-origin bioactives. From reviewing the status of marine biotechnology in the UK and the perceived gap between research outputs and industrial uptake, it would seem sensible to explore whether a Knowledge Transfer Partnership could be funded, which could identify suitable collaborative projects, ultimately across the breadth of sectors to which marine-derived materials could contribute.

In addition, local and regional networking helps to identify fruitful sources of knowledge and technology for transfer. Certainly, regional networks could be approached to sensitise them to the exploitation potential of marine resources.

Regional biotechnology networks and support organisations

These can be the first port of call for scientists investigating industrial opportunities and companies wanting to know more about local research relevant to their needs, as well as support programmes and funding for business and product

[147] see http://www.businesslink.gov.uk/

[148] see http://www.scottish-enterprise.com/sedotcom_home/sig/academics/proofofconceptfund.htm

[149] T Stone, A Harvey University of Glasgow, *pers. comm.* 2004

development. For general business help, local BusinessLinks are also important[150].

TABLE 55: SOME REGIONAL NETWORKS AND SUPPORT ORGANISATIONS

NAME	RÔLE	WEB-SITE
Bio Sci North	works with One North-East (RDA for NE England)	www.biosci.co.uk
BioDundee	based on University of Dundee's activities in supporting, promoting and spinning-out its bioscience activities; a collaboration between public, private and academic sectors	www.biodundee.co.uk
BioElf	previously Western Biotech, a combination of Universities and NHS Trusts, funded by a DTI BEP II Award and now memberships, focusing on biotechnology and healthcare in the SW Peninsula of Devon and Cornwall, helping to identify, protect, exploit and manage innovations arising in the region	www.bioelf.org
BioNow	the Northwest's support, promotion and economic development organisation for biosciences and biotechnology	www.bionow.co.uk
Bioscience York	supporting development and expansion of healthcare and biotechnology activities with the aim of establishing a self-sustaining cluster and centre of excellence	www.biosciencevork.org.uk
ERBI	began as a DTI-supported regional network and is now a membership company, supporting and promoting the East of England's biotechnology activities and managing business development and strategy projects with funding from development agencies and the EU	www.erbi.co.uk
I10	a collaboration between 10 HEIs in the East of England, to pool their resources and expertise and offer a co-ordinated response to industry needs, via a web-based portal	http://www.i10.org.uk
London Biotechnology Network	a forum for interchange and networking, based in London with regular meetings; a relatively recent response to the realisation that biotechnology activities in London and the immediate surroundings were fragmented, now in its successful 5th year	www.londonbiotechnology.co.uk
MerseyBIO	working with the life sciences sector on Merseyside and creating a community network	www.merseybio.com
Oxfordshire BioScience Network	was Oxford Biolink, is managed by Oxford Brookes University and promotes information exchange across the Oxfordshire biotechnology cluster	www.uk-extranet.com/oxbn
RDAs	Regional Development Agencies: Advantage West Midlands, East of England, East Midlands, London, One North East, North West, South East, South West, Yorkshire Forward	www.consumer.gov.uk/rda/info
Scottish Enterprise Biotechnology Group	consists of Scottish Enterprise, Highlands & Islands Enterprise and SE's network of 12 Local Enterprise Companies in Scotland; the Group assesses and funds individual projects to assist Scottish companies and institutions to develop products and businesses as well as supporting export activities	www.scottish-enterprise.com/sig-biotechnology
SEEBIO	the South East England bioscience portal for linkage between the region's industrial and academic biotech communities	www.seebio.net
Syben	The South Yorkshire Bioscience Enterprise Network, a joint public and private sector initiative	www.syben.org

[150] see http://www.businesslink.gov.uk/bdotg/action/home

5. A SWOT ANALYSIS OF THE PROSPECTS FOR UK MARINE BIOTECHNOLOGY

5.1 Introduction – Previous Workshops in Scotland, Spain and UK

Conducting a SWOT analysis was a specific requirement for this project. This exercise has in fact been undertaken previously on several occasions, with the output shown below.

Marine biotechnology strategy in Scotland

A previous workshop held in Scotland in October 2001 in the context of the prospects for marine biotechnology in the UK produced a SWOT analysis shown in a summarised form in **Table 56**.

TABLE 56: STRENGTHS, WEAKNESSES, OPPORTUNITIES AND THREATS – SCOTLAND 2001

STRENGTHS EXPRESSED	**CURRENT STATUS/COMMENTS**
Marine biotechnology as applied to the UK has a tremendous history and there is a lot of enthusiasm for applied marine science and marine biotechnology	this still pertains and can be capitalised upon; the NERC M&FMB programme has provided some good impetus in this area
There are many young people already involved in marine biotechnology and as, a result of the lack of defined training courses in marine biotechnology, there is a demand for more people with this type of expertise.	courses are developing that focus specifically on marine biotechnology and bioactives (UHIMI, HWU, for example) and can be built on
Though the UK research base for marine biotechnology is behind Asia and Japan, we are not so far behind we cannot catch up and overtake; there is good industrial support and Enterprise support in Scotland	NERC M&FMB programme has harnessed research talent and produced important within-UK momentum; the other regions are still way behind Scotland in terms of focus on marine bio[techno]logy
Culture collections of marine biotechnology in other countries are well known; in the UK our resources are just as good and we are especially skilful at natural products chemistry	marine-relevant collections are still too dispersed though move of Windermere collection to SAMS provides new opportunities
Geographically we are well positioned and there are world class strengths in potential UK and world markets; the system is flexible and supportive in the UK	too much of a gulf still between science and market, and NERC and DTI
WEAKNESSES EXPRESSED	**CURRENT STATUS/COMMENTS**
There is lack of fundamental knowledge in marine biosciences.	this will always be the case; the need therefore is to focus on the crucial areas of knowledge lack
Marine biotechnology may not be seen as a crucial area, either of academic science or as a science that has made a difference to the public.	whole-sector science marketing or 'branding' is required to achieve this
Marine biotechnology needs more focused public sector funding, and co-ordinated funding for particular areas; for companies involved in development, support funds come too slowly from the public sector.	without a firm focus on the viable opportunities for joining science and the market, support funds cannot be captured
We need to find the right way to get the media to help marine biotechnologists capture the public imagination; locally and nationally not enough is heard about this work	fellowships for science journalists might be a way forward; more profile with the Royal Institution perhaps?

TABLE 56: CONT

WEAKNESSES EXPRESSED	**CURRENT STATUS/COMMENTS**
Insufficient infrastructure in key areas such as cancer screens – UK researchers have to go to e.g. USA for capacity and expertise.	still the case, though infrastructure resource inventory is required, with knowledge of spare capacity and access-sharing potential
Other countries e.g. Germany have a higher proportion of research funding going into marine biotechnology than UK	not wholly relevant: preferable to benchmark quality of output and economic development based on research investment
OPPORTUNITIES EXPRESSED	**CURRENT STATUS/COMMENTS**
The UK has access to diverse habitats and can make the most of these resources	requires active agreements cross-discipline and with other activities to make the best use of access possibilities, otherwise resources will be eaten up too quickly
UK products and services in marine biotechnology such as biofouling, pollution monitoring and IPR services have a global market and the potential for export is enormous	let's get some success stories
In order to justify funding the UK needs key niche markets such as in marine biochemistry	finding the uptake within a market requires active prospecting and matching needs to capabilities; market size alone is not a reliable indicator
Schemes such as Proof of Concept, DTI R&D and Innovation Awards and venture capital are important for development and exploitation	these are indeed vital bridges between science and industry – what can be devised that is Marine Biotechnology specific?
The ECMB is an opportunity for all UK, with the potential to overtake other activities in Europe and become a world-class institute; there is a greater willingness to commercialise and it is much more possible for small companies to set up within the ECMB	will of course be watched closely over next 3 years
The science base can be used to raise public awareness of the good that marine biotechnology can do e.g. bioremediation	requires a concerted effort and perhaps a practical programme (Bio-Wise type) in which marine biotechnology can be embedded
THREATS EXPRESSED	**CURRENT STATUS/COMMENTS**
Developments in other countries are developing apace; if the UK does not take marine biotechnology forward then we will be missing an opportunity.	make use of our strengths!
There is definitely a lack of Research Council support in this area; if there was a programme manager promoting marine biotechnology to broad life sciences and engineers then this would be good.	cross-council co-ordination would be an advantage if feasible; the next best thing is projects which more than one council and funding body can buy into
Even after the effort of setting up a company, the IPR may be bought out and disappear overseas.	this is always a risk; if persistently true in the marine biotechnology sector, reflects inappropriate or inadequate support mechanisms that have failed to allow a start-up to reach critical survival mass

This is, of necessity, a starting point for any analysis that seeks to underpin future strategy, and we can ask ourselves how far forward we have gone in the relatively short time since then.

The column 'current status/comments' in the tables above are our views, based on information gained during the study.

In conclusion, this output is not historical or superseded; most of it is still current.

Brainstorming for Europe – Matalascañas 2003

A symposium on Marine Biotechnology: Basics and Applications was held in Feb-March 2003 in Matalascañas, Spain, at which a special multi-stream brainstorm session was convened, to pose and answer the question 'What to do in Marine Biotechnology'. The output from this is more in the nature of Opportunities than threats or weaknesses, but again there were some common conclusions that have an impact on a development strategy for marine biotechnology.

The general output was as follows:

- basic and applied aspects of marine biotechnology cannot be separated, but the *raison d'être* is application
- there are a number of philosophical issues to do with mutual respect amongst scientists of different disciplines, respect for the environment manifested through marine biotechnology, a need for more open-handed financial support and need for market-oriented approaches to application
- the basic science projects that excited most support were
- using marine biotechnology to elucidate cancers, and
- developing the genomics and proteomics of symbionts
- the applications that excited most support included
- antibacterial compounds for multi-resistant bacteria
- an underwater taxonomic DNA chip, and
- anti-HIV drugs
- the 'wildest dreams' developments that received the most support were
- non-stick cells as a monolayer for ships' hulls
- molecules that are anti-ageing
- a marine-derived product for erectile dysfunction
- a 'peace pill' from the sea
- 'green functional fish' containing photosynthesising symbionts

Ideas were also canvassed in more specific sectors including

Phototropic organisms, leading to practical suggestions for

- improved photobioreactors, including roof-top and continuous fermentation/harvesting types
- genetic improvement of algae for managed production
- creative ideas about changing heterotrophs into phototrophs, using algae for manufacture of haemoglobin and farming diatoms for industrial use

Heterotrophs, leading to the recommendations of

- much more emphasis on cultivation of 'unculturables'
- concentrated focus on using marine organisms for bioactives, enzymes and other components
- more investigation and application in aquaculture as foods and in environment and bioremediators

Invertebrates, where the emphasis was on

- bringing invertebrates into culture as cells or whole organisms
- understanding more about sponge transgenesis and virology
- applying more resource to genomics, proteomimics and metabolomics of invertebrate-symbiont assemblages

Many of these ideas, already started in some of the European support projects, will undoubtedly surface in future programme proposals.

Marine biotechnology strategy in UK – this project

As part of this project, we held a workshop/brainstorm in March 2004. The full report is given in Appendix 1, and the general output is summarised here:

Perceived problems and weaknesses

- There is a lack of understanding of what the sector is and an issue of positioning – better marketing of the science is required.
- Lack of continuity of funding is a real issue, as is lack of connectiveness at research council and higher levels; more practically, scientists often don't have enough knowledge of all the possible sources of funding and how to get the funds from them.
- An effective cross-discipline networking is lacking.
- Existing and past research support programmes have never had exploitation as a key goal and research is still not well linked to commercial exploitation.
- The landscape has changed since bioprospecting began, when molecules with new activity seemed eagerly sought after; big pharma now appears to see little added value in the 'natural' label and a barrier to uptake of bioactives is lack of appropriate data on activity.
- There are problems with an over-emphasis on regional economic development, possibly because maritime and sailing businesses are so heavily-represented in the marine sector – for marine biotechnology, job creation does not need to be associated with the marine environment, in other words once the starting material has been sourced the business could operate from anywhere.
- In trying to exploit the outputs, there is a need for focus and differentiation; marine biotechnology has to compete with mainstream biotechnology for the same money, so it must be prepared to answer the question what makes marine biotechnology so special anyway?
- In establishing new companies, as is the case with other bioscience start-ups, lack of money is not so much the problem as lack of management expertise.
- Lack of a coherent approach to IP management and exploitation is a handicap.

Opportunities that are here in the short-term

- Creative thinking on added-value opportunities in existing marine-related opportunities – collaborative work eg on maximising value of production streams (seaweeds is an example).
- Understanding and manipulating biofilms and microbial communities.
- Anti-fouling applications outside the marine sector.
- In the health field, anything that can fight MRSA – including marine phage technology.
- Marine viruses, since these are a strength.
- The interaction of marine biotechnology and the environment eg gas and pollutant cycling and bioremediation.

Targets for action, strategic opportunities and practical tactics

- Looking at the research outputs, there is a challenge in visualising what we need to do to get the good ideas moving forward – we need to identify the 2-10 factors that must be satisfied in order to get academics and industry together and working properly. Looking for the quick wins e.g. novel enzymes, may be a realistic way forwards, and we should identify what else can be achieved in the short-, mid- and long-term, using technology mapping. We should try to establish a mechanism for a conduit or pipeline that will join the two ends of the value chain, in an overall concept of 'Technology Streaming'. For any development, we can then define the whole pipeline so we can understand the elements and deal with them. One option is to use Technology Translators to help. For longer-term targets such as new medicines, it is vital to have generated strong, meaningful data, pre-clinical if the molecule is really novel, early clinical if it is close to an existing product.
- The potential breadth of marine biotechnology means that we must focus on the Top 5 prospects, but how do we find these? Benchmarking is important. Derive a best practice model from marine biotechnology activities elsewhere in the world; study existing products and work out how UK research can add value to them. Setting up businesses in this area may be a valid short-term activity. Knowing better what is happening at the moment in terms of commercial developments and market dynamics is vital, as well as understanding how to attract private money into developing the marine-derived products sector. Improvements in bioprocessing chimes in with the opportunity identified by the BIG team for healthcare.
- We should aim for an easy information flow and ready dissemination of reports. Define a marine biotechnology network, with relationships to existing networks across disciplines. This will also help promote the UK's science and technology in this area, so that it has a 'brand image'.

5.2 Comments During our Project

We have asked a number of people to provide factual information about their marine biotechnology activities and also some contextual comments and opinions. The following summarises the feedback from those we contacted, and provides an interesting counterpart to the results of SWOT exercises:

Positive

- Support for promising ideas appears to be relatively easy to obtain.
- Research councils are taking the marine biotechnology issues more seriously these days, which is refreshing to see.
- Incubator sites with ‘on-tap’ professional advice linked in with academic organisations seems a sensible way forward for encouraging technology transfer and exploitation.
- Suggestion: national programmes or even a national centre to focus on marine biotechnology development would be a really excellent way to promote this type of wealth creation activity.
- Good support from Scottish Enterprise for marine bio[techno]logy developments and for SMEs.

Negative

- Getting funding for eventual commercialisation will be problematic.
- Knowing who to trust is always a problem.
- There is no effort in UK companies to attempt to exploit the research-expertise in the environmental science community in our experience. At best we have been told that if we discover something useful, then companies will talk to us. However, this is pretty unlikely without funding. There are good examples in the US where companies are funding bioprospecting activities in marine, polar and other environments (ie Diversa Corp.).
- Insufficient funding in environmental biotechnology dealing with commercial projects. Lack of understanding, in some cases, by evaluation panels asked to consider the funding of projects.
- Key constraints relate to the availability of modest venture capital
- There’s a kind of institutional or cultural void between the people with relevant academic competencies and the ultimate end users (oil companies, pharmaceuticals, etc). Other sectors have a fertile middle ground of “appliers” – IT, for instance.
- Academics who are good at being academics are not always the risk-coping entrepreneurs that these high-investment high-tech outputs demand.
- The market for one brilliant idea is more finite than university researchers expect. The tricky bit is not to have ideas, but to keep a flow of them going into the market, so as to capture the necessary scale-economies.

5.3 UK Marine Biotechnology – SWOT

Based on the results of our project, we see the following:

UK Strengths

- Excellent intra-national collaborations fostered by NERC and earlier BBSRC funded programmes.
- Good move to establish a M&FMB Technology Translator.

- Excellent activity in marine actinomycetes.
- Excellent activity in marine biofouling.
- Excellent activity in marine viruses.
- Potentially excellent culture collections.
- Strengths in advanced engineering for ocean explorations.
- Strengths in bioprocessing technology and some institutional desire to move ahead and fund this.
- Access to Faraday Partnerships for best practice and Knowledge Transfer Networks/Partnerships for enhancing science-base/industry collaboration.
- Ability to build on what natural resources activities we already have (mariculture, seaweed processing, aquaculture) and exploit added-value opportunities.

UK Weaknesses

- Lack of UK co-ordinated framework for marine biotechnology.
- Fragmented research community (in spite of NERC programme) with no planned cohesion, lacking clearly-visualised Centres of Excellence.
- Few large-scale or productive international collaborations.
- Still on the whole a mismatch between perceptions of value in the academic sector and in the commercial sectors.
- Not much follow-through from research findings to practical applications.
- Low investment base in business ideas arising from marine biotechnology or biosciences research.
- Few companies of any size and momentum to take new ideas forward.
- Reluctance of larger companies in pharmaceutical sector to take on marine bioactives.
- No inventory of resources.
- No integrated training programmes that start at base-line with marine biotechnology.

Opportunities for UK

- Some viable business opportunities have already been identified that capitalise on the UK's science strengths in marine bio[techno]logy; these include applications of biofilm knowledge in anti-fouling, use of marine viruses, development of new enzymes for biocatalysis, development of bioactives for infections (rather than cancers).
- The UK's work in marine bacteria and cell-to-cell signalling is highly relevant to R&D and commercial opportunities in other fields such as medicine and cancer prevention.
- Scientists working in marine bio[techno]logy are aware that building a network will enhance interactions and improve opportunities for working with industry – the DTI's Knowledge Transfer Networks programme gives the opportunity to do this.

- Individual centres of excellence exist (Southampton for deep-sea technologies, Plymouth for marine viruses, Newcastle for actinomycetes, Aberdeen for bioactives, Heriot-Watt for biofilm and applied marine biotechnology, SAMS for biocides, surfactants and development, for example).
- There is an opportunity to use the SAMS experience of establishing the European Centre for Marine Biotechnology to explore the possibility of establishing other Centres of Excellence, either real or virtual.
- Funding programmes exist in Scotland (Proof of Concept projects, the Intermediary Technology Institutes) and the rest of UK (Follow-on-Fund, Knowledge Transfer Partnerships, SBRI programme, DTI R&D and Innovation awards) to move science-industry developments forward in application of the output of marine bio[techno]logy.

Threats to UK

- France has significant strengths in deep-sea exploration and deep-sea bacteriology, which are somewhat in advance of ours.
- The French programme supporting exploitation of marine algae has also been important in legitimising commercial activity in this area.
- German investment in marine bioactives has been significantly greater and earlier than the UK's; Greifswald and other institutes are definitely focused on commercial opportunities; and MPI and GBF have strengths in genomics.
- If funding priorities are switched away from continuation of fundamental work to emphasise applied and exploitable aspects, there is a risk of falling away from the cutting-edge of science.
- The investment community currently fails to regard marine outputs with any seriousness; discussions are required.

6. FINDINGS & CONCLUSIONS, RECOMMENDATIONS

6.1 Findings and Conclusions

Marine bio[techno]logy can address a multiplicity of end-use sectors, to the extent that focus is required. There are short-term possibilities for exploitation of marine-derived materials, though these may need some strenuous efforts to ensure that funds and resources are found to validate them well enough to enter the end-user's pipeline.

The UK has a great deal of activity in marine biotechnology and is world-class in some areas of good market potential – actinomycetes and their metabolites; marine viruses; biofilms, microbial assemblages and quorum molecules; extremophiles and their enzymes; advanced marine engineering. The momentum generated by earlier BBSRC funding and added to by NERC Biofouling and M&FMB cannot be underestimated and is a force for energising this sector. In our view it needs to be maintained.

There are coherent and realistic actions that can be taken to build on strengths and counteract weaknesses and threats. A number of these are presented in the next section. At this stage, the cost implications of carrying these out are not clear, but **Volume 2** explores the selection of feasible steps and an outline approach to the scale of costs in more detail.

6.2 Recommendations for Action

Our recommendations fall into six activity areas:

- Commercialisation
- Networking
- Centres of Excellence
- Focus on Funding
- Training
- Scientific PR and marketing

Commercialisation

Identifying viable business opportunities that the market wants, benchmarking these and assessing their feasibility.

- realistic candidates for the above process seem to us to be:
    - applications for marine biofilm knowledge in medical and other industrial anti-fouling.
    - marine viruses for environmental and industrial use.
    - microbial enzymes for biocatalysis, including those from marine viruses.
    - bioactives for infections (rather than cancers).
    - added-value materials from raw material processing.
    - make full use of the Technology Translator concept.

   - develop a technology transfer methodology that can then be applied to future outputs.
   - the potential for transfer to other sectors of the UK's knowledge in marine bacteria and cell-to-cell signalling should be explored at an early stage.
   - identify technology gaps – areas of need for industry, including non-biomedical, where marine biotechnology could provide an effective solution.

Networking

Create a community for scientists working in marine bio[techno]logy

- establish a new web-site or build on an existing one
- provide:
   - scientific content
   - market information relevant to development and commercialisation of the outputs of marine biotechnology
   - a discussion forum for scientists and industrialists
   - virtual conferencing
   - resource matching between science and industry.
- since Knowledge Transfer Network funding might be appropriate for this, make a case to DTI for support of this for marine biotechnology

Centres of Excellence

Reviewing resources within the marine sciences including biotechnology, and creating accessibility:

- create an inventory of marine bio[techno]logy resources: map the expertise, equipment and other useful facilities of each research and development group or centre that could serve as a community-wide resource
- examine the feasibility of setting up virtual or real cross-sector resources that call on the strengths of individual researchers and organisations, evaluating the potential of each HEI or institute to form part of such centres:
   - a Centre of Excellence for Marine Biotechnology Chemistry and Analytics, which isolates, characterises, establishes synthetic methods and develops appropriate analytical tools for novel bioactives and biomaterials from marine sources
   - a Bioprocessing and Scale-Up Centre, which finds the best ways to mass-culture source organisms, whether open cultivation, closed bioreactor or by use of genetic engineering, and builds and validates the industrial-scale systems required, as well as putting in place the relevant knowledge from chemistry and analytics
   - a Centralised Marine and Industrial Culture Collection facility, with suitable depository, viable storage and validation facilities, running at commercial rates
   - a Centre for Marine Biotechnology Pharmaceutics & Formulation, which establishes the commercially-viable forms for marine

bioactive-based or biomaterials-based products, in collaboration with industry.

- this will require evaluation of the potential of each HEI or institute to form part of such centres.

Focus on Funding

- make use of Scottish Proof of Concept projects and Intermediary Technology Institutes, using Scotland's marine scientists as the entrée.
- make use of UK Follow-on-Fund, Knowledge Transfer Projects and SBRI service for directed development of the research outputs of marine bio[techno]logy.
- provide some centralised planning and assistance for marine biotechnology researchers and SMEs via information, web-site links and, if appropriate, a hands-on service
- the investment community continues to be interested in innovative approaches to manufacture, healthcare and high-tech, and there should be no barrier to marine biotechnology feeding into this, provided that the targets are clear and the business strategies for reaching them are well-argued; this requires the marine biotechnology community as a whole to promote what is on offer to the investment community, using well-thought out seminars, conferences and partnering activities.

Training

Create a co-ordinated cross-disciplinary training effort

- build on existing excellent marine science and biology courses and the two marine biotechnology courses that are available
- benchmark, review and if appropriate transfer best practice from within the Faraday Partnerships in establishing modular cross-institution courses.

Scientific PR and marketing

Address concerns about the marketing and image of the sector

- organise science missions, GlobalWatch missions, involve more scientists in trade missions
- encourage and support the presence of UK marine biotechnology scientists at conferences and workshops that relate to end-users
- prepare publicity using case studies of successful development and application of marine bio[techno]logy, targeted at four sectors – academic, industrial, public and intermediaries (including government and funders)
- use whatever additional Government sponsorship is possible for disseminating information on biotechnology and innovation
- enhance opportunities for the UK to reach level pegging and aim to overtake France and Germany using appropriate, strategic collaborations, funded by EC programmes or other instruments depending on scale and scope
- use sensitive and consistent lobbying to ensure a realistic balance in support between fundamental marine bioscience, including biotechnology, and development and commercialisation of the sector.

To act on the above, the MBG in collaboration with a network of researchers and companies already established in the sector, however small, could move them forward, with support from appropriate bodies (RCUK, OST, DTI, NESTA). HIE/SE's Marine Science Strategy for Scotland recommends that major participants in marine bio[techno]logy should hold periodic brainstorms to maximise enthusiasm and opportunities for synergy; this can easily be adopted on a nation-wide basis.

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7.3 Contacts and Respondents

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Alex Rogers, British Antarctic Survey

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7.4 Attendees at Workshop/Brainstorm

Sue Armfield, DTI

John Roberts, Defra

Ian Gallett, SUT

Don Lennard, Fore*sight* Marine Panel Marine Biotechnology Group

Meredith Lloyd-Evans, BioBridge Ltd

Alasdair Munro, Top Country Development (ex-HIE)

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Catherine Side, Inside Consulting Ltd

Robin Teverson, Finance Cornwall

Dave Woodwark, FIRST Faraday Partnership & M&FMB Technology Translator

APPENDIX 1: THE PROJECT WORKSHOP/BRAINSTORM SESSION 08.03.04

Fore*sight* Marine Panel Marine Biotechnology Group

Marine Biotechnology Prospects Study

08/MAR/04 – DTI, 1 VICTORIA STREET, LONDON

1 **Attendees** Fore*sight* Marine Panel Marine Biotechnology Group	Professor Graham Shimmield, SAMS – Chair [GS] Jo Oliver, IJ Knowledge – Co-chair [JO] (*Project Executive of European Centre for Marine Biotechnology project at SAMS*) Ian Gallett, SUT – Acting Secretary [IG] Sue Armfield, DTI – member [SA] (*responsible for agribusiness, plant and marine biotechnology*) Don Lennard – member [DL] Alasdair Munro, Top Country Development. – member [AM] (*recently retired from Highlands & Islands Enterprise*) John Roberts, DEFRA – member [JR] Robin Teverson, Finance Cornwall – member [RT] (*also non-exec chairman of a small marine biotech company*)
BioBridge Ltd	Meredith Lloyd-Evans – Facilitator, Consultant for marine biotechnology prospects study [MLE]
Fenners Chambers	Daniel Owen – author of Legal Framework study [DO]
Pro-Bio Faraday Partnership	Geoff Pollard [GP]
GlaxoSmithKline Research	Michelle Scott [MS]
Inside Consulting Ltd	Catherine Side [CS] (*consultant to Biomar SA and the Hispanagar group and previously to PharmaMar SA*)
NERC M&FMB programme	Dave Woodwark [DW] (*FIRST Faraday Partnership & M&FMB Technology Translator*)
Great acknowledgements are due to Dr Jo Oliver for recording the meeting as the verbatim draft on which this report is based	

2	**Introduction** GS provided a brief Introduction to the day's proceedings and to the purpose of the Foresight Marine Panel – Marine Biotechnology Group in commissioning the projects on Legal Framework and Marine Biotechnology prospects, before asking those present to introduce themselves. GS noted that the sector review being carried out by BioBridge built on the work already done in Scotland, including a Marine Sciences Strategy currently in draft.
3	**Outline of the morning** MLE provided an overview of the brainstorm process and described the project and its progress briefly before open debate. The critical points in brainstorming are to generate ideas without prior censorship, and to prioritise issues and actions at the end.
4	**Open Debate** This began with discussion of an agreed definition of marine biotechnology: in the past, genetically modified organisms (GMOs) had not been included. From industry's point of view (MS - GSK), this would remove any interest in marine biotechnology, as genetically-enhanced micro-organisms are seen as the way forward in terms of process development. Laboratory-based genetic engineering is included, as a tool to facilitate or enhance production of specific material from micro or macro-organisms, but the development of GM marine vertebrates intended for consumption is not (JO). What is included is bioprospecting, the use of organisms, genetically-enhanced or otherwise, in process engineering and as model systems, and applications of materials from marine organisms in biofouling, bioremediation, healthcare, nutraceuticals etc (GS). For the avoidance of doubt,

	vertebrate biology is excluded and fisheries are included only in so much as they are a potential market for products of marine biotechnology.
	The Open Debate continued until lunch-break, with discussion summarised by MLE as follows: There needs to be better networking; we need to give serious consideration to where the money is going to come from; the DTI are on board if 'high-value job creation' is involved; better marketing of the science is required; there is a requirement for management expertise to take the science forward, IP (Intellectual Property) issues present a challenge as do the varied needs and drivers of the diverse sectors involved; lastly, big pharma appears to see little added value in the 'natural' label at present. The next sections represent a distillation of the entire discussions. In the final session, MLE asked each person present to identify the single biggest issue they saw from their perspective and what they believed should or could be done about it; the issues of focus/definition and funding the research base were not discussed – better networking and collaboration and how to understand and achieve economic development from marine biotechnology were the major questions addressed.
5	**Existing markets and new opportunities** MLE had already made a plea that existing or conventional uses of marine organisms should not be neglected. Many people do not realise the existing extensive use of marine-derived materials: the bulk come from outside the UK (CS), e.g. ISP alginates in Girvan currently buy seaweed from countries with low drying costs but are interested in switching supply back to the UK if appropriate drying technology can be developed (AM). One question is whether effort should be aimed at import substitution (MLE). The conclusion here is that it didn't matter where the materials came from, as long as value could be added in UK. There is already interest in collaboration between companies wanting high value products from seaweeds and those interested in processing for lower-grade material from the same biomass (JO) – ISP's waste could be further processed for higher-value material (AM) – and 2nd and 3rd stream products can be obtained from algae, e.g. phycobilirubins as high-value diagnostic reagents (CS, referring to PharmaMar and BioMar). Several important prospects stem from marine biotechnology research (DW). One is biofouling, particularly when one considers the science behind attachment, detachment etc, which makes it of interest in the biomedical field and industrial processing. The classic industrial microbiology approach is to look at single strains, but nature isn't like this – the interesting science comes from the relationship between different organisms. Anti-MRSA (methicillin-resistant *Staphylococcus aureus*) technology is the second, via looking for new antibiotic compounds or phage technology. Marine viruses is the third area – those that infect algae have novel enzymes and endonucleases with an immediate market. The fourth is in environmental monitoring, e.g. looking at bromine levels as an indicator of climate change.
6	**Issues identified** <u>General</u> Focus There is still a **lack of understanding of what the sector is** – it is all too 'fluffy' (RT). Part of the challenge is that the drive for biotechnological advancement comes primarily from the healthcare sector, which gives a certain image, but market realisation often occurs first in other sectors, where the route to market is less onerous in terms of time, money, and regulation (JO). And there is an **issue of positioning** – all other biotechnology businesses position themselves according to the market sector they serve – diagnostics, therapeutics etc. In contrast, marine biotechnology has chosen, deliberately or otherwise, to position itself according to where the starting material comes from, which is more often than not irrelevant in the market place. This makes all the hurdles that much higher (JO, echoed by DW and IG).
	<u>Science base</u> Funding **Lack of continuity of funding is a real issue**, especially as the research councils support programmes for a fixed period, thinking that this is enough to get the process started (DW). The view is that the academic community always asks for more money, so it is important to justify this in a strategic context (MLE). The concept of generating an income stream from research programmes and then using this to fund further research (MLE) does not appear to be a priority or indeed possible, for a variety of reasons including IP complexity (DW). And, overall, **scientists don't have**

enough knowledge of all the possible sources of funding and how to get the funds from them (DL).

Absence of effective networks

Effective cross-discipline networking is lacking and is very difficult because of the diverse markets for the products of marine biotechnology and because so many different research and technology groups are involved (JO). This underlines the lack of an academic network in marine biotechnology that knits with existing networks in other areas (GP).

Building capacity and co-operation at infrastructure level

There are some concerns that the current **lack of connectiveness at research council and higher levels** hampers effective action in funding the development of the outputs of marine biotechnology research to the stage where they can be commercialised and their value realised (GS, echoed by DL).

Science-industry links

Poor linkage between 'science push' and 'market pull'

Experience in the M&FMB programme is that the **research is still not well linked to commercial exploitation** – the UK is still considered to be pretty strong in the natural product field, and yet this subject is not 'in vogue' with big pharma, where there is a general view that nature has been well harvested, and now combinatorial chemistry is considered the way forward (DW). The **landscape has changed** since bioprospecting began – in the past PharmaMar has worked with Bayer, Sandoz, GlaxoSmithKline, supplying marine derived samples for high-throughput screening. These days GSK and other pharmaceutical companies are more interested in a single compound rather than the mix of products present in a marine extract (CS). Another issue is that **existing and past research support programmes have never had exploitation as a key goal** – the addition of a Technology Translator to the M&FMB programme is a welcome move (DW). **Scientists at the coal-face are too divorced from the market need** (DW) and, though there may be plenty of potential in the research achievements, without a market pull this will not be taken up (MLE). This is illustrated by GSK's approach (MS) – they are only interested if a novel substance comes to them already with pre-clinical data. Actually, the source of the material is to some extent irrelevant. Therefore, **the barrier to uptake of bioactives by the pharmaceutical industry is lack of appropriate data**.

Business-building

Lack of Business Development skills and exploitation efforts

The area will not succeed unless the focus of interest is on exploitation – problems with commercialisation are normally to do with the market and the normal commercialisation route does not seem to fit marine biotechnology (RT). There are **problems with an over-emphasis on regional economic development**; it is unlikely that job creation would be associated with the marine environment – in other words once the starting material has been sourced the business could operate from anywhere (DW). There is also a need to recognise that the UK can build businesses based on materials from elsewhere (MLE, DW). However, it is estimated that marine biotechnology will be worth $2 billion by 2007, and if the UK wants to share in this, more commercial activity is required (AM); the serious questions are 'Are we missing out on spawning the new companies?' (SA) and how we stimulate those.

Marine biotechnology has to compete with mainstream biotechnology for the same money – this imposes **a need for focus and differentiation** (MS). Money alone is not the main constraint, venture capital groups are falling over themselves to give money; **lack of management expertise** is a much bigger problem (RT, echoed by MS, who added 'access to sustainable finance').

IP (Intellectual Property) and exploitation

Lack of a coherent approach to IP management and exploitation is a handicap – there are currently 31 projects being funded in NERC's M&FMB programme but the IP is spread widely across the network and is handled in very different ways in different institutions (DW). We still do not know how companies would respond to any scheme for access to marine organisms and benefit-sharing. If companies felt that benefit-sharing obligations might be imposed on them retrospectively regarding R&D work they are currently carrying out, the uncertainty might be a disincentive for them to proceed

	(DO).
7	**Targets for action** ***<u>Effective networks</u>*** It would be useful to have a list of all relevant networks as a basis for cross-discipline knowledge flow (GP). Indeed, the NERC's knowledge transfer fund in this area is open at the moment – this encourages networking and collaboration (DW). And the emphasis of the Fore*sight* Marine Panel on technology combinations for longer-term opportunities (e.g. renewable energies and coastal protection) is appropriate for marine biotechnology (DL). Certainly, we need to ask whether getting research and commerce to speak effectively together is something we should focus on (DL). Though Faraday Partnerships might be a good model, since they link research and industry, with a strong emphasis on training, and are nationally-based, there are 20+ at present and it is highly unlikely that there will be any more (DW). It is worth mentioning a comment Jo Oliver made in one of the reports she has written on this subject – that there is value in looking to collaborate with countries with complementary rather than competing marine resources, for example deep and cold studies linking with shallow and hot (MLE). ***<u>Building capacity and co-operation at infrastructure level</u>*** The forthcoming NERC/BBSRC meeting is a good opportunity to build bridges. The DTI is particularly interested in the areas where the UK has real competitive advantage and where high-value, skills-based jobs can be created (SA). <u>Science-industry links</u> Poor linkage between 'science push' and 'market pull' We can identify opportunities for new or expanded UK business, some of which are relatively well-established or obvious (alginates and chitosans – AM, chitosans as seed coatings and other agricultural use – MLE, the whole area of biocatalysis, biosensors, bioremediation – GP, agarose beads for research and biocatalysis – CS) and some are larger and less easy to address (using biotechnological intervention in the toxic algal blooms that close seafood beds for months of the year or intervening in global warming by seeding the oceans – DW) but there is a challenge in visualising what we need to do to get the good ideas moving forward (DW). We need some kind of conduit (MS) or pipeline (AM) in place to join the two ends of the value chain, in an overall concept of 'Technology Streaming' (MLE). The Technology Translator approach is valuable in this context, as is adapting activities in other sectors in the UK, e.g. the BBSRC's newly-announced 'proof of concept' fund that allows an individual to spin out based on a BBSRC-funded project (SA). And it would be very helpful if we could identify the 2-10 factors that must be satisfied in order to get academics and industry together and working properly (DL).
	In general terms, it seems that a two-pronged approach is needed, maximising the outputs from marine biotechnology by thinking in a 'value-chain' kind of way, and establishing some sort of 'marine biotechnology marketing board' as the conduit to do this; there are too many pieces of the jigsaw for one person or group to cope with (MLE). On a more specific front, that of developing medicines from marine bioactives, the key issue is strong, meaningful data to show relevance to the potential licensee: for a product with therapeutic potential for a new indication, pre-clinical data might be enough; for a product targeting existing markets, clinical data would be needed in addition; and the IP position needs to be clean (MS). <u>Business-building</u> Lack of Business Development skills and exploitation efforts Establishing new biotech businesses has not been helped by the 'numbers game', in which Germany and the UK have competed for many years to have the most biotech companies – it masks the true picture of what is sustainable business development and how to achieve it (MS). What will be really helpful will be to promote the success stories, wherever from, (GP), look for the quick wins e.g. novel enzymes (DW) and identify what else can be achieved in short-, mid- and long-term by technology mapping (MLE, GP). Studying existing products, adding value to them and setting up businesses in this area may be a valid short-term activity (GP), as well as looking at improvements in

	bioprocessing, which chimes in with the opportunity identified by the BIGT (Bioscience Innovations and Growth Team) for healthcare (SA). Moving forward can be done if we derive a best practice model from marine biotechnology activities elsewhere in the world, learn from other sectors and start cherry picking, including areas such as business incubation, bridging the gap between research and commerce; we need to do some straightforward benchmarking (RT, echoed by SA). Knowing better what is happening at the moment in terms of commercial developments and market dynamics is vital, as well as understanding how to attract private money into developing the marine-derived products sector (CS).
8	**A selection of ideas from round the table – for work-up in the Final Report and/or consideration as policy and strategy issues in fora outside this report** ***Graham Shimmield:*** Communication is the most important issue to tackle. It is worth mentioning a European initiative – BlueBioNet, which has a strong focus on keeping and maintaining skills. (*MLE already intends to list relevant networks, societies, associations and other sources of community, including BlueBioNet, in the Final Report.*) The pre-commercialisation framework for research that is being used at present means that there is an urgent need to improve communication between market positioning and research endeavour. Think about the equivalent of Faraday partnership. ***Sue Armfield:*** We should follow up the concept of 'technology translators' and build on existing knowledge networks including the Pro-Bio and FIRST Faraday partnerships, to assist cross-sectoral transfer of ideas between the science base and businesses. ***Don Lennard:*** The potential breadth of marine biotechnology means that we must focus on the Top 5 prospects, but how do we find these? (*tools include listing prospects and ranking by pros and cons across a number of criteria including technical ease, market size, time to market, barriers to market etc*) ***Geoff Pollard:*** There is a need for easy information flow and ready dissemination of reports. Define a marine biotechnology network, with relationships to existing networks across disciplines, to maximise the potential. The other networks can then be asked for their help in managing complex developments. Focus on prospects will be aided by listing and ranking them in a technology roadmap, showing short, medium, and long-term plans and what has already been achieved. ***MLE:*** We should look at ways of promoting the UK's science and technology in this area, so that it has a 'brand image', and examine whether the 'natural product' tag restricts exploitation. ***Alasdair Munro:*** There is a need to deal with conservatism in the market, so for any development, we should define the whole pipeline so we can understand the elements and deal with them. An underlying theme of many comments was ***what makes marine biotechnology so special anyway?*** Other comments from the 'round the table' exercise have already been included earlier in the text.

APPENDIX 2: QUESTIONNAIRE USED FOR OBTAINING RESPONSES TO SWOT ANALYSIS AND RECOMMENDATIONS

As a result of Stage 1 of a project profiling marine biotechnology activities in the UK in an international context and assessing a case for scientific and economic development, a number of strengths, weaknesses, opportunities and threats have been identified, which have prompted recommendations for action. These are given in no specific order of importance, nor do they take into account the relative resources that might be required to achieve them or whether they will be achievable in practice. ***Could you please identify the three or four recommendations that in your view would make the most impact on the development of marine biotechnology in the UK and should therefore be priorities for action, as well as providing feedback on the outcomes so far.*** *You can use free text or a score from 1 = very important to 5 = least important, if you prefer.*

Please respond as fully as possible. The main purpose is to ensure that the perceived strengths, weaknesses, opportunities and threats reflect experience in the sector and the recommendations are ones that, if and when carried forward, will be seen as feasible and worthwhile. If any of the ***strengths, weaknesses, opportunities, threats*** *appear to you to be inappropriate or irrelevant, please strike them out of the lists (electronically using Format, Font, (Effects), Strikethrough or Double strikethrough). If any have, in your opinion, been missed out, please add into the table below or direct into the lists, which will expand if you wish to add more:*

Strengths, weaknesses, opportunities, threats

UK Strengths	***UK Weaknesses***
➢	➢
➢	➢
➢	➢
➢	➢
Opportunities for the UK	***Threats to the UK***
➢	➢
➢	➢
➢	➢
➢	➢

The recommendations flow from identified SWOT elements. Please review the list on page 3; comments and feedback on priorities, feasibility, relevance, and additional activities that might serve to *strengthen research, development and commercialisation of marine biotechnology are especially welcome, as well as comments on how to take actions forward; again you can add here or add to the list itself:*

Comments on recommendations
My top 3 priorities are: 1. 2. 3.

Identification of some strengths, weaknesses, opportunities and threats

UK Strengths	*UK Weaknesses*
➢ NERC and earlier BBSRC funded programmes	➢ Lack of UK co-ordinated framework in MBT
➢	➢ programme)
➢	➢
➢	➢
➢	➢ compared with US (COMB or Scripps)
➢	➢ collaborations
➢	➢ academic sector and in the commercial sectors
➢	➢ research findings to practical applications
➢	➢ marine biotechnology or biosciences research
➢	➢ new ideas forward
➢	➢ sector to take on marine bioactives
➢	➢
➢ explorations	➢ base-line with marine biotechnology
➢ institutional desire to move ahead and fund this	
➢	
➢ enhancing science-base/industry collaboration	
➢ (mariculture, seaweed processing, aquaculture) and exploit added-value opportunities	

Opportunities for the UK	***Threats to the UK***
➢ - applications of biofilm knowledge in anti-fouling, use of marine viruses, development of new enzymes for biocatalysis, development of bioactives for infections rather than cancers ➢ bacteria and cell-to-cell signalling in other fields such as medicine and cancer prevention ➢ community that building a network will enhance interactions and improve opportunities for working with other scientists and industry ➢ Biotechnology as the catalyst for development & commercial activity in this sector ➢ enable the proof of concept and development beyond prototype of products ➢ programmes (Proof of Concept & Intermediary Technology Institutes in Scotland; Follow-on-Fund, Knowledge Transfer Partnerships, DTI Business Support Products in rest of UK; EU Framework Programme 6)	➢ through competitive patenting and commercialisation activities: ➢ ➢ bacteriology ➢ legitimised commercial activity in this area ➢ commercial focus of Greifswald and other institutes and genomics strengths of MPI and GBF ➢ continuation of fundamental work to emphasise applied and exploitable aspects risking a falling away from the cutting-edge of science ➢ marine outputs with any seriousness; discussions are required ➢ and government department level may hinder coherent development of MBT and returns from outputs

Recommendations
Commercialisation

➢ in:
  ➢
  ➢
  ➢
  ➢
  ➢
➢
➢
➢
➢ solution

Networking
➢ ➢ ➢ of MBT, a discussion forum, virtual conferencing, resource matching between science and industry ➢

Infrastructure

- facilities of each research and development group or centre that could serve as a community-wide resource
- individual researchers and organisations, evaluating the potential contribution of each HEI or institute:
- synthetic methods and develops appropriate analytical tools for novel bioactives and biomaterials from marine sources
- appropriate genetic engineering, and builds and validates the industrial-scale systems required, as well as putting in place the relevant knowledge from chemistry and analytics
- validation facilities, running at commercial rates
- forms for marine bioactive-based or biomaterials-based products, in collaboration with industry

Focus on Funding

- information, web-site links and, if appropriate, a hands-on service, to aid access to sources of funds

Training

- are available
- initiatives in establishing modular cross-institution courses

Scientific PR and marketing

- targeted at four sectors – academic, industrial, public and intermediaries (including government and funders)
- appropriate, strategic collaborations, funded by EC programmes or other instruments depending on scale and scope
- bioscience, including biotechnology, and development and commercialisation of the sector

Free space for further comments if desired:

General comments on a strategy for UK marine biotechnology

Thank you very much for your input. This project has been commissioned from BioBridge Ltd by the UK Foresight Marine Panel's Marine Biotechnology Group with the support of DTI and SWRDA, the South West of England Regional Development Agency. Note that, as the project is still on-going, the above are initial views for discussion and have not necessarily been endorsed by the sponsors. Eventual publication of part or all of the project's findings is foreseen.

Please send your responses to:

Meredith Lloyd-Evans, Managing Director

or

Chris Massey, Marketing Officer

BioBridge Ltd, 45 St Barnabas Road, Cambridge CB1 2BX

tel 01223 566850 fax 01223 470222

email mlloydevans@biobridge.co.uk *or* admin@biobridge.co.uk

Please telephone if you would like further information or discussion before responding.

Meredith Lloyd-Evans

August 2004

APPENDIX 3: IACMST LIST OF HEIS IN MARINE SCIENCE AND BIOTECHNOLOGY[151]

University Research on the Biology of Marine Organisms

Department of Engineering, University of Aberdeen
Department of Zoology, University of Aberdeen
School of Biosciences, University of Birmingham
Department of Earth Sciences, University of Bristol
Department of Applied Mathematics and Theoretical Physics, University of Cambridge
School of Life Sciences, University of Dundee
School of Biological Sciences, University of Exeter
Institute of Biomedical and Life Sciences, Division of Infection and Immunity, University of Glasgow
Department of Biological Sciences, University of Hull
Department of Biology, University of Leicester
Oceanography Laboratories, Department of Earth Sciences, University of Liverpool
Port Erin Marine Laboratory, University of Liverpool
School of Veterinary Science, Department of Veterinary Clinical Science, University of Liverpool
Department of Marine Sciences and Coastal Management, University of Newcastle upon Tyne
Department of Biological Sciences, University of Plymouth
School of Biological Sciences, Institute of Marine Sciences, University of Portsmouth
School of Ocean and Earth Science, University of Southampton
School of Biology, University of St Andrews
Department of Biological Sciences, University of Stirling
Institute of Aquaculture, University of Stirling
Department of Civil Engineering, University of Strathclyde
School of Health, Natural and Social Sciences, Ecology Centre, University of Sunderland
School of Ocean Sciences, University of Wales, Bangor
Department of Biological Sciences, University of Wales, Swansea

University Research on Ecology

Department of Zoology, University of Aberdeen
School of Conservation Sciences, University of Bournemouth
Centre for Environmental and Applied Sciences Research, University of Derby
School of Biological and Biomedical Sciences, University of Durham
Scottish Association for Marine Science, University of the Highlands and Islands Millennium Institute
Port Erin Marine Laboratory, University of Liverpool
Department of Biological Sciences, University of Plymouth
School of Biology, University of St Andrews
School of Health, Natural and Social Sciences, Ecology Centre, University of Sunderland
School of Ocean Sciences, University of Wales, Bangor

University Research on Bio-fouling

School of Biosciences, University of Birmingham
Glasgow Marine Technology Centre, University of Glasgow
Department of Offshore Engineering, University of Newcastle upon Tyne
School of Biological Sciences, Institute of Marine Sciences, University of Portsmouth
School of Ocean Sciences, University of Wales, Bangor

University Research in Marine Biotechnology

Department of Biological Sciences, Heriot-Watt University
Department of Marine Sciences and Coastal Management, University of Newcastle upon Tyne
School of Ocean Sciences, University of Wales, Bangor

[151] source The Inter-Agency Committee on Marine Science and Technology (IACMST) 2004

APPENDIX 4: HEIS IN UK WITH TEACHING ACTIVITY IN MARINE BIOSCIENCES AND MARINE BIOTECHNOLOGY

TABLE 57: TEACHING ACTIVITY IN UK

ENGLAND	
HEI	**ACTIVITIES**
Anglia Polytechnic University Dept of Life Sciences, East Road, Cambridge CB1 1PT T: 01245 493131 F: 01245 348 772	Marine Biology options in Animal Behaviour, Animal Welfare, Biomedical Science, Cell & Molecular Biology, Ecology & Conservation and Wildlife Biology
Bath Spa University College Newton Park, Newton St Loe, Bath, Somerset BA2 9BN T: 01225 875845 F: 01225 875491	PhD/MPhil in Environmental Biology, including culture of micro-organisms and marine algae, Biological Effects of Pollution & Marine Phycology
Blackpool and the Fylde College Bispham Campus, Ashfield Road, Blackpool Lancs FY2 0HB T: 0125 3504322 F: 0125 3500479	HND in Coastal Conservation with Marine Biology
Bournemouth University Fern Barrow, Poole, Dorset BH12 5BB T: 01202 595470 F: 01202 595287 Centre for Coastal Conservation and Education, School of Conservation Sciences T: 01202 595444 F: 01202 595255 consci@bmth.ac.uk	Has related MSc/PGDip & PhD/MPhil/PGDip in Coastal Zone Management (the first in Europe) and Environment issues, including uses of coastal resources, coastal zone law; marine pollution, agro-ecosystems, marine conservation, Public Understanding of Science and Technology
Bristol, University of Biogeochemistry Research Centre	
Cambridge, University of Scott Polar Institute, Kellet Lodge, Tennis Court Road, Cambridge CB2 1QJ T: 01223 333308	MPhil in Polar Studies, including ecology and marine environment
Cranfield University Cranfield, Bedfordshire, MK43 0AL T: 01234 754090 F: 01234 752462	PhD in Marine Technology with integrated studies and practical activities
East Anglia, University of School of Environmental Sciences, Norwich. NR4 7TJ	
Essex, University of Wivenhoe Park, Colchester, Essex C04 3SQ T: 01206 873666 F: 01206 873423	offers a BSc in Marine and Freshwater Biology, PhD in Environmental Biology, including microbial ecology, marine ecology, environmental biotechnology; research activities include identification of sources of faecal pollution in environmentally sensitive waters, actinomycetes as a source of bioactive compounds. Also offers an MSc/MRes in Biotechnology & MEnv in Environment, Science and Society

TABLE 57: CONT

ENGLAND	
HEI	**ACTIVITIES**
The College of Falmouth Killigrew Street, Falmouth, Cornwall, TR11 3QS T: 01326 310310 F: 01326 310300 falenquiries@cornwall.ac.uk	offers degrees in Marine Sciences, Marine Biology & Ecology; part of the Combined Universities in Cornwall group.
Hull College Queens Gardens, Kingston Upon Hull, East Riding of Yorkshire HU1 3DG T: 01482 598744	offers a BSc in Marine Biology
Hull University Scarborough Campus, Filey Road, Scarborough, North Yorkshire YO11 3AZ T: 0148 246 6904 F: 0148 246 6554 Institute of Estuarine and Coastal Studies	IECS is a research and consultancy organisation; interests include benthic and pelagic organisms as well as other coastal issues
King's College London Strand, London WC2R 2LS United Kingdom T: 020 7836 5454 F: 020 7848 3460	Offers MSc in Aquatic Resource Management (environmental analysis; fishery management; marine, freshwater and estuarine ecosystem utilisation and conservation; ecotoxicology and pollution)
Liverpool, University of School of Biological Sciences, 6 Abercromby Square, Liverpool L69 3BX T: 0151 794 6730 F: 0151 794 6733 Marine Station, Port Erin Marine Laboratory Breakwater Rd, Isle of Man IM9 6JA T: 01624 831000	Offers BSc in Marine Biology and PhD/MPhil/MRes in from the School of Biological Sciences (departmental specialisms include applied ecology, Marine Biology, cellular regulation, gene structure and function, molecular and environmental microbiology)
Kingston University School of Life Sciences, Cooper House, 40-46 Surbiton Road, Kingston upon Thames, London KT1 2HX T: 020 8547 7516 F: 020 8547 7080	Offers a BSc in Marine and Freshwater Biology
Newcastle upon Tyne, University of School of Marine Science and Technology, Armstrong Building Newcastle NE1 7RU T: 0191 222 6718 F: 0191 222 5491	Offers Marine Biology and a multidisciplinary Marine Sciences PhD / MPhil; particular strengths in tropical and temperate marine biology; owns a research vessel. Departmental specialisms: environmental signal transduction in marine organisms; marine ecosystem dynamics; well-established marine engineering department.

TABLE 57: CONT

ENGLAND	
HEI	**ACTIVITIES**
Plymouth, University of The Institute of Marine Studies, Drake Circus, Plymouth, Devon PL4 8AA T: 01752 232400 F: 01752 232406	Offers a very wide range of marine-oriented courses at all levels, including marine biology, marine biosciences, applied marine sciences, marine algae, biomolecular sciences and many others. Marine Biology is taught in collaboration with the Marine Biological Assoc.
Portsmouth, University of School of Biological Sciences, King Henry Building, King Henry I Street, Portsmouth PO1 2DY T: 0239 2843488 F: 0239 2843538 Institute of Marine Sciences, Ferry Road, Eastney, Portsmouth PO4 9LY	Offers BScs in Marine Biology, Marine Environmental Science, MSc/PGDip in Aquaculture Economics freshwater and marine and MSc/PGDip/PGCert Coastal and Marine Resource Management
Queen Mary, University of London Mile End Road, London E1 4NS T: 020 7882 3066 F: 020 7882 5556	Offers BSc in Marine and Freshwater Biology
Reading, University of Whiteknights, PO Box 217, Reading RG6 6AH T: 0118 378 8111 F: 0118 975 2252	Offers Environmental Systems Science Centre PhD / MPhil (Departmental specialism includes Marine Science).
Royal Holloway, University of London School of Biological Sciences, Egham, Surrey, TW20 0EX T: 01784 443182 F: 01784 470756	Offers Biology MPhil/PhD; extensive aquaria (freshwater and marine), cell/tissue culture facilities. Departmental specialisms: Evolutionary and Environmental Biology, Biomedical and Animal Molecular Biology
Southampton Institute East Park Terrace, Southampton SO14 0YN T: 02380 319422 F: 02380 319412	Offers BSc in Marine Biology with Oceanography, Marine Environmental Science and Maritime Studies (Coastal & Ocean Management) MSc/PGDip/PGCert (marine exploration, resource conservation, environmental management)
Southampton, University of Southampton Oceanography Centre, School of Ocean & Earth Science, European Way, Southampton SO14 3ZH T: 02380 592681/595899 F: 02380 593052	Offers degrees in Ocean and Earth Science, Oceanography; specialisms include marine biology and marine chemistry
Warwick, University of Coventry CV4 7AL T: 02476 523706 F: 02476 524337	Offers Biological Sciences degrees; specialisms include ecosystems analysis, marine ecology, resource management, ethics and governance, biomathematics, epidemiology, remote sensing and image technology.
York, University of Heslington, York O10 5DD T: 01904 433534 F: 01904 434268	Offers degrees in Environmental Management including sustainable use of terrestrial, marine and freshwater resources; specialisms include wetlands and coastal zones including marine reserves

TABLE 57: CONT

SCOTLAND	
HEI	**ACTIVITIES**
Aberdeen, University of Aberdeen Institute for Coastal Science & Management, Fraser Noble Building, King's College, Aberdeen AB24 3UE T: 01224 274474/272522, F: 01224 272497 aicsm@abdn.ac.uk Oceanlab, Newburgh, Aberdeenshire AB41 6AA T: 01224 274401, F: 01224 274402 oceanlab@abdn.ac.uk	Offers BScs in Marine Biology and various aspects of Marine Resource Management; Marine and Fisheries Science: Sustainable Management of Living Marine Resource, marine molecular ecology
Glasgow, University of Institute of Biomedical and Life Sciences, Anderson College, Glasgow G11 6NU T: 0141 330 3999, F: 0141 330 4045 University Marine Biological Station, Millport, Isle of Cumbrae Scotland KA28 0EG	offers MRes in Ecology & Environmental Biology and Marine & Freshwater Ecology & Environmental Management
Heriot Watt University Riccarton, Edinburgh, EH14 4AS T: 0131 451 3707, F: 0131 451 3630	offers BScs in Applied Marine Biology and Marine Biotechnology and PhD/MPhil degrees in a variety of biological and environmental subjects, including molecular biology of marine organisms, molecular systematics and biodiversity in marine systems (a new programme), marine microbial biotechnology and bioengineering, marine resource development and management
The International Centre for Island Technology Old Academy, Back Road, Stromness, Orkneys KW16 3AW T: 01856 850 605, F: 01856 851 349 icit@hw.ac.uk	is a specialist unit of Heriot-Watt University, with a focus on marine resource management, including sustainable development, environmental economics, marine bioresources and biodiversity, waste disposal systems; also houses H-W's Diving Unit and supports H-W's practical marine science activities
Napier University 219 Colinton Road, Edinburgh EH14 1DJ T: 0131 455 6331, F: 0131 455 6334 School of Life Sciences, 10 Colinton Road, Edinburgh EH10 5DT, T: 0131 455 2490	Offers a BSc in Marine and Freshwater Biology
North Atlantic Fisheries College Port Arthur, Scalloway, Shetland ZE1 0UN T: 01595 772000, F: 01595 772001 admin@nafc.ac.uk www.nafc.ac.uk	training in fisheries science
St Andrews, University of Old Union Building North St, St Andrews, Fife KY16 9AJ T: 01334 462245, F: 01334 463388 Gatty Marine Laboratory, St Andrews, Fife KY16 8LB T: 01334 463441, F: 01334 463443	Offers BSc in Marine and Environmental Biology and Division of Environmental and Evolutionary Biology PhD / MPhil
Stirling, The University of Dept of Biological Sciences, Stirling FK9 4LA T: 01786 467042, F: 01786 466800	Offers Marine Biology BSc (Hons) and important degrees in aspects of Aquacultural Science, including coastal aquaculture and marine pathobiology, molecular life sciences, crustacean biology

TABLE 57: CONT

SCOTLAND	
HEI	**ACTIVITIES**
UHI Millennium Institute SAMS Dunstaffnage Marine Laboratory, PO Box 3, Oban, Argyll PA34 4AD T: 01463 279000, F: 01463 279001	A new development – the University of the Highlands and Islands: offers Marine Science BSc (Hons) and proposes to offer **Marine Biotechnology** from next 2 years
WALES	
HEI	**ACTIVITIES**
Aberystwyth, University of Wales Institute of Biological Sciences, Edward Llwyd Building, The University of Wales Aberystwyth Ceredigion SY23 3DA T: 01970 622316 F: 01970 622350	Marine & Freshwater Biology BSc
Bangor, University of Wales School of Ocean Sciences, Centre for Applied Oceanography, Menai Bridge, Anglesey, LL59 5AB Marine Science Laboratories Menai Bridge, Anglesey, LL59 5EY T: 01248 382846 F: 01248 716367 enquiries@sos.bangor.ac.uk	School of Ocean Sciences is one of largest in Europe. A range of BScs in marine subjects (including Applied Marine Biology and Ecology), Marine Chemistry, an MSc in Marine Environmental Protection and advanced degrees in Oceanography & Marine Biology, and Ocean Sciences. The School's specialisms also include Larval Biology, Hydrothermal Vents and Cold Seeps, Genetics & Benthic Ecology
Glamorgan, University of School of Technology, Pontypridd, Wales CF37 1DL T: 01443 483413/482885 F: 01443 482525/48292 School of Biological Sciences	offers a BSc in Marine Sciences
Swansea, University of Wales Singleton Park, Swansea, SA2 8PP T: 01792 205678 F: 01792 295618	Offers Marine Biology and Ecology degrees; specialisms include ecology and taxonomy of marine fish, turtles, plankton and benthic invertebrates, environmental biology and coastal management.
NORTHERN IRELAND	
HEI	**ACTIVITIES**
Belfast, Queen's University University Road, Belfast BT7 1NN T: 02890 335088, F: 02890 335089 School of Biology and Biochemistry, Medical Biology Centre, 97 Lisburn Road, Belfast BT9 7BL T: 02890 975787, F: 02890 975877 sobb.office@qub.ac.uk	BSc in Marine Biology, PhD in Marine Biology including Molecular Ecology and Evolution, Molecular Microbiology & Marine Systems
Ulster, University of School of Biological and Environmental Sciences, Cromore Road, Coleraine, Co. Londonderry BT52 1SA, T: 08700 400 700	Offers Marine Science BSc (Hons)

APPENDIX 5: RESEARCH VESSELS OPERATING FROM THE UK

TABLE 58: UK RESEARCH VESSELS

NAME	BASE OR ORGANISATION	WORKING SCOPE
Aora	UMBS, Millport	Scottish West Coast, North Irish Sea
Aplysia	UMBS, Millport	Scottish West Coast, North Irish Sea
Beagle	MoD, HSS	Coastal Waters
Bernicia	Dove Marine Laboratory	Northumberland Sea Area
Bill Conway	SOC	Solent, Channel and Poole Bay
Bulldog	MoD, HSS	Coastal Waters
Calanus	NERC, CCMS, DML	Scottish West Coast
CEFAS Endeavour	CEFAS	North & Irish Seas, Channel & SW Approaches
Charles Darwin	NERC Research Ship Unit	Worldwide
Clupea	SERAD, FRS	North Sea, West Coast of Scotland
Coastal Guardian	EA, National Marine Service	UK Home Waters
Colonel Templer	MoD, DERA	Worldwide
Corystes	CEFAS	North Atlantic, North Sea
Discovery	NERC Research Ship Unit	Worldwide
Ernest Shackleton	NERC, BAS	Worldwide, Polar Seas
Gleaner	MoD, HSS	Inshore Waters
Hecla	MoD, HSS	Worldwide
Herald	MoD, HSS	Worldwide
James Clark Ross	NERC, BAS	Worldwide, Polar Seas
Lough Foyle	DANI	Irish Shelf and Celtic Sea.
Newton	MoD, RMAS	Worldwide
Prince Madog	U of W, Bangor, SOS	Shelf Seas West of Britain
Roagan	Port Erin Marine Laboratory	Irish Sea
Roebuck	MoD, HSS	Shelf and Coastal Waters
Scotia	SERAD, FRS	North East Atlantic, North Sea
Sea Vigil	EA, National Marine Service	UK Home Waters
Seol Mara	NERC, CCMS, DML	Inshore Waters
	NERC, CCMS, PML	Inshore and Estuarine Waters
Squilla		Inshore Waters
Sula	Port Erin Marine Laboratory	Isle of Man Coastal Waters
	NERC, CCMS, PML	Inshore and Estuarine Waters
Vigilance		UK Home Waters
Water Guardian	EA, National Marine Service	UK Home Waters

APPENDIX 6: EUROCEAN LIST OF UK INSTITUTIONS AND SOCIETIES INVOLVED IN MARINE-RELATED ACTIVITIES[152]

TABLE 59:UK INSTITUTIONS INVOLVED IN MARINE ACTIVITIES

Aberdeen University Lighthouse Field Station
Atmospheric Chemistry Studies in the Oceanic Environment (ACSOE)
Britain and Ireland Association of Aquatic Sciences Libraries and Information Centres (BIASLIC)
British Antarctic Survey
British Atmospheric Data Centre (BADC)
British Dynamics of Earth and Ocean Systems (DEOS)
British Geological Survey (BGS)
British Marine Life Study Society
British Marine Life Study Society
British Ocean Sediment Core Repository (BOSCOR)
British Oceanographic Data Centre (BODC)
Cardiff University Marine Institute
Cardigg School of Earth, Ocean and Planetary Sciences
CEFAS Lowestoft Laboratory
Centre for Environment, Fisheries and Aquaculture Science (CEFAS)
Cetacean Research & Rescue Unit (CRRU)
Coastal Studies Research Group (CSRG)
Coastal Zone Research Network (COZONE)
Dunstaffnage Marine Laboratory
Fisheries Research Services
Glasgow College of Nautical Studies Faculty of Maritime Studies
Glasgow University UMBS Millport
Hadley Centre for Climate Prediction and Research
Heriot-Watt University: Ocean Systems Laboratory & Centre for Marine Biotechnology
Imperial College Of Science and Technology Oceanography Laboratory
Inter-Agency Committee on Marine Science and Technology (IACMST)

NERC Arctic Environmental Metadata Centre
Sciences and Coastal Management (MSCM)
North Atlantic Fisheries College
Oxford University:Atmospheric, Oceanic and Planetary Physics & Marine Group
Plymouth Marine Laboratory
Proudman Oceanographic Laboratory (POL)
Reading University Oceanography Group
Royal Meteorological Society
Scott Polar Research Institute (SPRI)
Scottish Association for Marine Science (SAMS)
Scottish Environment Protection Agency (SEPA)
Sea Fish Industry Authority (Seafish)
Society for Underwater Technology (SUT)
The Scottish Association for Marine Science (SAMS)
The Sir Alister Hardy Foundation for Ocean Science (SAHFOS)
U.K. Ocean Drilling Program
UK GLOBEC - Marine Productivity
UK Met Office Research and Development
United Kingdom Hydrographic Office (UKHO)
United Kingdom Met Office
University of Aberdeen: Centre for Marine and Coastal Zone Management & Department of Zoology - Marine Studies
University of East Anglia Physical Oceanography
University of Edinburgh Institute for Meteorology
University of Glasgow Marine Technology Centre (GMTC)
University of Liverpool: Oceanography Laboratories & Port Erin Marine Laboratory

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152 source: EurOcean website – covering all aspects of marine science and technology

TABLE 59: CONT

International Centre for Island Technology
Joint Nature Conservation Committee (JNCC)
Land-Ocean Interaction Study (LOIS)
Marine Biological Association of UK
Marine Sciences and Coastal Management
National Maritime Museum (NMM)
National Oceanographic Library
Natural Environment Research Council (NERC)
Natural Environment Research Council (NERC).

University of Plymouth: Institute of Marine Studies & School of Earth, Ocean and Environmental Sciences
& Sea Mammal Research Unit
University of Stirling: Institute of Aquaculture & Marine Environmental Research Laboratory
University of Ulster Coastal Studies Research Group (CSRG)
University of Wales: Centre For Applied Oceanography & School of Ocean Sciences

APPENDIX 7: EXISTING UK INITIATIVES WITH MARINE BIOTECHNOLOGY NETWORKING POTENTIAL

TABLE 60: UK NETWORKING INITIATIVES – BMI CHALLENGE

BABRAHAM BIOINCUBATOR Dr David Hardman Babraham BioIncubator The Babraham Institute Babraham, Cambridge CB2 4AT Tel: 01223 496 205 Fax: 01223 496 020 email: david.hardman@bbsrc.co.uk Web site: http://www.bi.bbsrc.ac.uk	**NORWICH BIO-INCUBATOR** Dr John Carter Norwich Bio-Incubator Norwich Research Park Colney Lane, Norwich NR4 7UH Tel: 01603 218102 Fax: 01603 450000 e-mail: j.carter@norbio.com
BIOFORM Dr Linda Naylor / Dr Tom Hockaday Isis Innovation Limited Ewert House, Ewert Place Summertown, Oxford OX2 7BZ Tel: 01865 272 414 Fax: 01865 272 412 e-mail: l.naylor@isis.oxac.uk Web site: http://www.isis-innovation.com	**OXFORDSHIRE BIOTECHNET** Mr Nigel Wild Oxfordshire BiotechNet Ltd Littlemore Park Tel: 01865 405 100 Fax: 01865 405 101 email:nigel.wild@biotechnet.co.uk Web site: http://www.biotechnet.co.uk
BIOINCUBATOR YORK Dr Rukmal Abeysekera Bioincubator York Innovation Centre York Science Park York YO10 5DG Tel: 01904 433 026 Fax: 01904 433 030 e-mail: incubate@york.ac.uk Web site: http://www.york.ac.uk/org/bioincubator	**PROGENY BIOVENTURES** Theresa Wallis Progeny bioVentures ANGLE Technology Surrey Technology Centre Guildford, Surrey GU2 5YG Tel: 01483 295830 Fax: 01483 295386 Web site: http://www.angletechnology.com/
BIOTECH BUSINESS BUILDING (3B's) Dr Ceri Batchelder Manchester Innovation Limited Manchester Incubator Building Grafton Street, Manchester M13 9XX Tel: 0161 606 7200 Fax: 0161 606 7300 email: ceri.batchelder@maninv.com Web site: http://www.3BsProject.com	**TETRICUS** Dr Clive Duggleby Tetricus Ltd Porton Down Science Park Salisbury, Wiltshire SP4 0JQ Tel: 01980 556 514 Fax: 01980 556 515 e-mail: info@tetricus.co.uk Web site: http://www.tetricus.co.uk
IMPERIAL COLLEGE COMPANY MAKER Ms Dominique Kleyn Imperial College Innovations 12th Floor, Electrical and Electronic Engineering Department London SW7 2AZ Tel: 020 7581 4949 Fax: 020 7589 3553 e-mail: d.kleynk@ic.ac.uk Web site: http://www.icinnovations.co.uk	**WHEB VENTURES LIMITED** Dr Rob Wylie & Mr Kim Heyworth 7 Hertford Street London W1J 7LP Tel: 020 7493 9977 Fax: 020 7493 9933 email: rob@whebventures.com or kim@whebventures.com Web site: http://www.whebventures.co.uk/
MERLIN VENTURES 33 King Street, St. James's London SW1Y 6RJ Tel: 020 7811 4000 Fax: 020 7811 4001 email:mailbox@merlin-ventures.co.uk Web site: http://www.merlin-ventures.co.uk/	

TABLE 61: UK NETWORKING INITIATIVES – BEP CHALLENGE

Aber BioCentre BEP (Biomedical, pharmaceutical, biological processes, agriculture, environment) David Craddock Tel: 01970 622385 E-mail: david.craddock@aber.ac.uk Web site: www.aber.ac.uk/abc	**EnVision BEP** (Environmental biotechnology) Peter Ainsworth Tel: 020 7594 6563 E-mail: p.ainsworth@ic.ac.uk Web site: www.eett.co.uk
Beacon Bio BEP (Bioremediation, industrial processes, drug development and screening systems, CNS-related research, fungal and microbial diversity) Dr Helma Kaptein Tel: 01273 873267 or 873000 E-mail: h.kaptein@sussex.ac.uk Web site: www.sussexip.com	**manIP & TrusTECH BEP** (Biological instrumentation and healthcare, biomaterials, diagnostics, gene tissue, medical devices, pharmaceuticals) Dr Richard Deed Tel: 0161 276 5763 E-mail: RichardDeed@trustech.org.uk Web site: www.trustech.org.uk
BioElf Ltd BEP (Food and plant, environment, healthcare, medical devices) Prof. Howard Slater Tel: 01823 430052 E-mail: info@bioelf.org Web site: www.bioelf.org	**STEP 2000 BEP** (Biomedical, diagnostics, gene therapy, medical devices, pharmaceuticals) Dr Sharron Bennett Tel: 020 7848 3325 E-mail: sharron.bennett@kcl.ac.uk Web site: www.step2000bio.co.uk
Bioscience Partnership BEP (Healthcare) Dr Kay Callaghan Tel: 0191 222 7700 E-mail: kay.callaghan@ncl.ac.uk Web site: www.biosciencepartnership.co.uk	**UK MicroBEP** (Microbial biotechnology) Dr Jan Chojecki Tel: 01603 456500 E-mail: ajsc@pbltechnology.com Web site: www.pbltechnology.com
Bio-THRuST BEP (Nanotechnologies and microsystems in a range of bio-industry sectors) Dr Robert Carr Tel: 01980 611862 E-mail: biothrust@mma.org.uk Web site: www.mma.org.uk/biothrust.htm	**WessexBio BEP** (Regional healthcare and biomedical) Dr Elizabeth Fletcher Tel: 02380 593 095 E-mail: e.j.fletcher@soton.ac.uk
Cancer Research Technology (CRT) BEP Susan Harris Tel: 020 7269 3640 E-mail: sharris@cancertechnology.co.uk Web site: www.cancertechnology.co.uk	**Western Arc BEP** (Biomedical, pharmaceutical, biological processes, environment) Dr Wendy Ross Tel: 029 2087 4673 E-mail: rossw@cardiff.ac.uk
CENTECH BEP (Medical devices, environmental sciences, pharmaceuticals, therapeutics, diagnostics) Dr Lyndon B Davies Tel: 01223 262686 E-mail: lyndon@ldassoc.demon.co.uk	**White Rose BEP** Simon Donoghue Tel: 01904 435353 E-mail: cw21@york.ac.uk Web site: www.whiterose.ac.uk
(Diagnostic technologies) Lisa Mynheer Tel: 01865 811127 E-mail: l.mynheer@oxin.co.uk Web site: www.diagnox.co.uk	**Yorkshire BioEnterprise BEP** (Diagnostic and analytical technologies, biomedical, biomaterials processing, food and agriculture, environment) Dr David Parkinson Tel: 0114 225 3052 E-mail: D.Parkinson@shu.ac.uk

TABLE 62: FARADAY PARTNERSHIPS

NAME	THEME	WEB-SITE	COMMENT
FIRST	Innovative Remediation Science and Technology	www.firstfaraday.com	bioremediation, novel organisms, enzymes, sensors
FOOD PROCESSING	Developing the underpinning Materials, equipment and Process knowledge applicable to food processing	www.pera.com/foodfaraday/index.asp	marine products and food safety, processing
IMPACT	Innovative Materials Development and Product Formulation by the application of Colloid Technology	www.impactfp.org	
INSIGHT	High throughput technologies for new product and process development	www.insightfaraday.org	screen or reactor processes
INTERSECT	Intelligent sensors for control technologies	www.intersect.org.uk	sensor technology, robotics
MEDICAL DEVICES	Medical Devices	www.medical-devices-faraday.com	biomaterials, scaffolds, tissue engineering
IMAGING	Digital Imaging	www.imagingfp.org.uk	virtuality, deep-sea imaging
GENESIS	Farm Animal Genetics and Genomics	www.genesis-faraday.org	– parallels
IMSE	Industrial Mathematics and System Engineering	www.smithinst.ac.uk	modelling, algorithmic profiling
INREB	Integration of new and renewable energy in buildings	www.inreb.org	maybe H2 or renewable energy units
MINI-WASTE	Novel Technologies and processes for the minimisation of industrial waste	www.mini-waste.com	marine-origin materials
PACKAGING	Practical Innovation for fast-moving consumer goods (fmcg) packaging, its manufacture and supply	www.faradaypackaging.com	marine-origin materials
PINPOINT	Global navigation satellite systems (GNSS) applications	www.pinpoint-faraday.org.uk	biodiversity mapping
PLASTICS	critical technological challenges of the plastics sector	www.faraday-plastics.com	new materials, biocatalysts, remediation
PRIME	Smart Products (products with inter-dependent mechanical and electronic parts)	www.primefaraday.org.uk	nanostructures, novel biocatalysts, piezophile molecules
PRO-BIO	Bio-catalytic processes for manufacturing	www.pro-bio-faraday.com	novel enzymes
SMART OPTICS	Smart Optics	www.smartoptics.org	advanced marine materials, nanostructures
TECHNITEX	Technical textiles		marine-origin fibres, materials

APPENDIX 8: COUNTRY PROFILES – THE EU

THE EU AND ITS RTD SUPPORT

Marine biotechnology and biodiversity

The EU has funded about 75 projects in marine bio[techno]logy, of which about 40 are real marine biotechnology[153]. Under FP6, one specific objective of the ERA-NET cross-border support programme is to strengthen Baltic marine science (see later), as well as to build a European Marine Research Area to complement other ERAs. In the Cell Factories programme of FP5, Extremophiles as Cell Factories received about € 7 million, for example.

The next EurOCEAN European conference on marine science and ocean technology will take place in Galway, Ireland, from 10 to 13 May 2004[154]. Although this includes all marine science, and in the past has tended toward maritime engineering, transport and environmental issues, the forthcoming conference has a strong focus on biodiversity and the potential of marine resources for added value:

TABLE 63 MARINE BIOTECHNOLOGY & BIODIVERSITY-ORIENTED PRESENTATIONS AT EUROCEAN 2004[155]

Marine biotechnology and biodiversity: use of marine organisms as sources of pharmaceuticals and other biologically active compounds	Dr. Adrianna Ianora (Italy) Stazione Zoologica "A. Dohrn"
ERA and FP6 marine research in Europe	Mr. Pierre Mathy (EU), Directorate General for Research
Marine Research Infrastructures- need for a better co-ordination	Dr. Rudy Herman (Belgium), Science and Innovation Administration
European Marine Science in the Global context	Dr. Jean-Francois Minster (France), IFREMER
European strategy for the management of the marine environment- science requirements	Mr. Patrick Murphy (EU), Directorate General for Environment
FP6 NoE "Marine Genomics" Management and Co-ordination	Prof. Adelino Canario (Portugal) University of Algarve

The inclusion of these topics, the conference's adoption as an explicit Irish Presidency Event and the current scale of EU funding for marine bio[techno]logy suggest that marine biotechnology is genuinely becoming a focus for more effort and that the EU has an accelerating potential to act as a significant multiplier of well-networked national activities, despite the absence of an explicit marine biotechnology focus in FP6.

FP6 has funded a very large Network of Excellence (NoE) on marine biodiversity research, 'MARBEF' - Marine Biodiversity and Ecosystem Functioning[156] – with a consortium of 56 institutes co-ordinated by Carlo Heip of NIOO-CEME, Yerseke – the

153 see www.cordis.lu
154 see http://www.eurocean2004.com
155 source: EurOcean 2004 web-site
156 see http://www.marbef.org

Netherlands. The opening meeting took place on 17-19 March 2004 in Bruges Belgium. The European Register of Marine Species, an output of the ERMS project funded from 1998-2000 in the EU's MAST programme, will be incorporated into the data available through MARBEF. There is also a NoE on Marine Genomics, co-ordinated by the Marine Biology Station/CNRS Roscoff, France, in the name of the GIS on Marine Genomics set up in 2002 in France (see next section). The proposal for this NoE recognised that, compared to other fields, the marine sciences community is fragmented across Europe and has therefore benefited less from the genomics revolution. There are 9 institutions in the Core Partners' Group, 32 others. 11 of the 41 are from UK - the University of Birmingham, the Antarctic Genome Laboratory at the School of Ocean and Earth Science, Southampton (both core partners), the Universities of Newcastle, Hull, Oxford, Wales-Bangor, Wales-Cardiff and Warwick, the Plymouth Marine Biology Laboratory, Southampton Oceanography Centre and CEFAS Weymouth.

Research vessels

Research vessels, RVs, are critical to marine biodiversity and bioprospecting operations. The European Science Foundation's Marine Board reported recently on Integrating Marine Science in Europe, shortly followed by the Academy of Finland on infrastructure[157]. One aspect covered is the situation with regard to RVs and vehicles. There is a European research fleet of more than 190 RVs, the majority of which were built between 1962 and 1995. It is a misnomer that this is a 'European fleet', since productive co-operation has only recently begun, in 1996 for a tripartite BMBF-IFREMER-NERC Anglo-German-French agreement, for individual 2- or 3-way groupings focused on individual RVs or projects and, more recently, via the European Science Forum Marine Board's network of Operators of European Research Vessels.

Currently, France, Norway and Finland are planning small RVs, and there is a joint Navy-IFREMER initiative in France for 2 large RVs, a German-led consortium approach to a new Arctic icebreaker that is expected to cost at least € 250 million to build and € 15 million to run each year and proposals are with the UK Government for a replacement to the RV *Charles Darwin.* A further 11 RVs of over 30 metres are planned, 4 by Germany, 2 by Norway, 1 each by France, Spain, Poland, Ireland and UK, between 2003 and 2105. The UK currently has 33 RVs and survey vessels, including two polar vessels.

Undersea vehicles are rather few in number in Europe. France had two manned submersibles, but one was taken out of service in 2003, Greece has one and Portugal operates one in the waters off the Azores. IFREMER has one deep-sea remotely operated vehicle (ROV), which works waters from 1000m to 6000m and requires a large support vessel, Germany has one operating to 4000m and one to 1000m, Norway has one to 2000m, and the Southampton Oceanographic Centre has another ROV, operating to 6500m and more flexible in terms of support size. Autonomous underwater vehicles, AUVs, of which NERC has one example to 1500m, Portugal one to 200m and Germany and Netherlands are building others, have been very successful, partly because of their ease of deployment and flexibility. Sea-bed Observatories are widely regarded as being a constructive way forward in mapping and understanding the

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[157] see *Integrating Marine Science in Europe*, ESF Marine Board Position Paper 5, November 2002, and *European Strategy on Marine Research Infrastructure*, Academy of Finland April 2003, from which information on RVs and undersea vehicles is taken

physical and biological environment around Europe, and collaborative use is strongly recommended.

FRANCE

TABLE 64: RESEARCH ACTIVITIES IN FRANCE

INSTITUTE/ORGANISATION	COMMENTS
CNRS Institut National des Sciences de l'Univers (INSU) IFREMER National Natural History Museum (MNHN)	These are the main organisations involved in funding marine science and technology, often of the same departments or unités, resulting in a plethora of abbreviations connected with these (CNRS UBO MNHN, for example); CNRS units are often in or affiliated with Universities
Centre de Recherche sur les Ecosystèmes Marins et Aquacoles de l'Houmeau (CREMA L'HOUMEAU)	Mariculture, disease prevention, molecular approaches to populations
IFREMER Institut Français de Recherche pour l'Exploitation de la Mer, Issy-les-Moulineaux	Bioactives from marine extremophiles, algae and other marine products; marine microbes as contaminants; pollution; ecology of marine organisms
Institut National des Sciences et Techniques de la Mer (INTECHMER), Laboratory of Marine Research and Studies, Cherbourg	Marine biotechnology group working on extremophiles and marine environment research group working on sediment pollutant exchanges with the sea
European Institute for Marine Studies (IUEM), Plouzane	One of the CNRS's National Network of Marine Stations and part of the regional "Blue Network" of civilian and military Marine Sciences institutes
National Natural History Museum (MNHN), Station de Biologie Marine de Concarneau; Unité Biologie des Organismes Marins BOME-CNRS; Université de Bretagne Occidentale Laboratoire de Chimie, Paris	Activities across the National Natural History Museum (MNHN), CNRS and the University of Brest - biofouling; bioactives from marine organisms; bioactives and added-value from marine wastes; antibiotics from fish mucus; molecular evolution & physiology in crustacea & molluscs; biomineralisation Bioactives from tunicates and their symbionts
NAUSICAÄ, Boulogne-sur-Mer	The French National Sea Experience Centre, dedicated to informing people about the sea and the need for sustainable management of marine resources.
Université de Bretagne Occidentale (UBO) Unité LEBHAM-LCHO, Plouzane Unité FRE 2125 Chimie et Biologie des Substances Naturelles, Quimper	Fundamental and applied research in algae and seaweeds; bioactives from marine and coastal plants; population ecology; bioactives synthesis
Université de Caen, Laboratoire de Biologie et Biotechnologies Marines (IBBA IFREMER), Laboratoire de Biochimie (IRBA CNRS UPRES)	Biofouling by marine algae; cell cultures of the mollusc *Haliotis* and production of molluscan extracellular matrix
Université de Corse, Equipe Ecosystèmes Littoraux	Marine ecology, studying species of commercial interest, biomarkers.
Université des Sciences et Technologies de Lille, Station Marine de Wimereux, Villeneuve d'Ascq	Carbon cycling in the oceans; pollutant cycling
Université de la Méditerranée, Marseille, Centre d'Oceanologie de Marseille	
Université Pierre et Marie Curie, Paris/CNRS Observatoire océanologique, Banyuls-sur-Mer Marine Biology Station Roscoff, Phytoplankton Group, Cell Cycle Group and Cellular Physiology Research Group Observatoire Océanologique de Villefranche-sur-Mer	Impact of marine organisms on the environment and ecosystems Marine biological and biogeochemical cycles, Characterisation of picoplanktonic populations using proteins from photosystems I and II
Centre d'Étude et de Valorisation des Algues (CEVA), Pleubian	Seaweed and algal research for foods, industrial, ecological use
Université d'Evry Génoscope	The facility at which marine genomics is being carried out as part of the GIS GENOMER

France sees itself as particularly strong in marine genomics[158]. The Brittany region funded a programme GENOMER in 1999, based on the Roscoff Marine Biology Station, involving 54 research units across disciplines, with about 800 researchers. As a result, a Scientific Interest Group in marine genomics 'GIS GENOMER' was established in July 2003 with funding from the regional government, the Ministries of Fishing and Research and CNRS. The focus is to continue sequencing marine algae, using the facilities of the Génoscope at the University of Evry, and move on to transcriptomics and proteomics. The GIS also has access to the EU Network of Excellence (NoE) Marine Genomics, initiated in Spring 2004, via the CNRS-University of Paris 6 Unité mixte at Roscoff, co-ordinator of the NoE, and IFREMER.

France is also particularly active in enhancing industrial value of bioscience and other research, which has been given the specific word 'valorisation', somewhat more attractive than the English equivalent 'exploitation'. There are a number of centres in France where valorisation of marine algal biomass is carried out and in particular, at the Centre d'Étude et de Valorisation des Algues in Brittany[159]. Set up in 1982 to attack encroachments of seaweeds along the coast, focus changed to encompass development of new products from seaweed. CEVA is based at Presqu'Île de Pen Lan in Pleubian and includes microalgae and marine plants as well as seaweeds in its remit. Although many products are at what could be called the non-sophisticated end of the market – food, fertilisers, petfoods – the potential for seaweed products in the cosmetic and pharmaceuticals sectors and for bioremediation is also being progressed.

Research and development services available at CEVA include

- the conception and development of new products
- finalising and developing basic marine ingredients. (PAI, active agents, base materials)
- the extraction and purification of molecules extracted from algae
- the designation and evaluation of ingredients : their composition, functional, nutritional and biological properties.
- the elaboration and preparation of algal extracts in response to special requirements
- the development and validation of analysis techniques adapted to the raw material of algae

Significantly and characteristically this French centre is also embracing new technologies and is involved with new National marine genomics programmes. Pharmaceutical laboratories and biotech companies will therefore have access to a constantly growing pool of information on the diversity of marine genomes. Further knowledge of the genetics of marine populations could also prove useful to canning industry, to fisheries and aquaculture.

The Marine Biology and Biotechnology Lab at the University of Caen, studies the cellular and molecular aspects of metabolic processes in molluscs and algae. This research is relevant to the shellfish farming, cephalopod and bivalve fishing and macro-algae

158 see http://www.ceva.fr/actualites.html and www.sb-roscoff.fr

159 see www.ceva.fr

exploitation industries. At the national level and within a shared department with IFREMER, the MBBL deals with the key aspects of the algal growth and reproduction.

IFREMER has a research programme on molecules extracted from marine algae. This includes:

- Macro-algae : research deals with sulphated polysaccharides extracted from brown algae (application in treatment of cardiovascular diseases). The project is conducted within the framework of the URM* N °2 (University of Paris XIII) (industrial partnership supported by the ANVAR). CEVA is taking part in the project in the preparation of algae polysaccharides and patent supervision.
- Micro-algae : this project began with the study of diatoms (Skeletonema costatum) produced using saline groundwater. The aim is to optimise production in open areas, to find compounds that can be developed and to develop equipment to produce these compounds (LAMP, artificial light, average productivity, photobioreactors).

IFREMER[160] also has an internationally recognised deep-sea marine research infrastructure, consisting of ships and submersibles that are among the most advanced in the world, along with Japan and US facilities. There is access to French oceanic and external territories for exploration and biodiversity work, led by Georges Barbier.

IFREMER's bioactives R&D is focused on molecules from hydrothermal micro-organisms, including

- thermostable enzymes: in response to industrial firms wishing to use enzymes with thermostability or new enzymes, IFREMER is studying and developing replication factors, ligases, polymerases, alcohol dehydrogenase, esterase and glucosidases.
- there is a programme highlighting the chemical and rheological characterisation of new bacterial polysaccharides of hydrothermal origin, with the objective of evaluating the potential of these macromolecules in the fields of heavy metal bioremediation, new functional components of food and health, especially the nutraceutical, cosmeceutical or direct pharmaceutical applications of the exopolysaccharides.

The Marine Biology Station (Centre d'Etudes d'Óceanographie et de Biologie Marine) at Roscoff has already been carrying out marine genomics and, with the Génoscope at Evry, has sequenced the genomes of the picoplanktonic cyanobacteria *Prochlorococcus* and *Synechococcus*. Collaborators also included the University of Warwick, the Scripps and Woods Hole Institutions and Alexander-Humboldts-Universität.

Researchers at Roscoff, in collaboration with the University of Athens, have isolated a novel compound 6-bromoindirubin-6'-oxime (BIO) from *Hexaplex trunculus*, the source of the dye Tyrian purple. As a result of a sabbatical by the Roscoff researcher Laurent Meijer at Rockefeller University, Rockefeller is now using BIO to stabilise mammalian embryos and embryonic stem cells and stimulate differentiation.

Commercial activity in France is strong in the cosmetics sector, driven by the Government's programme of support for exploitation of seaweed resources and by a pre-existing R&D buoyancy in this industry.

[160] see www.ifremer.fr

TABLE 65: COMPANIES INVOLVED IN MARINE BIOTECHNOLOGY OR MARINE-DERIVED PRODUCTS – FRANCE

COMPANY	COMMENTS
Aventis Pharma	Strasbourg-based international company, working on girolline from *Pseudaxinyssa* sponge and, with the US company Inflazyme, on a synthetic analogue of contignasterol for inflammatory diseases.
Laboratoires Codif SA	based in St Malo, makes bioactive algal extracts from microalgae and seaweeds for skin repair (high-protein extract from *Chlorella vulgaris*) and treatment of acne ('phycosaccharides' from *Laminaria digitata*); also uses omega-3 fatty acid rich oil from *Odontella aurita* extracted using a supercritical CO_2 process
CTPP	Boulogne-based fish-processing cooperative, produces marine-origin materials for cosmetic products, including elastin, oligosaccharides, gelatine from fish skin and peptides (claimed to be Immunomodulating and to stimulate cell growth); for foods, it produces enzymatically-hydrolysed marine collagen, pure chondroitin sulphate and derivatives from skate and siki (Portuguese dogfish) - cartilage, elastin and processed cartilage (a blend of mucopolysaccharides, minerals and cartilage proteins); more conventionally, CTPP makes refined oils, flavour extracts from scallop, shrimp, crab, squid, lobster or mussel by-products, peptones for industrial fermentation and nucleic acids for laboratory use
Laboratoires Goëmar	St Malo-based, an extracter of beta-glucans from seaweed and developer of products for cosmetics, crop protection and healthcare, under the name Phycarine®, using a liquid nitrogen freezing and extraction process; funds research at the CNRS-Université Paris VI Unité 'Végétaux marins et biomolécules' Roscoff, part of the French GIS Génomique Marine
Sederma	a subsidiary of the UK firm Croda International, sells Skin Tightener from marine sources, for anti-wrinkle use. Hydrergy is a skin toner with algal extracts and Capigen, for preventing hair loss, contains synthetic, marine and biotech ingredients[161]; also sells 'DNA Gel', obtained from marine sources, and Ichthyocollagen, both indicated for skin repair; has recently been developing a product Venuceane™ containing enzymes and other molecules produced by fermentation from *Thermus thermophilus*, collected from a hydrothermal vent from the Gulf of California, obtained under licence from CNRS France - the enzymes are anti-oxidant and according to the company prevent free radical damage to skin fibroblasts[162].
Lanatech SA	Lanatech's product Abyssine 657 contains an exopolysaccharide from the deep-sea vent bacterium *Alteromonas macleodii* as a skin protectant, developed by and based on work at IFREMER Brest, with whom Lanatech has an arrangement for marine bioproducts; Lanatech has named the molecule 'Deepsan' and has found it reduces skin damage from inflammatory insults, as measured by reduced ICAM-1 activity; has also launched 'Lanablue', based on extracts from a cyanophycean alga harvested from Lake Klamath, Oregon USA; bought In November 2003 by the Canadian group Atrium[163]

GERMANY, AUSTRIA AND SWITZERLAND

Germany's strong support of natural product programmes, coastal and coldwater research and biotechnology as a whole has led to a very strong scale and scope of

[161] see http://www.sederma.fr/

[162] see http://www.newscientist.com/hottopics/tech/article.jsp?id=99991503&sub=Extra

[163] Atrium is also owner of Aeterna, which is developing shark cartilage extracts for medical use.

potentially fruitful research. The UK will need to consider what level of support might be needed for the UK sector to allow it to keep up with this.

In Austria, the Marine Biology department at the University of Vienna is involved in benthic ecology and invertebrate-symbiont studies. In Switzerland, the Novartis Venture Fund is a lead investor in Nereus Biosciences, the company based on Bill Fenical's discoveries at the Scripps Institution of Oceanography, La Jolla California. The fund was established in the late 1990s, and was initially aimed at assisting ex-Novartis employees to set up their own businesses. Managed from Basel, the fund has investments widely spread, and has the goal of 'creating a home for many innovative technologies that can be developed faster and more efficiently in smaller start-up companies than in the larger pharmaceutical world'.

TABLE 66: RESEARCH ACTIVITIES IN GERMANY AND AUSTRIA

INSTITUTE/ORGANISATION	COMMENTS
University of Vienna, Austria, Department of Marine Biology	Marine Ecology, especially of benthic systems; symbioses between bacteria and animals.
BioCon Valley Initiative, Bioregio Greifswald-Rostock	Technocommercial initiative to bring biotechnology research and companie together
Universität Bonn, Institut für Pharmazeutische Biologie	Projects to explore the biosynthetic capabilities of marine fungi, especial fungi living as endophytes in marine algae
Gesellschaft für Biotechnologische Forschung mbH (GBF), Braunschweig	Detection of pharmacologically active natural products using ecology, including Indopacific marine invertebrates and sponge-derived fungi
Universität Bremen, Departments of Biology, Marine Zoology, Marine Botany Centre for Tropical Marine Ecology (ZMT) Marum - Centre for Marine Environmental Sciences	Ecophysiology and biochemistry of marine organisms; new assay method under the EU Water Framework Directive; dimethyl sulfonium propionate (DMSP) in toxic dinoflagellates, picoplankton and *Tetraselmis*; interactions between Antarctic ice diatoms and epiphytic bacteria; ecophysiology of Antarctic ice algae and proline as protection against salt and temperature stress Focus on reefs, plankton, nutrient metabolism, population genetics, ecology, baseline data for fisheries and mariculture
Max-Planck-Institute for Marine Microbiology, Bremen, Department of Biogeochemistry, Microsensors Group, Group for Flux Studies, Department of Microbiology, Department of Molecular Ecology	Interaction of marine microbial and geochemical processes in sediments, ecology and physiology of cold-adapted bacteria and nitrate-storing bacteria, transformations of sulphur, iron and manganese and their interactions in marine sediments, the chemistry and degradability of complex macromolecular organic material in marine sediments, distance monitoring and high-performance sensing for N, O and S cycles in sediments and microbial mats, flux processes in sediments and across boundaries, physiology and diversity of bacteria from the carbon, nitrogen, sulphur and iron cycles, culture and characterisation, hydrocarbon- and oil-degrading bacteria, molecular methods for studying biofilms, symbiotic associations and planktonic or benthic bacterial communities.
Alfred Wegener Institute for Polar and Marine Research (AWI), Bremerhaven Department of Marine Chemistry and Marine Natural Products	Violacein and desoxyviolacein as non-biocidal antifoulants, Δ12-desaturase from the cold-resistant polar algae *Fragilariopsis cylindrus*, chemical ecology of marine invertebrates, use of mollusc gills as bioassay, molecular studies of cold adaptation and cold acclimation in marine ectothermic animals
Christian Albrechts University of Kiel, Research and Technology Centre Westcoast, Büsum	kinetics of photosynthetically-active algae; analysis of excitation spectra for algae group detection and chlorophyll-a determination

TABLE 66: CONT

INSTITUTE/ORGANISATION	COMMENTS
Westfälische Wilhelms-Universität, Münster, Marine Biology Wadden Sea Station Carolinensiel, Institut für Zoophysiologie	Working on bioactives from natural sources including marine
Heinrich-Heine-Universität Düsseldorf, Institut für Pharmazeutische Biologie	Marine natural products, marine medicines, chemical ecology; working with GBF Braunschweig on bioactives from Indopacific marine invertebrates and sponge-derived fungi
Friedrich-Alexander-Universität Erlangen, Institute of Bioprocess Engineering	Potential of phototrophic micro-organisms, cultivation techniques, a bioreactor system for *Medusa*, photobioreactor screening modules (PSMs)
Senckenberg Centre for Biodiversity Research, Frankfurt	Deep-sea hydrothermal research
KliniPharm, Frankfurt	Working on bioactives such as avarol from *Dysidea avara* and aspects of sponge culture of *Geodia cydonium* for bioactive metabolites
Institute for Coastal Research, Geesthacht	Uses physical and chemical analysis to look at impacts on the Coastal Zone from substances, and as a resource for natural substances of potential value such as pharmaceuticals or food supplements
Institute for Marine Biotechnology Greifswald (IMaB)	Bioactive compounds; screening and characterisation of cyanobacteria and marine fungi producing substances with antibacterial, antifungal, antiviral, cytostatic, immunomodulatory or enzyme inhibitory properties – drug development based on marine natural products; Isolation, structure elucidation and analysis of bioactive compounds; cultivation of marine micro-organisms; Target analyses (Proteomics of marine bacteria) Cold-adapted enzymes; Screening of psychrophilic microorganisms with cold-adapted enzymatic activities; Cloning and expression of cold-adapted enzymes Enzyme production processes; Development of bacterial expression systems for the overproduction of thermolabile or insoluble enzymes; Optimisation of bacterial fermentation processes; Quality control of recombinant enzymes by proteomics
Universität Hamburg, Institut für Meereskunde, Institute for Biogeochemistry and Marine Chemistry (IfBM) The German Society for Marine Research (Meeresforschung)	Boreal Sponges-Sources of Marine Natural Products Porifera in deep cold-water reefs: Habitat-analysis and natural products inventory
Forschungszentrum Jülich GmbH	Programme includes marine and polar research
Hans-Knöll-Institut für Naturstoff-Forschung eV, Kiel	Has a library of organisms and extracts and isolates and characterises natural products, including from marine sources
Universität Mainz, Institut für Physiologische Chemie, Abteilung Angewandte Molekularbiologie	Initiation of an Aquaculture of *Geodia cydonium* sponges for the Sustainable Production of Bioactive Metabolites in Open Systems
Wilhelms-Universität Münster	Ectoines from halophiles as cosmetic components
Universität Regensburg, Lehrstuhl für Mikrobiologie	Cultivation, isolation, and characterisation of microorganisms from marine invertebrates
Carl von Ossietzky Universität Oldenburg, Institut für Chemie und Biologie des Meeres (ICBM)	Significance of particle-associated marine bacteria producing secondary metabolites

TABLE 66: CONT

INSTITUTE/ORGANISATION	COMMENTS
University of Würzburg, Biozentrum, Institut für Molekulare Infektionsbiologie	Research: Extracts from marine sponges screened for their antimicrobial and antifungal activities; Marine Surfaces and the Expression of Specific Byssal Adhesive Protein Variants in Mytilus; Antimicrobial Activities and Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry of *Bacillus* Isolates from the Marine Sponge *Aplysina aerophoba* Collaborations with : Institut für Chemie, Arbeitsgruppe Biochemie und Molekulare Biologie, Technische Universität Berlin, Institut für Biochemie, Freie Universität Berlin, Institut für Pflanzengenetik und Kulturpflanzenforschung, Abteilung Molekulare Genetik, Corrensstrabe 3, D-06466 Gatersleben & Institut für Organische Chemie, Universität Würzburg
University of Kiel, IFM-GEOMAR, Leibniz-Institut für Meereswissenschaften	Research includes biological oceanography, fisheries biology and marine chemistry.

Marine Biotechnology in Germany is clustered in Northern Germany around Bremen, Wilhelmshaven, Greifswald and Helgoland. Advances have particularly been made in studying micro-organisms of North Sea sediments. The Institute for Marine Biotechnology at Greifswald is a new development focussing on more applied and commercially near-market research projects. On the other hand, the Biological Institute on Helgoland (BAH)[164] conducts basic research into marine life, focusing primarily on the North Sea and the Wadden Sea. Another notable institute is GBF Braunschweig.

Funding of marine biotechnology is being taken seriously and it is recognised as a distinct growth area that will lead to new companies and employment. The BioCon Valley Initiative has been set up in Bioregio Greifswald-Rostock, within the overall Land programme for Life Science in Mecklenburg-Vorpommern. Project support is underpinned by a very large investment in new research vessels and ocean-going ships, one of which is costing around €55 million. This infrastructure will allow Germany to maintain its activities in oceanographic research in general but also in the study of marine ecosystems around the world, in particular the polar regions.

In the Kiel region, the “Kompetenznetz Meerestechnik” has been set up by the regional authorities, which brings together a very wide range of institutions and companies working in marine technology, and therefore available to help in realising projects and commercial activities in marine biotechnology. The consultancy company Coastal Research and Management is part of this.

Germany launched the second round of its Marine Materials research program in 2001 with the aim of harnessing marine biotechnological compounds. The new funding was used to initiate new industry-academia co-operations, set up Centres of Excellence, and support young scientists' research groups. Marine biotechnology is a field which can have a very short path between basic research and ready-to-buy products, and several such products (such as microbial enzymes) are being developed at the Institute for Marine Biotechnology in Greifswald[165]. While the first 30-million-DM round of funding focused more on basic research, the emphasis is now growing on applied research.

[164] see http://www.awi-bremerhaven.de/BAH/index.html

[165] see http://www.marine-biotechnologie.de/index.html

The BOSMAN II Project, BOreal Sponges-Sources of MArine Natural Products, aims to identify bioactives from poriferan sponges and their associated microbes, establish new bioassays, isolate new industrial enzymes and extend the 'Porifera database'. BOSMAN II is part of the Federal Ministry of Education, Research and Technology's programme Marine Natural Product Research, established in 1999, and is coordinated by the Institute of Biogeochemistry and Marine Chemistry, Hamburg. The project includes Novozymes Deutschland as industrial partner and institutes at four universities across Germany.

The Department of Molecular Natural Products Research at the Hans-Knöll-Institut für Naturstoff-Forschung eV, Jena, carries out discovery research for new drugs or agrochemicals, and develops tools to study eukaryotic cell signalling in vitro and in vivo. Targets include new or rare coryneforms, nocardioforms and sporoactinomycetes, as well as endophytic and marine fungi and microalgae. After isolation programs and combinatorial chemistry, molecules are tested and characterised in biological assay systems before being offered to external collaborators for specific testing or further development. The Hans-Knöll-Institut maintains the Natural Products Pool, a collection of more than 5000 pure compounds that are provided by about thirty German laboratories, for screening by various industrial partners.

TABLE 67: PARTNERS IN GERMANY'S BOSMAN II PROJECT

PARTNER	RESPONSIBILITY
Universität Hamburg	SP 1: Natural products from sponges and associated microbes from coldwater environments – Institut für Biogeochemie und Meereschemie SP 6: Identification and biosynthesis of secondary metabolites from sponges and associated microbes - Institut für Organische Chemie
Universität Göttingen	SP 2: Geobology and diversity of Arctic Porifera - Geowissenschaftliches Zentrum Göttingen, Abteilung Geobiologie
Universität Bonn	SP 3: Pharmaceutical potential of microbial natural products - Institut für Pharmazeutische Biologie
Technische Universität Berlin	SP 4: Microbiology of Porifera in coldwater reef systems - Institut für Technischen Umweltschutz, Fachgebiet Ökologie der Mikroorganismen SP 5: Screening and synthesis of bioactives from Porifera and their symbionts - Max-Volmer-Institut für Biophysikalische Chemie und Biochemie, Abteilung Biochemie und Molekulare Biologie
Novozymes Deutschland GmbH, Mainz	SP 7: Identification of new industrial enzymes from sponge-associated microbes

The Max Planck Institute for Marine Microbiology is based at Bremen[166]. The genomes of 3 marine organisms, Pirellula, Desulfobacterium psychrophila and Desulfotalea autotrophicum have been sequenced here.

Dr Manfred Hofle of GBF Braunschweig[167], heads the EU-funded Aquagenome project and is currently a member of the Environmental Microbiology Research Group at GBF. The overall objective of the research project is the development and application of a new

[166] see http://www.mpi-bremen.de/english/profil_eng.html

[167] see www.gbf.de

molecular strategy to turn the biodiversity of marine bacteria into novel biotechnological products. This strategy using metagenomics is based on an integrated molecular approach using bacterial DNA and RNA obtained directly from the marine environment, to circumvent the need for cultivation. The German Culture Collection, Deutsche Sammlung von Mikroorganismen und Zellen (DMSZ) in Braunschweig, has also used PCR on total DNA extracts to examine the potential of symbionts of the bryozoan Flustra foliacea to produce polyketide synthases or halogenases.

Other universities are involved in aspects of marine biotechnology and resource utilisation. The Heinrich Heine University in Düsseldorf has been working on clinical research using the photolyase from the blue-green alga Anacystis nidulans as a treatment for skin damage due to excess sunlight, in work supported by the EU. The Forschungszentrum Terramare, Wilhelmshaven, is the Centre for Research on Shallow Seas, Coastal Zones and the Marine Environment. Greifswald and the University of Rostock are collaborating on isolating, identifying and characterising bioactives from Baltic Sea organisms, and screening them for potential medical activity. In 2002, they reported that they had obtained a number of anti-bacterial, anti-fungal and antiviral agents. They are also combining the antimicrobials with biopolymers to produce antibiotic implants.

The Westfälische Wilhelms-Universität Münster and the Rheinische-Westfälische Wilhelms-Universität Bonn have collaborated in work on ectoines, salt-protectant molecules found in halophile and extreme-halophile bacteria, Halomonas spp., establishing bioreactor culture for extreme halophiles as well as gene transfer to conventional E coli bioreactors. Merck KGaA of Darmstadt is commercialising the ectoines as cosmetic ingredients for skin protection. The Universität Mainz has developed a system for culturing structured cell clusters, primmorphs, of sponges, as a way of obtaining sufficient sponge-origin bioactives on land[168]. So far, Suberites domuncula, Dysidea avara and Geodia cydonium have been grown in this way, and natural secondary metabolites including avarol and the immunomodulator 2-5A have been produced.

The Swiss pharmaceutical company Novartis is investigating several bioactives for clinical use, including bengamide and synthetic analogues, for breast cancer, and discodermolide.

[168] see http://www.mpiz-koeln.mpg.de/~rohde/SchroederC.html

TABLE 68: COMPANIES INVOLVED IN MARINE BIOTECHNOLOGY OR MARINE-DERIVED PRODUCTS – GERMANY

COMPANY	COMMENTS
AMP - Lab GmbH	based at the University of Mainz, is obtaining marine natural products for drug discovery, from the intertidal zone
AnagnosTec GmbH	founded in 1988 in Luckenwalde, uses MALDI-TOF MS to characterise natural products; Anagnostec is partner and/or subcontractor in the EU-project MICROMAR (Lead potential of marine microorganisms from coastal, shelf and deep-sea sediments, analysing sponge extracts), EU projects CYANOTOX and TOPIC (Cyanobacterial toxins) and EUROFUNG (products from terrestrial fungi) and the BMBF-project BOSMAN "Boreale Schwämme als Naturstoffquelle
Coastal Research and Management	based in Kiel, an aquaculture, algal bloom and ecology consultancy with a seaweed farm and a join venture in Chile with Plancton Andino Ltda for sustainable development
Faustus Forschungs Compagnie GmbH	based in Leipzig, has acquired anti-cancer molecules from a variety of sources and intends to be a virtual development company; has collaborations with molecule providers or screeners in Latin America, USA and Australia (AIMS) as well as Europe, and will license-out or co-develop once the molecules, many of them natural products, have been demonstrated to be of value
GPC Biotech	based at Martinsried, Munich, GPC had obtained Orphan Drug Status in the EU for bryostatin I as a treatment for oesophageal cancer and was going through phase II and into phase II/III studies, when further work was stopped in March 2004 as a result of inconsistent efficacy and too many side-effects
KliniPharm GmbH	based in Frankfurt, currently screening marine sponge extracts for chronic skin diseases, skin ageing, infections, inflammations and Alzheimer's disease, partnering with research institutes and universities in Germany, Greece, Holland, Italy, Estonia, and Croatia; has established a sponge farm in Greece to cultivate medically interesting sponges; extracting marine sponge collagen for medicine, drug delivery, nutrition, cosmetics and anti-ageing products, avarol for psoriasis and an enzyme for targeted destruction of cancer tissues; holds several patents on manufacture and use
Merck KgaA	The Darmstadt company is commercialising ectoines from halophiles as cosmetics ingredients
Novozymes Deutschland GmbH, Mainz	Involved in the BOSMAN II project as industrial partner testing new industrial enzymes for utility

BELGIUM, IRELAND AND THE NETHERLANDS

TABLE 69: MARINE BIOTECHNOLOGY RESEARCH IN BELGIUM, IRELAND AND THE NETHERLANDS

BELGIUM	
Flanders Marine Institute, Oostende (VLIZ)	Belgium's leading institute for biodiversity work, leader of the MAST project ERMS and manager of the European Register of Marine Species
Marine Biology Laboratory, University of Mons-Hainault	Bioadhesives from Sea Cucumber
Université de Liege, Unité d'Océanographie Chimique & MARE Interfaculty Centre for Marine Research	Ecological and systematic research of marine ecosystems; biodiversity and systematic databases for nematodes and mysids ('NEMASLAN' & 'MYSIDLAN' resp.)
Rijksuniversiteit Ghent: Marine Biology Section & Morphology and Systematics; Renard Centre of Marine Geology; Laboratory of Environmental Toxicology and Aquatic Ecology	Fouling of marine structures; bioremediation; development of fluorescence biomarker techniques for detecting toxic stress; development of in vivo fluorescence test systems with freshwater and marine invertebrates
Vrije Universiteit Brussel, Belgian Scientific Research Programme on the Antarctic	
IRELAND	
Marine Institute, Dublin (policy HQ), Galway (research HQ)	POLBIOSENSOR - Research and development of an economical Biological Sensor for detection of Marine Pollution by Hydrocarbons (with Stocker Yale Ltd.)
National University of Ireland, Martin Ryan Marine Science Institute, Galway, Depts of Marine Botany, Marine Microbiology, Oceanography, Marine & Estuarine Zoology	Taxonomy, biosystematics and ecology of marine algae and bacteria; harvesting and processing of seaweed; phytoplankton ecology; algal aquaculture; marine bacteria and biogeochemical fluxes; sediment chemistry; determination of metals and pigments in algae.
Sherkin Island Marine Station, Co Cork	Locally-active marine centre focused on ecology, natural history and public communication, as well as economic potential of the sea
THE NETHERLANDS	
Netherlands Institute for Sea Research (NIOZ), Den Burg	Marine biogeochemistry & toxicology; molecular analysis of marine organisms and sediments; impacts of man-made organic compounds on marine ecosystems
Wageningen University: Marine Biotechnology Group; Food and Bioprocess Engineering Group	and energy; bioreactors for algae and sponges; production of high-value secondary metabolites; hydrogen production by *Rhodopseudomonas* sp.; functional bioreactor for hydrogen production using anoxygenic phototrophic bacteria
University of Groningen, Biological Center, Dept. of Marine Biology	Marine benthic ecology; ecophysiology of microalgae; ecology ecophysiology and bioenergetics of zooplankton, zoobenthos and nekton; coral reef ecology
Netherlands Institute of Ecology (NIOO-KNAW), Nieuwersluis	Research projects include DYNATOX, focusing on toxic freshwater cyanobacteria, MACROPATH, the effects of antagonists produced by macroalgae on phyto- and zooplankton, and PHOBIA, phototrophic biofilms and their potential applications (an EU project)
Netherlands Institute for Fisheries Research (RIVO), IJmuiden	

Belgium is important as host to the EU-supported European Register of Marine Species, based at VLIZ, Ostend. There is some marine biotechnology activity, including involvement of the Universities of Liège and Ghent in the MICROMAT consortium that is bioprospecting in the Antarctic, but it is not as well-established as in the Netherlands.

Ireland has some presence in marine biotechnology, at the National University Galway. There is also a strong commitment from national Government for science and economic development of the marine sector as a whole. The budget of the Marine Institute Ireland and related institutions was **Ir£13.5 million** in 1998. Given the surge of activity in Ireland in general marine biology matters, though not all of this is biotechnology-oriented, the budget for 2004 is likely to be at least double that.

In 1998 the Irish Government sponsored a paper from the Marine Institute[169] that set out 'the way forward for the accelerated advancement of Marine Research, Technology, Development and Innovation (RTDI) which is vital for Ireland's future'. The Strategy went far beyond marine biosciences to embrace marine tourism, leisure and food, and had a challenging target of increasing marine sector turnover from Ir£940 million to Ir£1,370 million and employment from 32,000 to 39,000 within 5 years. The budget for the support of marine RDTI was then Ir£30 million (€52 million, currently **£35 million**[170]), using a combination of state, EU, international and private funding and income from RTDI services, and the Marine RTDI Measure was introduced as a component of the National Development Plan 2000-2006. About 60% of the programme (€30 million, **£20 million**) has been committed to a new research vessel, the RV *Celtic Explorer*, designed by Irish and Norwegian organisations and built in the Netherlands and Romania.

The Marine Institute has published an interim report for the period to 2002[171]; there are two projects focusing on toxic algal bloom and azaspiracid toxins in shellfish, the former a collaboration between NUG and Woods Hole Massachusetts, the latter between the Marine Institute Galway, University College Dublin, Chiba and Tokohu Universities in Japan, the Japan Food Research Laboratories and the Center for Coastal Environmental Health Charleston USA. It is too soon to decide whether the programme has successfully achieved its targets.

Coralline seaweed, maerl, is still harvested off the Irish coast for use as soil improvers and fertilisers, by Celtic Sea Minerals, who take about 5,000 tonnes a year for local processing. Marigot Ltd have added some value to this by developing additional health supplement products from the processed materials. The Irish company élan owns Neurex, the developer of ziconotide (ziconitide) for pain-control.

The Netherlands has the strongest marine biotechnology presence of these three, in the Marine Biotechnology group at Wageningen University. There is a strong emphasis on algal bioreactors and photobioreactor technology. The Wijffels group in Food and Bioprocess Engineering works extensively on continuous fermentation of microalgae and bacteria in bioreactors, for the production of secondary metabolites, PUFAs, and carotenoids such as astaxanthin. Research includes photobioreactor design and

[169] *A Marine Research, Technology, Development and Innovation Strategy for Ireland – A National Team Approach*, Marine Institute 1998

[170] at € 1.49 = £1.00

[171] *Productive Sector Operational Programme: Marine RTDI Measure Interim Report 2000-2002*, the Marine Institute Dublin 2003

optimisation, engineering photobioreactor growth of *Monodus subterraneus* and two-phase bioreactors for astaxanthin production from *Haematococcus pluvialis*. The continuous bioreactor production of materials such as carotenoids and PUFAs is referred to by Wageningen as 'milking'.

Wageningen is also part of the BioHydrogen programme, and has optimised *Rhodopseudomonas*, a purple bacterium, for this use, as well as designing bioreactors to obtain biological hydrogen production from acetate. This project is funded as part of the Netherlands government's BWP II (Biological Hydrogen Production II) programme, sponsored by the EET platform - Economy, Ecology and Technology. It is a follow-up to several other projects investigating biological hydrogen formation in which Process Engineering has taken part during the last 5 years, and involves a consortium of about 6 Universities and institutes and 7 industrial companies.

René Wijffels's lab at Wageningen is also one of the world's leading centres for applied biology of sponges. Their work includes:

- Cultivation of sponges as functional animals in controlled, closed bioreactor systems.
- Design and optimisation of a growth medium.
- Production of high-value metabolites on cheap and selective media.
- Modelling of growth and development of primmorphs.

Poriferan sponges produce a variety of interesting compounds: cytotoxins, antibiotics, anti-viral agents, anti-inflammatory and cardiovascular therapeutics, and anti-fouling substances. Biotechnological production methods for sponge biomass are needed to enable durable exploitation of this valuable natural resource. The Dutch group is following a strategy for the production of sponge biomass by cultivation of sponges as functional animals in controlled, closed bioreactor systems, so-called ecoreactors that mimic natural cycles seen in the sea.

TABLE 70: MARINE BIOTECHNOLOGY COMPANIES IN IRELAND AND THE NETHERLANDS

COMPANY	COMMENTS
Icon Foods Ltd	Sligo-based company freeze-drying marine nutraceuticals and probiotics to pharmaceutical standard, extracting flavours from fish and shellfish and producing therapeutic petcare products.
Marigot Ltd	Irish seaweed processor; sells products based on mineralised *Lithothamnion* seaweed Aquamin for foods and dietary supplements, aimed at osteoporosis. The seaweed is harvested by Marigot's sister company Celtic Sea Minerals at Castletownbere, West Cork. The company Microferm Ltd (HQ in Malvern UK) manufactures for Marigot. Marigot has now launched AquaMin as a calcium-rich ingredient for bread. Marigot also sells face masks based on seaweeds, including *Lithothamnion* and *Laminaria digitata*
Porifarma[172]	Ronald Osinga, of the Wijffels group in Wageningen, is planning this start-up, which will use the new cultivation technology of sponge biomass for metabolite production; the first target is the Mediterranean *Dysidea avara*, which produces the compound avarol, used in ointments for the treatment of skin disorders such as psoriasis

[172] see www.porifarma.com

SCANDINAVIA, ICELAND AND GREENLAND, THE BALTIC STATES

TABLE 71: MARINE BIOTECHNOLOGY RESEARCH IN SCANDINAVIA, ICELAND AND THE BALTIC STATES

DENMARK	
Danish Institute for Fisheries Research	Better understanding of mechanisms underlying algal blooms, oxygen depletion events and degradation of organic pollutants; risk analysis of GMOs (not so far in marine context)
Departments of Marine Ecology & Aquaculture, Marine Fisheries, and Seafood Research	
National Environmental Research Institute	
Departments of Marine Ecology and Wildlife Ecology & Biodiversity	
CREAM Center for Research and Monitoring of the Marine Environment	A Marie Curie Training Site hosted by the National Environmental Institute (NERI)
ESTONIA	
Estonian Marine Institute, University of Tartu & Department of Marine Biology, Tallinn	Mainly projects and research relating to ecological and environmental aspects of biogeological and pollution processes, e.g. impact of alien species
Marine Systems Institute, Tallinn Technical University	Partner in SEA-SEARCH marine information and data network in Europe
FINLAND	
Tekes, Helsinki	Funding a number of projects in marine biotechnology with industrial focus, including discovery of arctic micro-organisms for biotechnological applications
Finnish Institute of Marine Research	Mainly geophysical and oceanological research
Marine Science and Technology Society of Finland	Boosts the Finnish contribution to national and international marine technology and science
ICELAND	
Sandgerdi Marine Centre, Iceland	Conducts research on the marine environment around Iceland and its living resources
Dept. of Marine Biotechnology, The Norwegian College of Fishery Science	Has research groups on plankton, marine genomes and fish feeds; mainly concerned with ecobiology and fishieries/aqauaculture
Institute of Marine Research, Bergen	Microheterotrophs and Viruses, Phytoplankton and Primary Production, Zooplankton and Secondary Production, Reproductive and Developmental Biology, Larval Fish Physiology, Larval Fish Ecology, Marine Juvenile Production, Diseases of Marine Organisms, Environmental Health, Molecular Marine Biology, Marine Biodiversity and Habitats
University of Bergen	
Department of Fisheries and Marine Biology	
Sars International Centre for Molecular Marine Biology	
Norwegian University of Science and Technology, Trondheim Biological Station	

TABLE 71: CONT

SWEDEN	
University of Göteborg and Chalmers University of Technology, Analytical and Marine Chemistry	Research on organic substances
Kristineberg Marine Research Station, Fiskebacksil	Behavioural ecology, benthic ecology benthic monitoring, biological oceanography & plankton research , ecophysiology , ecosystem research , ecotoxicology , functional morphology , macroalgae, physiology of shallow coastal communities , marine genomics
University of Stockholm Marine Research Centre (SMF)	Biodiversity of marine organisms, Chemical defence in marine organisms against marine fouling and other attacks etc
Tjärnö Marine Biological Laboratory, Strömstad	Investigating the presence of chemical defences in diatoms in the Baltic Sea
Umeå Marine Sciences Centre	

Norway has a very strong presence in marine bio[techno]logy, largely driven by its well-established fisheries and aquaculture sectors. The Norwegian culture collection of algae is held by the Norwegian Institute for Water Research NIVA.

The combination of the focus on biotechnology at the European level and the position stated by the Nordic Council, that regional co-operation raises the level of competences, has stimulated the development of a joint Norwegian-Baltic-Icelandic initiative, ScanBalt[173], to capitalise on small but excellent groups at national universities and institutes in the region. This ScanBalt BioRegion comprises Denmark, Estonia, Finland, Iceland, Latvia, Lithuania, Norway, Poland, Sweden, the northern part of Germany and the north-western part of Russia. The ScanBalt activities range across innovative biosciences – for example, their next event is a Spring School on Regenerative Medicine and Stem Cells in Neurodegenerative Diseases, from 26.4.04-9.5.04 at the University of Rostock, Germany.

Marine biotechnology does not have a Nordic or Baltic platform for communication and interaction and it is recognised that those working in the area are fragmented and situated in very diverse types of research organisations. At the second ScanBalt Forum in Gdansk, Poland, in May 2003, a specific Marine Biotechnology network was proposed by a working group led by Professor Peter Aleström from the Norwegian School of Veterinary Science in Oslo. A 2-day workshop was held in Copenhagen on 15-16 January 2004, supported by a Nordic Industrial Fund (Norfa) grant, at which the possibility of a specific marine biotechnology network was crystallised and a decision made to apply in May 2004 to Norfa for further funding. The Nordic Baltic Sea Marine Biotech Network was launched at the 3rd ScanBalt Forum in August 2004. 5-year funding is being sought for the network, which will include discussion and agreement on areas of strategic collaboration in marine biotechnology, analyses of the strengths and weaknesses of the collaborating centres and the opportunities provided by collaboration, setting up post graduate student training and mobility and looking for future funding possibilities.

173 see www.scanbalt.org

TABLE 72: COMPANY ACTIVITY IN SCANDINAVIA IN MARINE BIOTECHNOLOGY AND PROCESSES

COMPANY	COMMENTS
BioProcess A/S	Danish company with production processes and equipment for high-value products from algae, beginning with astaxanthin; operates subsidiaries in Scotland and Iceland
Biotec Pharmacon ASA	established in Tromsø Norway, specialising in DNA-modifying enzymes from marine organisms living in Arctic waters; also manufactures beta-glucans for use in immune system maintenance in humans and animals, shrimp alkaline phosphatase, shrimp nuclease produced in an enhanced yeast *Pichia pastoris* and Uracil DNA n-glycosylase from Arctic cod; lysozyme from scallops and cod pepsins
Cultor	one of the largest dairy, foods and feeds companies in Europe, based in Finland, with diversified interests; the world's second largest consumer of astaxanthin as an additive for animal and aquaculture feeds, sourced from microalgal cultivation in Hawai'i
Fiskeriforskning	Fiskeriforskning is a research company within the NORUT Group Ltd, based in Tromsø Norway; covers all main aspects of the fisheries and aquaculture industry, including biochemical compounds from marine raw materials
Galilaeus OY	named after *Streptomyces galilaeus*, the company is based in Kaarina Finland; has expertise in using microbes as mini-factories for pharmaceuticals, based on molecular biochemistry knowledge and genetic engineering of *Streptomyces* to allow the expression of natural products derived from different sources. Galilaeus is co-ordinating EU project CYANOMYCES and is a partner in MICROMAR and EUKETIDES
NovaMatrix	NovaMatrix is a newly created business unit of the US company FMC BioPolymer, based in Drammen, Norway, selling ultrapure grades of sodium alginate and chitosan salts from marine sources and fermentation-produced sodium hyaluronates
Primex ehf	Primex, based in Siglufjordur Iceland, is the successor of Genis ehf, which acquired the Norwegian company PrimexIngredients ASA in September 2001; in addition to chitin-based products, Primex also supplies partially-hydrolysed marine proteins for various applications in the food and feed markets.
Zymetech Marine Enzyme Products	this Icelandic company extracts enzymes from viscera waste of Atlantic codfish, used in skin creams as Penzim, for de-scaling, smoothing and skin protection in psoriasis, acne, other irritations and inflammations; collaboration between Uni Virginia USA and Uni Iceland Reykjavik; trials at the Iceland Institute of Natural Sciences

GREECE, ITALY, PORTUGAL, SPAIN, MALTA & TURKEY

TABLE 73: MARINE RESEARCH IN SOUTHERN MEDITERRANEAN COUNTRIES

GREECE	
Institute of Marine Biology of Crete (IMBC), Iraklion & NCMR Anavissos, now joined as	Use of genetics/molecular biotechnology in studying fish; involved in MAST project ERMS
Hellenic Centre for Marine Research (**HCMR**), Anavissos; Institute of Oceanography University of Athens	Investigation of genes from marine bacteria that are resistant to antibiotics, taxonomy and ecology of cyanobacteria from extreme environments

TABLE 73: CONT

ITALY	
Universita degli Studi di Napoli Federico II, Dipartimento di Chimica delle Sostanze Naturali	Marine metabolites, structure elucidation, anticancer agents, antimicrobial agents, immunomodulating agents, lead compounds from marine organisms
International Marine Centre (IMC), Torregrande, Sardinia	Working with fish, algae, seaweeds, developing species-specific genetics fingerprints, biogeochemical cycles of nutrients and heavy metals, marine physiological ecology, hosting international marine bio[techno]logy events
CNR Istituto di Scienze Marine (ISMAR)	Neurotoxin Quinolinic Acid in *Suberites*
Istituto per la Chimica di Molecole di Interesse Biologico, Pozzuoli	Biological oceanography and marine and lagoon biology, including interactions between marine organisms and toxic pollution
Istituto di Scienze Marine, Venice	Mediterranean marine biodiversity, long- term studies of species and ecosystems
Santa Teresa Marine Environment Research Centre, La Spezia	Applied and theoretical marine fisheries research, including biodiversity, ecology.
CNR IRPEM (Istituto di Ricerche sulla Pesca Marittima)	
MALTA	
University of Malta, Marine Ecotoxicology Laboratory	Pollution and biomonitoring in the Mediterranean
PORTUGAL	
University of Coimbra, **IMAR**-Institute of Marine Research,	IMAR includes about 200 researchers, belonging to institutions from all over the country, and covers the majority of research areas in Marine Science and Technology. Research includes studying micro-organisms in deep-sea vents and marine hot springs as sources of potentially valuable biochemicals
University of Algarve, Faculty of Ambient and Marine Sciences, Faro	Research includes Molecular Biology of Marine Organisms
New University of Lisbon, Faculty of Sciences and Technology, Monte da Caparica	Natural products, medicinal plants, bio-guided isolation
SPAIN	
Institute of Marine Sciences	Analysis and total synthesis of bioactives; molecular design of mimics or antagonists to bioactives; biological investigations
Centro Mediterráneo de Investigaciones	Cultivation and exploitation of marine species of economic interest; ecotoxicological biomarkers
Marinas y Ambientales (CMIMA), Barcelona	
CSIC, Departamento de Química Biorgánica	
ICMAN, Institute of Marine Sciences in Andalusia	
TURKEY	
The Scientific and Technical Research Council of Turkey, Ankara	Research on organic substances

Marine-origin bioactives, indirubins, have been isolated from *Hexaplex trunculus*, a Mediterranean marine mollusc that is one source of the dye Tyrian purple, by the Marine Biology Station Roscoff, and characterised and synthesised at the Department of Pharmacognosy and Natural Products Chemistry in the University of Athens. These compounds appear to be useful in cytological and embryological research and in management of stem cells. The Hellenic Centre for Marine Research is the result of a merger in 2003 between the National Centre for Marine Research Anavisso and the Institute of Marine Biology of Crete in Heraklion.

In Italy, phycological and algal research is carried out at the University of Florence by Mario Tredici and others. The University is collaborating with CMARC, Australia's Marine Algal Research Centre, on bioreactor technology for economic land-based culture of marine microalgae, to harvest PUFAs, colorants and other higher-value materials.

The Institute of Natural Products and Agro-Biology (IPNA) is a department of the Spanish Scientific Research Council based on the University of Tenerife's Science Campus in the Canary Islands. Research is being carried out on bioactive substances from marine organisms, including macro- and microalgae, collected from the Canary Islands, the Antarctic and Easter Island in the South Pacific. So far, more than one hundred compounds have been isolated, including macroalgal anti-inflammatory phospholipase A2 antagonists from Tenerife and Easter Island, anti-PLA2 compounds from seaweeds including species of *Sargassum*, *Cystoseira*, *Taonia* and *Desmarestia*, which are also cytotoxic to leukaemia cells, polyhalogenated antimicrobials from *Plocamium* red seaweeds from the coast of Chile and the Antarctic, halogenated insecticidal compounds from an Easter Island *Laurencia*, an antibiotic from *Delisea*, and a series of new terpenes from an Antarctic seaweed.

TABLE 74: COMPANIES INVOLVED IN MARINE BIOTECHNOLOGY AND MARINE-DERIVED MATERIALS IN SPAIN

COMPANY	COMMENTS
Instituto BioMar	exploitation of marine organisms as sources of new bioactives-derived molecules
PharmaMar SA	the major European company developing marine-origin bioactives for human medicine
Hispanagar	more conventional colloids (agars, carrageenans) used in foods, cosmetics etc., microbiological agars, and agaroses used in molecular biology and laboratory research

Instituto BioMar, based near Léon, obtains marine samples including algae and invertebrates and isolates the associated micro-organisms, identifying and characterising secondary metabolites. The collection has over 20,000 strains, increasing at a rate of about 3,000 a year, with a library of over 15,000 extracts. Instituto BioMar has fermentation facilities and is also able to work on synthetic and semi-synthetic analogues of isolates. The company works with potential licensees in the pharmaceutical, chemical, cosmetic and environmental industries. It has a collaboration with the US company Aphios in which it is testing 20 of Aphios's extracts for anti-cancer activity.

PharmaMar, a subsidiary of the Zeltia Group based in Tres Cantos, Madrid, is completely focused on anti-cancer uses of marine bioactives, as the table below shows.

TABLE 75: PHARMAMAR'S PRODUCT PIPELINE 2002[174]

MOLECULE	SOURCE	STAGE OF DEVELOPMENT
ET-743 Yondelis™	*Ecteinascidia turbinata* warm-water tunicate	phase II
aplidine Aplidin™	*Aplidium albicans* Mediterranean tunicate	phase II
Kahalalide F	*Elysia rufescens* Pacific sea-slug	phase II
ES-285	*Spisula polynyma* North Atlantic clam	phase I
thiocoraline A	*Micromonospora marinia* Mozambique actinomycete	pre-clinical
variolin B	*Kirkpatrickia varialosa* Antarctic sponge	pre-clinical
8 others		pre-clinical

PharmaMar aims to move production into synthesis or semi-synthesis at an early stage, to remove the need for unsustainable harvesting of source materials. For ET-743, PharmaMar bought the rights to the compound and started to culture *Ecteinascidia* in aquaculture in warm waters in Spain. Mode of action work has been carried out by the Mario Negri Research Institute in Milan, Italy. Dr Elias Corey of University of Harvard has developed a total synthesis method for ET-743[175] but the company uses a semi-synthetic method, starting with the related safracin B produced by a conventional strain of *Pseudomonas fluorescens* in fermentation, followed by chemical conversion. The product Yondelis™ is being developed in agreement with Ortho Biotech Products L.P, who have paid milestones to PharmaMar.

PharmaMar is working with the Universidad Autonoma of Madrid, in the Instituto de Investigaciones Biomedical Alberto Sols, on pre-clinical work with kahalalide F for cancers and with the Netherlands Cancer Institute, Amsterdam on clinical studies. The company has also had an arrangement with the University of Canterbury, New Zealand, for screening for anti-cancer activity in marine bioactives from New Zealand and Antarctic waters.

2003 was not a good year for PharmaMar – the EMEA rejected its application for marketing approval of Yondelis for the treatment of soft tissue sarcoma in November 2003, leading to a need to conserve its resources; the previous year it had embarked on an expansion programme, establishing a European marketing structure in anticipation of gaining approval, which has now been closed down. Yondelis is still undergoing development for ovarian cancer and PharmaMar hopes to gain approval in 2006. Aplidin has been in early-stage trials against thyroid carcinoma and childhood leukaemia.

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[174] source Abstracts Int. Symp. Natural products from marine micro-organisms ESMB Greifswald June 2002; various web news items 2004

[175] see http://www.nih.gov/news/NIH-Record/09_19_2000/story04.htm

EASTERN EUROPE

TABLE 76: SOME MARINE RESEARCH IN EASTERN EUROPE

CROATIA	
Institute of Oceanography and Fisheries, Split, Laboratory of Marine Microbiology Ruđer Bošković Institute Center for Marine Research Rovinj Center for Marine and Environmental Research (CMER), Zagreb	Ecological and maricultural studies, Marine flora and fauna; bioactives; ecophysiology, biochemistry, and molecular biology of marine organisms; culture methods for sponge *Geodia* for bioactive production (with Uni Mainz, KliniPharm, MariMirna Rovinj) Biogeochemical cycles of inorganic and organic constituents, inorganic and organic pollution, impact of metals on marine organisms & exposure biomarkers in Northern Adriatic and inland waters
POLAND	
Institute of Oceanology, Polish Academy of Sciences Dept of Genetics and Marine Biotechnology, Gdynia Sopot Laboratory of Molecular Biology, Marine Biology Center, Gdansk University of Gdansk, Institute of Oceanography, Gdynia & Department of Biochemistry, Gdansk	Genetic and physiological mechanisms of functioning marine organisms, principles of marine biotechnology, genetic and endocrinological mechanisms in marine fish and invertebrates, genetic polymorphism of some marine and fresh water species with the application of molecular markers, biological role of bacterial bioluminescence in the marine environment, Role of the oceans in climate change and its effects for the European Seas, Natural and anthropogenic variability of the Baltic Sea environment, Contemporary changes of the coastal ecosystems in the shelf seas; bioactives and characterisation
RUSSIA	
Institute of Marine Biology, Vladivostok Pacific Institute of Bioorganic Chemistry, Far East Branch of the Russian Academy of Sciences, 690022, Vladivostok-22, Russia	Filamentous Marine Fungi

Poland has the most active marine biotechnology efforts in Eastern Europe. The marine research institutions on the far east coast of Russia, on the north-west Pacific edge, are also working on bioactives from seaweeds and marine micro-organisms.

MariMirna JSCG, of Rovinj in Croatia, is collaborating with the University of Mainz, KliniPharm GmbH and Ruđer Bošković Institute Center for Marine Research Rovinj on sustainable production of bioactives from open system culture of the sponge *Geodia cydonium*.

APPENDIX 9: EUROPEAN HEIs AND ORGANISATIONS WITH MARINE BIOSCIENCE OR MARINE BIOTECHNOLOGY ACTIVITIES

TABLE 77: HEIS COUNTRY BY COUNTRY

AUSTRIA	
University of Vienna, Department of Marine Biology	Marine Ecology, especially of benthic systems; symbioses between bacteria and animals.
BELGIUM	
Flanders Marine Institute, Oostende (VLIZ) Marine Biology Laboratory, University of Mons-Hainault Université de Liege, Unité d'Océanographie Chimique & MARE Interfaculty Centre for Marine Research Rijksuniversiteit Ghent, Marine Biology Section & Morphology and Systematics Renard Centre of Marine Geology University of Ghent, Laboratory of Environmental Toxicology and Aquatic Ecology Vrije Universiteit Brussel, Belgian Scientific Research Programme on the Antarctic	Belgium's leading institute for biodiversity work, leader of the MAST project ERMS and manager of the European Register of Marine Species Bioadhesives from Sea Cucumber Ecological and systematic research of marine ecosystems; biodiversity and systematic databases for nematodes and mysids ('NEMASLAN' & 'MYSIDLAN' resp.) Fouling of marine structures; bioremediation; development of fluorescence biomarker techniques for detecting toxic stress; development of in vivo fluorescence test systems with freshwater and marine Invertebrates Provides the scientific basis for: the rational and sustainable exploitation/management of living marine resources
CROATIA	
Institute of Oceanography and Fisheries, Split, Laboratory of Marine Microbiology Ruđer Bošković Institute Center for Marine Research Rovinj	Ecological and maricultural studies, Marine flora and fauna; bioactives; ecophysiology, biochemistry, and molecular biology of marine organisms; culture methods for sponge *Geodia* for bioactive production (with Uni Mainz, KliniPharm, MariMirna Rovinj)
Center for Marine and Environmental Research (CMER), Zagreb	Biogeochemical cycles of inorganic and organic constituents, inorganic and organic pollution, impact of metals on marine organisms & exposure biomarkers in Northern Adriatic and inland waters
DENMARK	
Danish Institute for Fisheries Research Departments of Marine Ecology & Aquaculture, Marine Fisheries, and Seafood Research National Environmental Research Institute	Better understanding of mechanisms underlying algal blooms, oxygen depletion events and degradation of organic pollutants; risk analysis of GMOs (not so far in marine context)
Departments of Marine Ecology and Wildlife Ecology & Biodiversity CREAM Center for Research and Monitoring of the Marine Environment	A Marie Curie Training Site hosted by the National Environmental Institute (NERI)

TABLE 77: CONT

ESTONIA	
Estonian Marine Institute, University of Tartu & Department of Marine Biology, Tallinn Marine Systems Institute, Tallinn Technical University	Mainly projects and research relating to ecological and environmental aspects of biogeological and pollution processes, e.g. impact of alien species Partner in SEA-SEARCH marine information and data network in Europe
FINLAND	
Tekes, Helsinki Finnish Institute of Marine Research Marine Science and Technology Society of Finland	Funding a number of projects in marine biotechnology with industrial focus, including discovery of arctic micro-organisms for biotechnical applications Mainly geophysical and oceanological research Boosts the Finnish contribution to national and international marine technology and science
CNRS Institut National des Sciences de l'Univers (INSU), Paris IFREMER National Natural History Museum (MNHN)	These are the main organisations involved in funding marine science and technology, often of the same departments or unités, resulting in a plethora of abbreviations connected with these (CNRS UBO MNHN, for example); CNRS units are often in or affiliated with Universities
Centre de Recherche sur les Ecosystèmes Marins et Aquacoles de l'Houmeau (CREMA L'HOUMEAU)	Mariculture, disease prevention, molecular approaches to populations
IFREMER Institut Français de Recherche pour l'Exploitation de la Mer, Issy-les-Moulineaux	Bioactives from marine extremophiles, algae and other marine products; marine microbes as contaminants; pollution; ecology of marine organisms
Institut National des Sciences et Techniques de la Mer (INTECHMER), Laboratory of Marine Research and Studies, Cherbourg	Marine biotechnology group working on extremophiles and marine environment research group working on sediment pollutant exchanges with the sea
European Institute for Marine Studies (IUEM), Plouzane	One of the CNRS's National Network of Marine Stations and part of the regional "Blue Network" of civilian and military Marine Sciences institutes
National Natural History Museum (MNHN), Station de Biologie Marine de Concarneau; Unité Biologie des Organismes Marins BOME-CNRS; Université de Bretagne Occidentale Laboratoire de Chimie, Paris	Activities across the National Natural History Museum (MNHN), CNRS and the University of Brest - biofouling; bioactives from marine organisms; bioactives and added-value from marine wastes; antibiotics from fish mucus; molecular evolution & physiology in crustacea & molluscs; biomineralisation Bioactives from tunicates and their symbionts
NAUSICAÄ, Boulogne-sur-Mer	The French National Sea Experience Centre, dedicated to informing people about the sea and the need for sustainable management of marine resources.

TABLE 77: CONT

FRANCE	
Université de Bretagne Occidentale (UBO) Unité LEBHAM-LCHO, Plouzane Unité FRE 2125 Chimie et Biologie des Substances Naturelles, Quimper	Fundamental and applied research in algae and seaweeds; bioactives from marine and coastal plants; population ecology; bioactives synthesis
Université de Caen, Laboratoire de Biologie et Biotechnologies Marines (IBBA IFREMER), Laboratoire de Biochimie (IRBA CNRS UPRES)	Biofouling by marine algae; cell cultures of the mollusc *Haliotis* and production of molluscan extracellular matrix
Université de Corse, Equipe Ecosystèmes Littoraux	Marine ecology, studying species of commercial interest, biomarkers.
Université des Sciences et Technologies de Lille, Station Marine de Wimereux, Villeneuve d'Ascq	Carbon cycling in the oceans; pollutant cycling
Université de la Méditerranée, Marseille, Centre d'Oceanologie de Marseille	
Université Pierre et Marie Curie, Paris Banyuls-sur-Mer Observatoire Océanologique de Roscoff, Phytoplankton Group, Cell Cycle Group and Cellular Physiology Research Group Observatoire Océanologique de Villefranche-sur-Mer	Impact of marine organisms on the environment and ecosystems Marine biological and biogeochemical cycles, Characterisation of picoplanktonic populations using proteins from photosystems I and II
GERMANY	
Universität Bonn, Institut für Pharmazeutische Biologie	Projects to explore the biosynthetic capabilities of marine fungi, especially fungi living as endophytes in marine algae
Universität Bremen, Departments of Biology, Marine Zoology, Marine Botany Center for Tropical Marine Ecology (ZMT) Marum - Centre for Marine Environmental Sciences	Ecophysiology and biochemistry of marine organisms; new assay method under the EU Water Framework Directive; dimethyl sulfonium propionate (DMSP) in toxic dinoflagellates, picoplankton and *Tetraselmis*; interactions between Antarctic ice diatoms and epiphytic bacteria; ecophysiology of Antarctic ice algae and proline as protection against salt and temperature stress Focus on reefs, plankton, nutrient metabolism, population genetics, ecology, baseline data for fisheries and mariculture

TABLE 77: CONT

GERMANY	
Max-Planck-Institute for Marine Microbiology, Bremen, Department of Biogeochemistry, Microsensors Group, Group for Flux Studies, Department of Microbiology, Department of Molecular Ecology	Interaction of marine microbial and geochemical processes in sediments, ecology and physiology of cold-adapted bacteria and nitrate-storing bacteria, transformations of sulfur, iron and manganese and their interactions in marine sediments, the chemistry and degradability of complex macromolecular organic material in marine sediments, distance monitoring and high-performance sensing for N, O and S cycles in sediments and microbial mats, flux processes in sediments and across boundaries, physiology and diversity of bacteria from the carbon, nitrogen, sulphur and iron cycles, culture and characterisation, hydrocarbon- and oil-degrading bacteria, molecular methods for studying biofilms, symbiotic associations and planktonic or benthic bacterial communities.
Alfred Wegener Institute for Polar and Marine Research (AWI), Bremerhaven Department of Marine Chemistry and Marine Natural Products	Violacein and desoxyviolacein as non-biocidal antifoulants, Δ12-desaturase from the cold-resistant polar algae *Fragilariopsis cylindrus*, chemical ecology of marine invertebrates, use of mollusc gills as bioassay, molecular studies of cold adaptation and cold acclimation in marine ectothermic animals
Gesellschaft für Biotechnologische Forschung mbH (GBF), Braunschweig	Detection of pharmacologically active natural products using ecology, including Indopacific marine invertebrates and sponge-derived fungi
Christian Albrechts University of Kiel, Research and Technology Centre Westcoast, Büsum	Measuring the influence of nutrients and contaminants on fluorescence kinetics of photosynthetically-active algae; analysis of excitation spectra for algae group detection and chlorophyll-a determination
Westfälische Wilhelms-Universität, Münster, Marine Biology Wadden Sea Station Carolinensiel, Institut für Zoophysiologie	
Heinrich-Heine-Universität Düsseldorf, Institut für Pharmazeutische Biologie	Marine natural products, marine medicines, chemical ecology; working with GBF Braunschweig on bioactives from Indopacific marine invertebrates and sponge-derived fungi
Friedrich-Alexander-Universität Erlangen, Institute of Bioprocess Engineering	Potential of phototrophic micro-organisms, cultivation techniques, a bioreactor system for *Medusa*, photobioreactor screening modules (PSMs)
Senckenberg Centre for Biodiversity Research, Frankfurt	Deep-sea hydrothermal research
KliniPharm, Frankfurt	Working on bioactives such as avarol from *Dysidea avara* and on sponge culture of *Geodia cydonium* for bioactive metabolites
Institute for Coastal Research, Geesthacht	uses physical and chemical analysis to look at impacts on the Coastal Zone from substances, and as a resource for natural substances of potential value, such as pharmaceuticals or food supplements

TABLE 77: CONT

GERMANY	
Institute for Marine Biotechnology Greifswald (IMaB)	Bioactive compounds • Screening and characterisation of cyanobacteria and marine fungi producing substances with antibacterial, antifungal, antiviral, cytostatic, immunomodulatory or enzyme inhibitory properties – drug development based on marine natural products • Isolation, structure elucidation and analysis of bioactive compounds • cultivation of marine microorganisms • Target analyses (Proteomics of marine bacteria) • Screening of psychrophilic microorganisms with cold-adapted enzymatic activities • Cloning and expression of cold-adapted enzymes • Development of bacterial expression systems for the overproduction of thermolabile or insoluble enzymes • Optimisation of bacterial fermentation processes • Quality control of recombinant enzymes by proteomics
Meereskunde, Institute for Biogeochemistry and Marine Chemistry (IfBM) The German Society for Marine Research (Meeresforschung)	Boreal Sponges-Sources of Marine Natural Products Porifera in deep cold-water reefs: Habitat-analysis and natural products inventory
Forschungszentrum Jülich GmbH	Programme includes marine and polar research
Universität Mainz, Institut für Physiologische Chemie, Abteilung Angewandte Molekularbiologie	Initiation of an Aquaculture of *Geodia cydonium* sponges for the Sustainable Production of Bioactive Metabolites in Open Systems
Universität Regensburg, Lehrstuhl für Mikrobiologie	Cultivation, isolation, and characterisation of microorganisms from marine invertebrates
Carl von Ossietzky Universität Oldenburg, Institut für Chemie und Biologie des Meeres (ICBM)	Significance of particle-associated marine bacteria producing secondary metabolites
University of Würzburg, Biozentrum, Institut für Molekulare Infektionsbiologie	Research: Extracts from marine sponges screened for their antimicrobial and antifungal activities. Marine Surfaces and the Expression of Specific Byssal Adhesive Protein Variants in Mytilus Antimicrobial Activities and Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry of *Bacillus* Isolates from the Marine Sponge *Aplysina aerophoba* Collaborations with: • Institut für Chemie, Arbeitsgruppe Biochemie und Molekulare Biologie, Technische Universität Berlin • Institut für Biochemie, Freie Universität Berlin • Institut für Pflanzengenetik und Kulturpflanzenforschung, Abteilung Molekulare Genetik, Corrensstrabe 3, D-06466 Gatersleben • Institut für Organische Chemie, Universität Würzburg

TABLE 77: CONT

GERMANY	
University of Kiel, IFM-GEOMAR Leibniz-Institut für Meereswissenschaften	Research includes biological oceanography, fisheries biology and marine chemistry.
GREECE	
Institute of Marine Biology of Crete (IMBC), Iraklion	Use of genetics/molecular biotechnology in studying fish; involved in MAST project ERMS
Hellenic Centre for Marine Research (**HCMR)**, Anavissos	Institute of Oceanography
University of Athens	Investigation of genes from marine bacteria that are resistant to antibiotics, taxonomy and ecology of cyanobacteria from extreme environments
ICELAND	
Marine Research Institute Sandgerdi Marine Centre	Conducts research on the marine environment around Iceland and its living resources
IRELAND	
Marine Institute Dublin (policy HQ) Galway (research HQ)	POLBIOSENSOR – Research and development of an economical Biological Sensor for detection of Marine Pollution by Hydrocarbons (with Stocker Yale Ltd.)
National University of Ireland, Martin Ryan Marine Science Institute, Galway, Depts of Marine Botany, Marine Microbiology, Oceanography, Marine & Estuarine Zoology	Taxonomy, biosystematics and ecology of marine algae and bacteria; harvesting and processing of seaweed; phytoplankton ecology; algal aquaculture; marine bacteria and biogeochemical fluxes; sediment chemistry; determination of metals and pigments in algae.
Sherkin Island Marine Station, Co Cork	Locally-active marine centre focused on ecology, natural history, public communication and economic potential of the sea
ITALY	
Universita degli Studi di Napoli 'Federico II", Dipartimento di Chimica delle Sostanze Naturali	Marine metabolites, structure elucidation, anticancer agents, antimicrobial agents, immunomodulating agents, lead compounds from marine organisms
International Marine Centre (IMC), Torregrande, Sardinia	Working with fish, algae, seaweeds, developing species-specific genetics fingerprints, biogeochemical cycles of nutrients and heavy metals, marine physiological ecology, hosting international marine bio[techno]logy events
CNR Istituto di Scienze Marine (ISMAR)	
Istituto per la Chimica di Molecol di Interesse Biologico, Pozzuoli Istituto di Scienze Marine, Venice	Neurotoxin Quinolinic Acid in *Suberites* Biological oceanography and marine and lagoon biology, including interactions between marine organisms and toxic pollution
Santa Teresa Marine Environment Research Centre, La Spezia	Mediterranean marine biodiversity, long- term studies of species and ecosystems
MALTA	
University of Malta, Marine Ecotoxicology Laboratory	Pollution and biomonitoring in the Mediterranean

TABLE 77: CONT

THE NETHERLANDS	
Netherlands Institute for Sea Research (NIOZ), Den Burg	Marine biogeochemistry & toxicology; molecular analysis of marine organisms and sediments; impacts of man-made organic compounds on marine ecosystems
Wageningen University Marine Biotechnology Group Food and Bioprocess Engineering Group	Sustainable exploration of the sea for food, pharmaceuticals and energy; bioreactors for algae and sponges; production of high-value secondary metabolites; hydrogen production by *Rhodopseudomonas* sp.; functional bioreactor for hydrogen production using anoxygenic phototrophic bacteria
University of Groningen Biological Center, Dept. of Marine Biology	Marine benthic ecology; ecophysiology of microalgae; ecology, ecophysiology and bioenergetics of zooplankton, zoobenthos and nekton; coral reef ecology
Netherlands Institute of Ecology (NIOO-KNAW), Nieuwersluis	Research projects include DYNATOX, focusing on toxic freshwater cyanobacteria, MACROPATH, the effects of antagonists produced by macroalgae on phyto- and zooplankton, and PHOBIA, phototrophic biofilms and their potential applications (an EU project)
Netherlands Institute for Fisheries Research (RIVO), IJmuiden	Mainly fishing but also interested in toxic plankton
NORWAY	
Dept. of Marine Biotechnology, Norwegian College of Fishery Science	
Institute of Marine Research, Bergen	has research groups on plankton, marine genomes and fish feeds; mainly concerned with ecobiology and fishieries/aqauaculture
University of Bergen Department of Fisheries and Marine Biology Sars International Centre for Molecular Marine Biology	Microheterotrophs and Viruses, Phytoplankton and Primary Production, Zooplankton and Secondary Production, Reproductive and Developmental Biology, Larval Fish Physiology, Larval Fish Ecology, Marine Juvenile Production, Diseases of Marine Organisms, Environmental Health, Molecular Marine Biology, Marine Biodiversity and Habitats
Norwegian University of Science and Technology, Trondheim Biological Station	
POLAND	
Institute of Oceanology, Polish Academy of Sciences Dept of Genetics and Marine Biotechnology, Gdynia; Sopot; Laboratory of Molecular Biology, Marine Biology Center, Gdansk	Genetic and physiological mechanisms of functioning marine organisms, principles of marine biotechnology, genetic and endocrinological mechanisms in marine fish and invertebrates, genetic polymorphism of some marine and fresh water species with the application of molecular markers, biological role of bacterial bioluminescence in the marine environment, Role of the oceans in climate change and its effects for the European Seas, Natural and anthropogenic variability of the Baltic Sea environment, Contemporary changes of the coastal ecosystems in the shelf seas
University of Gdansk, Institute of Oceanography, Gdynia & Department of Biochemistry, Gdansk	bioactives and characterisation

TABLE 77: CONT

PORTUGAL	
University of Coimbra, IMAR-Institute of Marine Research,	IMAR includes about 200 researchers, belonging to institutions from all over the country, and covers the majority of research areas in Marine Science and Technology. Research includes studying microorganisms in deep-sea vents and marine hot springs as sources of potentially valuable biochemicals
University of Algarve, Faculty of Ambient and Marine Sciences, Faro	Research includes Molecular Biology of Marine Organisms
New University of Lisbon, Faculty of Sciences and Technology, Monte da Caparica	Natural products, medicinal plants, bio-guided isolation
RUSSIA	
Institute of Marine Biology, Vladivostok	
Pacific Institute of Bioorganic Chemistry, Far East Branch of the Russian Academy of Sciences, 690022, Vladivostok-22, Russia	Filamentous Marine Fungi
SPAIN	
Institute of Marine Sciences Centro Mediterráneo de Investigaciones Marinas y Ambientales (CMIMA), Barcelona	
CSIC, Departamento de Química Biorgánica	Analysis and total synthesis of bioactives; molecular design of mimics or antagonists to bioactives; biological investigations
ICMAN, Institute of Marine Sciences in Andalusia	Cultivation and exploitation of marine species of economic interest; ecotoxicological biomarkers
SWEDEN	
University of Göteborg and Chalmers University of Technology, Analytical and Marine Chemistry	Research on organic substances
Kristineberg Marine Research Station, Fiskebacksil	behavioural ecology, benthic ecology benthic monitoring, biological oceanography & plankton research , ecophysiology , ecosystem research , ecotoxicology , functional morphology , macroalgae, physiology of shallow coastal communities , marine genomics
University of Stockholm Marine Research Centre (SMF)	
Tjärnö Marine Biological Laboratory, Strömstad	Biodiversity of marine organisms, Chemical defence in marine organisms against marine fouling and other attacks etc
Umeå Marine Sciences Centre	Investigating the presence of chemical defences in diatoms in the Baltic Sea

TABLE 77: CONT

TURKEY	
The Scientific and Technical Research Council of Turkey, Ankara	Research on organic substances

APPENDIX 10: EUROCEAN LIST OF EUROPEAN INSTITUTIONS AND SOCIETIES INVOLVED IN MARINE SCIENCE AND TECHNOLOGY[176]

TABLE 78: EUROPEAN INSTITUTIONS INVOLVED IN MARINE SCIENCE

AUSTRIA
University of Vienna Department of Marine Biology
BELGIUM
Vlaams Instituut voor de Zee/Flanders Marine Institute (VLIZ)
Management Unit of the Mathematical Models of the North Sea (MUMM)
University of Ghent: Marine Biology Section, Maritime Institute; Renard Centre of Marine Geology
Université de Liège: Geohydrodynamics and environment research (GHER) and MARE - Interfacultary Center for Marine Research
Belgian Scientific Research Programme on the Antarctic
Royal Meteorological Institute of Belgium (RMI)
Integrated Marine Information System (IMIS)
Laboratory of Environmental Toxicology and Aquatic Ecology
Sea Fisheries Department
BULGARIA
National Institute of Meteorology and Hydrology (NIMH)
CROATIA
Institute of Oceanography and Fisheries
University of Rijeka Department of Maritime Studies
Rudjer Boskovic Institute, Center for Marine and Environmental Research
Republic of Croatia Meteorological and Hydrological Service
Croatian Information Service for Biodiversity
DENMARK
Danish Polar Centrum (DPC)
University of Copenhagen Department of Geophysics
North Sea Centre Danish Institute for Fisheries Research (DIFRES)
National Environmental Research Institute: Depts of Marine and Coastal Zone Ecology
Danish Meteorological Institute: Danish Center for Remote Sensing (DCRS)
University of Aarhus, Department of Earth Sciences
DHI Water & Environment
Technical University of Denmark, Section of Maritime Engineering
Centre for Maritime and Regional Studies
ESTONIA
Estonian Science Foundation (EstSF)
Estonian Marine Institute, University of Tartu
Research and development in Estonia (ERIS)

[176] source: EurOcean website – covering all aspects of marine science and technology

TABLE 78: CONT

ESTONIA
Marine Systems Institute, Tallinn Technical University
National Environmental Monitoring Program
Ministry of Environment: Environmental Strategy
FINLAND
Finnish Ice Service
Finnish Meteorological Institute
Marine Science and Technology Society of Finland
FRANCE
Systèmes d'Informations Scientifiques pour la Mer (SISMER)
Institut National des Sciences et Techniques de la Mer (INTECHMER)
Institut de Recherche pour le Développement (IRD)
Observatoire Océanologique de Banyuls-sur-Mer / Laboratoire Arago
Oceanic Environments and Paleoenvironments (EPOC)
Institut Universitaire Européen de la Mer (IUEM)
Station de Biologie Marine du Muséum National d'Histoire Naturelle, Concarneau
Laboratoire des Sciences du Climat et l'Environnement (LSCE)
Centre de Recherche en Ecologie Marine et Aquaculture de l'Houmeau
L'Université de la Méditerranée Centre d'Oceanologie de Marseille (CNRS)
Institut Français de Recherche pour l'Exploitation de la Mer (IFREMER)
Observatoire Océanologique de Roscoff
Observatoire Océanologique de Villefranche-sur-Mer
French national network of marine research stations
Service Hydrographique et Océanographique de la Marine Française (SHOM)
French Coral Reef Initiative (IFRECOR)
EUROSFAIRE
Union des Océanographes de France (UOF)
Institut Océanographique
Centre National d'Etudes Spatiales (CNES)
NAUSICAA - French National Sealife Centre
Laboratoire d'Ecophysiologie et de Biotechnologie des Halophytes et Algues Marines (LEBHAM)
Institut polaire français Paul Emile Victor (IPEV)
Station marine de Wimereux Laboratoire de Biogéochimie et Chimie Marines (LBCM)
Institut Pierre Simon Laplace (IPSL)
Base d'observation pour le suivi des côtes (BOSCO)
Conservatoire du Littoral
Université de Corse: Equipe Ecosystèmes Littoraux
ANTARES
Club des Organismes de Recherche Associés (CLORA)
Laboratoire d'Océanographie Dynamique et de Climatologie (LODYC)
Centre National de la Recherche Scientifique (CNRS)

TABLE 78: CONT

GERMANY
Federal Maritime and Hydrographic Agency - National Oceanographic Datacentre
University of Bremen: Institute for Environmental Physics & Departments of Geoscience, Marine Zoology, Marine Botany
Marum - Centre for Marine Environmental Sciences
Max-Planck-Institute for Marine Microbiology Bremen
Alfred Wegener Institute for Polar and Marine Research (AWI)
University of Münster Marine Biology Wadden Sea Station Carolinensiel
GKSS Research Center Institute for Coastal Research
Ernst-Moritz-Arndt-University of Greifswald: Institut for Ecology Hiddensee
Institut for Marine Biotechnology Greifswald
University of Hamburg: Centre for Marine and Climate Research (ZMK) & Faculty of Biology
German Centre of Marine Biodiversity (DZMG)
Technical University of Hamburg-Harburg - Mechanics and Ocean Engineering
Max-Planck-Institute for Meteorology
Federal Maritime and Hydrographic Agency of Germany (BSH)
German Climate Computing Centre (DKRZ)
Federal Waterways Engineering and Research Institute - Coastal Division (BAW-AK)
Federal Research Centre for Fisheries
German Society for Marine Research (DGM)
Biological Institute on Helgoland (BAH)
University of Kiel Institute of Marine Research (IFM)
University of Kiel Research Center for Maritime Geoscience (GEOMAR)
German Weather Service (DWD)
University of Oldenburg Institute for Chemistry and Biology of the Marine Environment (ICBM)
Research Unit Potsdam of the Alfred Wegener Institute
University of Rostock Department of Biology - Marine Biology
German Hydrographic Society (DHyG)
Baltic Sea Research Institute
Society for Maritime Technology (GMT)
German Museum of Marine Research and Fisheries
University of Kiel Institute for Polar Ecology (IPÖ)
Senckenberg Centre for Biodiversity Research
TERRAMARE Research Centre
German CLIVAR Ocean Program (CLIVAR-DecCen)
Fischerei in Deutschland
University of Bremen Oceanography Department
GFZ Data Center
German Remote Sensing Data Center (DFD)
University of Bremen : Center for Tropical Marine Ecology
Technical University of Clausthal Institute for Geotechnik
Potsdam Institute for Climate Research (PIK)
Institute for Geosciences Mainz
Marine Environmental Data Base (MUDAB)

TABLE 78: CONT

GERMANY
University of Rostock Baltic Sea Research Institute
GeoResearch Centre (GFZ)
University of Oldenburg Zoosystematics and Morphology Section
DFG-Research Center Ocean Margins
German Society for Marine Research (DGM)
German Society for Limnology
German Research Foundation (DFG)
Working Group on Climate Change: Federal Ministry of Consumer Protection, Food and Agriculture and Forests
GREECE
Hellenic National Oceanographic Data Centre (HNODC)
Hellenic Network of Marine Microbial Ecology
National Centre for Marine Research
Hellenic Institute of Marine Archaeology
ICELAND
Marine Research Institute (MRI)
Icelandic Fisheries Laboratories
University of Iceland Sandgerdi Marine Centre
Icelandic Meteorological Office
IRELAND
Irish Marine Institute
National University of Ireland Martin Ryan Marine Science Institute (MRI)
Irish Seaweed Industry Organisation
Irish Whale and Dolphin Group (IWDG)
Hydraulics and Maritime Research Centre
National University of Ireland Marine Microbiology Group
Sherkin Island Marine Station
Coastal and Marine Resources Centre (CMRC)
Environment Research Institute (ERI-ECOSITE)
Department of Communications, Marine and Natural Resources
Aquaculture Development Centre (ADC)
Environmental Protection Agency (EPA)
Geological Survey of Ireland (GSI)
Irish Maritime Development Office (IMDO)
Irish Coast Guard (IRCG)
Bord Iascaigh Mhara (BIM) - Irish Sea Fisheries Board

TABLE 78: CONT

ITALY
Italian National Research Council Marine Fisheries Research Institute (IRPEM) Università degli Studi di Pavia Centro Interdisciplinare di Bioacustica e Ricerche Ambientali Italian Malacological Society (SIM) Istituto Idrografico della Marina
Instituto Nazionale de Oceanografia, Marine Bioacoustics and Acoustical Oceanography International Marine Centre Istituto di Scienze Marine (ISMAR), CNR Institute of Atmospheric and Oceanic Sciences Marine Environment Research Centre Tethys Research Institute Central Institute for Scientific and Technological Research Applied to the Sea (ICRAM) Italian National Research Council Institute of Marine Biology (IBM) Venice Marina Militare Italiana Istituto Idrografico della Marina Italian Association for Oceanology and Limnology (A.I.O.L.)
LATVIA
Latvian Hydrometeorological Agency (LHMA) Marine Environment Board of Latvia
LITHUANIA
Lithuanian Hydrometeorological Service
MALTA
University of Malta Department of Biology
THE NETHERLANDS
National Oceanographic Data Committee (NODC) of the Netherlands Marine Information Service (MARIS) NetCoast Delft University of Technology Delft Institute for Earth-Oriented Space Research (DEOS) Netherlands Institute for Sea Research (NIOZ) University of Groningen Department of Marine Biology Netherlands Institute of Ecology (NIOO-KNAW) Netherlands Institute of Ecology Centre for Estuarine and Coastal Ecology (CEME) InterWad Zoological Museum Amsterdam Netherlands-Flanders Society for Aquatic Ecology (NECOV) Netherlands Institute for the Law of the Sea Netherlands Institute for Fisheries Research (RIVO)

TABLE 78: CONT

NORWAY
Havforskningsinstituttet/Institute of Marine Research (IMR)
University of Bergen: Department of Fisheries and Marine Biology, Geophysical Institute, Marine Food Chain Research Infrastructure & Sars International Centre for Marine Molecular Biology
University of Oslo: Geophysical Fluid Dynamics & Department of Geophysics
The Norwegian College of Fishery Science (NCFS)
Norwegian Polar Institute
Norwegian Meteorological Institute (DNMI): Oceanography
FishLarvae.com
Norwegian University of Science and Technology Faculty of Engineering Science & Technology
POLAND
Institute of Oceanology of the Polish Academy of Sciences
University of Gdansk Institute of Oceanography
University of Gdansk Institute of Oceanography Marine Station at Hel
Technical University of Gdansk Faculty of Ocean Engineering and Ship Technology
Numerical Forecast Office
Marine Bio-Optics Laboratory
Institute of Environmental Protection
Faculty of Environmental Sciences and Fisheries -University of Warmia and Mazury
PORTUGAL
University of Coimbra Institute of Marine Research
University of Algarve: Faculty of Ambient and Marine Sciences & Science Centre of the Sea (CCMAR
Department of Oceanography and Fisheries of the University of the Azores
Institute of Oceanography of the University of Lisbon
Instituto de Investigação das Pescas e do Mar (IPIMAR)
Lisbon Oceanarium
Institute of Marine Research (IMAR)
Institute of Meteorology
Section of Marine Biology and Oceanography of the University of Madeira
GUIA Marine Laboratory
ROMANIA
National Institute for Marine Research and Development
Institutul National de Meteorologie si Hidrologie
RUSSIA
Zoological Institute of the Russian Academy of Sciences

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SPAIN
Instituto de Ciencias Marinas de Andalucía (CSIC) & Andalusian Institute of Earth Sciences
Universidad de Cádiz Facultad de Ciencias del Mar
Ministerio de Medio Ambiente (MMA)
CSIC Coordinated Scientific Program for the Follow-up and the Evaluation of the Prestige Oil spill
Institute of Marine Sciences (ICM)
International Centre for Coastal Resources Research (CIIRC)
Universidad de Las Palmas de Gran Canaria, Facultad de Ciencias del Mar
Instituto Canario De Ciencias Marinas (ICCM)
AINCO-Interocean
Spanish Institute of Oceanography (IEO)
Mediterranean Institute for Advanced Studies (IMEDEA) Natural Resources Department
Universidad de Vigo Departamento de Geociencias Marinas y Ordenación del Territorio
Instituto de Investigaciones Marinas
TIERRA, el web de las Ciencias de la Tierra de España
Instituto Nacional de Meteorologia
Spanish Aquaculture Observatory (OESA)
Spanish Polar Committee
Scientia Marina - International Journal on Marine Sciences
Centro de Estudios Avanzados de Blanes (CEAB) Chemical Oceanography Group
Revista Aquatic - Electronic journal
Coto de Doñana Accidente de Aznalcóllar
MARINET: Forum for Marine Investigations
OESA - Spanish Aquaculture Observatory
Sociedad Española de Cetáceos (SEC)
Centro Tecnológico del Mar – Fundación CETMAR
Universidad Complutense de Madrid: Department of Geophysics and Meteorology
IMEDEA Natural Resources Department
Interdisciplinary Oceanography Group
Gabinete de Economia del Mar
Basque Country Fisheries and Food Technology Institute
Remote Sensing: IEO Santander (Spain)
SWEDEN
Kristineberg Marine Research Station
University of Göteborg and Chalmers
University of Technology Analytical and Marine Chemistry
University of Stockholm: Marine Research Centre (SMF), Meteorologiska Institutionen (MISU) & Department of Systems Ecology
Tjärnö Marine Biological Laboratory
Swedish Meteorological and Hydrological Institute (SMHI)
Göteborg University: Marine Research Center (GMF) & Department of Oceanography
Umeå Marine Sciences Centre

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TURKEY
Turkish State Meteorological Service
Department of Navigation, Hydrography and Oceanography (DNHO)
Underwater Research Society (SAD)
Derinsu Underwater Engineering & Consulting
Institute of Marine Sciences and Management, Istanbul
Institute of Marine Sciences, Middle East Technical Services
Institute for Marine Sciences and Technology, Izmir
YUGOSLAVIA
Federal Hydrometeorological Institute of Yugoslavia
Institute for Marine Biology

APPENDIX 11: NORTH AMERICA

UNITED STATES OF AMERICA

Introduction

In the USA, no single institution acts as the centre for marine biotechnology, although the NOAA (National Oceanic and Atmospheric Agency) National Sea Grant Colleges programme and NSF (National Science Foundation's) Microbial Observatories programme carry most of the burden of current federal support of marine biology, ecology and bioscience, that might be relevant to marine biotechnology. This makes it difficult to quantify spend, either historically or current. The rather fragmentary **Table 71** below indicates that at least $500 million, **£300 million** has been spent in the past 15 years, which is likely to be an underestimate for marine bioscience and biology. Discriminating marine biotechnology within this would be even more difficult.

Funding is generally by interaction between state support and individual programmes operated by the National Institutes of Health, NOAA, the National Science Foundation or the Office of Naval Research of the US Defense Department, in many cases with a requirement for partial or matching funding from the private sector.

Data is similarly fragmentary for capital expenditure on marine biotechnology or bioscience projects. A feasibility analysis for a marine technology centre in Rhode Island[177] suggested that $2.9 million would be needed for construction of 8000 sq ft of buildings, including 6000 sq ft for incubator/start-up space and 2000 sq ft shared and management facilities, and 7200 sq ft of on-land aquaculture greenhouses. Cumulative operating losses over the first 5 years of activities were estimated at $1.6 million, taking into account potential income from rents and usage fees of about $550,000. Thus total exposure (capital plus trading losses) would be of the order of $4.5 million, or **£2.76 million**.[178] The plan is now being reviewed, since the original concept was too restrictive to generate an economic return. This analysis also mentions the New Hampshire Biotech Incubator, not marine, but costing some $5 million to set up (£3 million).

A more concrete example is the **Florida Center of Excellence in Biomedical and Marine Biotechnology**, an example of a virtual CoE. This was officially opened September 23rd 2003. It is a new activity, with Florida Atlantic University as the lead and the Harbor Branch Oceanographic Institution as a major partner. Other academic collaborators include Florida International University, the Smithsonian Marine Station, Nova Southeastern University and the University of Florida. There are also a number of private companies involved, including Ixion Biotechnology, Acera Biosciences, Nabi Biopharmaceuticals, Edgetech, Custom Biologicals and Sunol Molecular. This new CoE[179] is funded to the tune of $10 million (over **£6 million**) and will accelerate the discovery, development and licensing-out of new medicines. This funding is being regarded as seed money to boost the nascent marine biotechnology industry in Florida

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[177] *Marine Technology and Aquaculture Center (MTAC) Feasibility Analysis* May 2003 Ninigret Partners, see http://www.crmc.state.ri.us, also accompanying reports

[178] Exchange rate 2003, £1.00 = US$1.63

[179] see http://www.floridabiotech.org/

and encourage further funding at Federal level and from commercial contracts. Part of the funding will support additional oceanic research expeditions.

TABLE 79: SOME MARINE BIOTECHNOLOGY FUNDING IN USA

WHO FUNDS	SITE/PROJECT	WHERE	HOW MUCH
Department of Energy	Microbial Genome Initiative	USA-wide	$3 million for 1-4 grants
Federal budget request	National Aquacultural Biotechnology Consortium	COMB Maryland, Institute of Marine Sciences Uni Southern Mississippi, Mote Marine Lab Florida, Oceanic Institute Hawai'i	$8 million p.a.
Federal funding Federal funding	overall marine biotechnology	USA-wide	1992 $44 million 1993 c. $50 million
Federal Interagency initiative	COMPASS (proposed in 1999)	USA-wide	$50 million
Florida state funding	Center of Excellence in Biomedical and Marine Biotechnology	Florida	$10 million
Harbor Branch	collection programme	Florida	1986-2001 $10 million
Industrial funding	Marine biotechnology applications	USA-wide	1992 $25 million
National Cancer Institute	Anti-cancer projects	Australia (AIMS) Shimizu, Rhode Island	$1 million $2 million
National Science Foundation NSF cellular bioscience	marine biotechnology marine organisms	USA-wide	1990 $1 million 1999 $12 million 1990 $5 million
NSF/UCal Berkeley/Hawai'i	MarBEC	Hawai'i	$12.4 million start-up
NOAA National Sea Grant Colleges Programme	University-based projects biotechnology	USA-wide	1989 $2.3 million 1999 $10 million $35 million (inc. match)
NOAA/State legislature	National Sea Grant College Programme	Hawai'i	$290 million for 1999-2003
Office of Naval Research/Maryland	Center of Marine Biotechnology COMB	Maryland	$6.7 million start-up $9 million p.a.
Office of Naval Research	molecular techniques extremophile research	in-house and contracted-out USA-wide	1990 $1.7 million 1999 $5.6 million 1990 $0.3 million
U California/ BioSTAR/ UC Discovery	isolation, screening, development, bioreactor development	mainly Bill Fenical	1998-2005 $2.3 million
U California/NOAA Sea Grant	UC Santa Barbara Marine Biotechnology Center	California	$8 million $1.5 million pa $2 million

The Florida Center already has an active programme of patenting, technology transfer and involvement of investors, venture capitalists and business angels in advising and funding start-ups, and the breadth of institutions in the partnership, together with the funding, is allowing an enhanced training programme for undergraduate, graduate and PhD researchers in marine biotechnology.

The **State of Maine's Technology Institute** (MTI) operates a Cluster Enhancement Award, to stimulate the formation and growth of technology sectors by attracting and supporting related businesses. MTI gives up to $500,000 (£300,000) per project. These include exploitation and management of natural resources in the state, such as wood products, trap fishing, oyster-farming and wild blueberry harvesting, and also higher-tech projects for media, digital technologies and biotechnology networks. A recent grant of $387, 000 (about £250,000) went to the University of Maine Center for Cooperative Aquaculture for new buildings to house the US subsidiary of the Newcastle-upon-Tyne company Seabait Ltd, to set up a lugworm nursery. The lugworms are used for shrimp and fish feed and anglers' baits.

As a comment on focus of funding in USA, the **State of Kentucky** has recently announced a $5 million (£3 million) Natural Product Fund, for early-stage companies commercialising compounds or products found in nature in plants, animals or micro-organisms. This is all-equity funding, of up to $50,000 (£30,000) in very early-stage, and up to $500,000 (£300,000) in later stage companies, providing that twice as much external funding is secured. There is also access to a fund that provides up to $100,000 a year (£60,000) for 2 years for R&D work.

The **Sea Grants Program** operated by NOAA (National Oceanic and Atmospheric Administration) has supported about 30 institutions throughout USA for work in marine biotechnology or advanced biosciences. The Sea Grant Marine Biotechnology programme was established by the House of Representatives and US Senate in 1993. It earmarked $20 million for each of 1994 and 1995, rising to $25 million for 1996 and 1997; only some of this was actually allocated. 168 projects have been funded that relate to marine biotechnology, with NOAA support of almost $22.3 million and matched funding of about $13 million[180], 30% (51/168) in California, 11% (19) in Washington State, 9% (15) in Florida, and 7-9 each in Hawai'i, Oregon, Delaware, Massachusetts and Maryland. The NSF's Microbial Observatories programme[181] had committed over $12.5 million (£7.5 million) to marine projects by 2003.

Space does not permit a full evaluation of projects in the Sea Grants Program; they cover all aspects from fundamental to applied research and exploitation of marine organisms and marine-derived products in industrial, food, chemical and disease-management sectors.

The USA's Microbial Observatories (MO) and Microbial Interactions and Processes (MIP) programmes are intended to discover and characterise novel microorganisms, microbial consortia, communities, activities and other novel properties, and to study their roles in diverse environments, covering terrestrial, marine and zoological sites. MO continues work begun in 1999, aimed at developing a network of "microbial observatories" in different habitats to study and understand microbial diversity over time and across environmental gradients. Microbial Interactions and Processes (MIP)

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[180] see http://www.oarhq.noaa.gov/seagrantasp/SG_Public_Search/SearchHome.asp

[181] see http://www.nsf.gov/pubs/2004/nsf04586/nsf04586.htm and http://www.nsf.gov/bio/pubs/awards/mo1999.htm (and mo01_02.htm and mo03.htm)

supports projects that are smaller and/or shorter in duration than MO projects, to explore novel micro-organisms and the processes that they carry out in the environment.

TABLE 80: SEA GRANT PROGRAMS INVOLVING COLLEGES AND OTHER INSTITUTIONS

Alaska
California
University of California, Santa Barbara
University of Southern California
Hawai'i
Illinois-Indiana
Maryland
COMB, University of Maryland
Center for Microbial Ecology, Michigan State University
Ohio
Oregon
Marine Bioremediation Program, University of Washington
Washington [State]
Wisconsin
Woods Hole Oceanographic Institution

43 MO and related projects have been supported since 1999 with approx. $31 million of funding. Of these, 17 involve marine microbes (including marine iguana-associated organisms) and 18 involve terrestrial or freshwater extremophiles. The diversity of universities involved is also wide, from the University of Alaska to the island Universities of Hawai'i and Puerto Rico. Most of these institutions are involved in diversity rather than biotechnology-based exploitations; exceptions are University of California San Diego and Santa Cruz, COMB and Oregon State University.

The USDA (US Department of Agriculture) operates a Biotechnology Risk Assessment Grant (BRAG) Program[182]. BRAG is specifically aimed at studies of the potential environmental impact of genetically-modified organisms, and the development of risk assessment methodology and risk management practices related to specific types of organisms and environments. Studies so far have been restricted to terrestrial organisms, with the exception of a study on transgenic fish, but this programme would support risk assessment of GM marine organisms.

Foremost amongst the centres of marine biotechnology in the USA are:

- COMB, the Center of Marine Biotechnology, Baltimore Maryland, which receives about $9m per year, almost 90% of this from Federal and State funds, for maintenance and research projects

[182] see http://www.reeusda.gov/crgam/biotechrisk/biotech.htm

- the Marine Bioproducts Engineering Center (MarBEC), a partnership between the University of Hawai'i and the University of California at Berkeley; founded in 1998, it is based at UH-Manoa and has attracted a number of industry partners, including Cyanotech (natural astaxanthins in food and feed)
- the Scripps Institution of Oceanography at University of California San Diego

The USA is strongly committed to making marine products contribute to the US economy[183] although Rita Colwell, one of the most ardent supporters, has pointed out that 15-20 years of effort and financial support of marine biology and biotechnology has resulted in discouragingly few medicines from bioactives. It is recognised that more effort is required to:

- develop culture methods for marine organisms
- establish alternatives to continued harvesting
- analyse and characterise gene products
- extend exploration beyond those areas of the sea already investigated
- sequence marine organism genomes
- apply the tools and systems of functional genomics and proteomics
- extend into molecular metabolic biology
- identify model species that are the equivalents of *Drosophila*, the fruit fly[184].

Overall, the National Academy of Sciences recommends revitalising the search for new bioactives by focusing on currently-unculturable micro-organisms and unexamined habitats and applying new methods for their detection and characterisation, making better use of marine biotechnology for environmental remediation and giving greater emphasis to commercialisation efforts. In the latter context, fostering relationships between researchers and innovative small companies, facilitating technology transfer and streamlining government regulations are particularly mentioned.

The marine biotechnology sector has entered the mental map of the biotechnology industry, albeit in the context of aquaculture, as can be seen in the US BIO's recent guide to biotechnology[185]

Corporate activity

There are a number of companies involved in the cultivation of marine micro-organisms, or the identification and isolation of bioactives or enzymes from these, and other 'bio' or 'technological' marine-related activities. 16 of these are profiled in the summary table below.

Albany Molecular Research maintains a large library of natural-origin extracts, including a significant number from marine sources. In 2002 it entered a new 3-year agreement with Bristol-Myers Squibb, in which up to 80,000 extracts from Albany's Diversity Library would be provided to BMS for screening. AMRI would then be involved in analysing and

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[183] see Executive Summary of *Marine Biotechnology in the Twenty-First Century: Problems, Promises and Products*, The National Academy of Sciences 2002

[184] *Marine Biotechnology in the Twenty-First Century: Problems, Promises and Products*, The National Academy of Sciences 2002

[185] *Editors' and Reporters' Guide to Biotechnology 2002-2003*, US Biotechnology Industry Organization , Washington USA, June 2002, pp64-65

synthesising promising candidates, using its expertise in medicinal chemistry, biocatalysis, microbiology and computational chemistry. The contract included fees for technology access and work performed as well as milestone fees for successfully-identified compounds and royalties on products. The envisaged milestone payments to Albany ranged from $500,000 to $7 million per compound, depending on how well it progressed along the development pathway.

TABLE 81: US COMPANIES ACTIVE IN SOME ASPECT OF MARINE BIOTECHNOLOGY

COMPANY	COMMENTS
Advanced BioNutrition	Based in Columbia, Maryland, and established in 2001 by a co-founder of Martek to develop the use of arachidonic acids in aquaculture, nutritional substitutes for fishmeal and fish oils, vaccines for fish and probiotics for shrimp
AGI Dermatics	Based in Freeport, Long Island, develops cosmetics and cosmeceuticals; incorporates a photolyase from blue-green alga *Anacystis nidulans* as a corrective for sun-damage on skin
AgraQuest	Based in Davis California, this company focuses on creating natural pest management products. It has screened over 20,000 microbes for bioactives and has launched Serenade™, a biofungicide isolated from a soil microbe; since February 2002 has been in a BioStar-funded project with Bill Fenical's lab at Scripps Institution of Oceanography, San Diego, to find new agricultural pesticides from marine microbes; also licensed a microbe from Montana State University as a biofumigant
Albany Molecular Research	Based in Bothell Washington State, Mount Prospect near Chicago and Albany, New York State. Identifies, extracts, characterises and exploits natural products. Also acts as a contract research organisation. Has three proprietary libraries of extracts, including the Diversity Library, with c. 110,000 primary fermentation samples from over 25,000 microbes, and the Premium Library, with c. 150,000 fractionated extract samples.
Aphios Corporation	Focusing on bioactives from natural sources, Aphios, a Woburn Massachusetts based company, has several bryostatins in development, using new extraction and formulation technologies, and an antibacterial
BiophoriX	A new company developing small molecules from marine and terrestrial sources, founded in Aurora Colorado, working temporarily from Carlsbad California, but relocating to Colorado and Hawai'i for access to terrestrial and marine extremophiles.
CalBioMarine	Focused on new manufacturing and gene transfer technologies for marine bioactives, this company ran out of financial steam in 2003
Cyanotech	One of the first commercial partners in the MarBEC initiative at University of Hawai'i in Manoa. Strictly speaking not a marine biotech company but has developed bioreactor culture of marine microbes to produce consistent carotenoids.
Diversa	Has a strong activity in screening, which has allowed it to discover large numbers of novel enzymes and other bioactive molecules for health, agriculture and industrial applications. Its partners have included Syngenta Biotechnology, Celera Genomics, Aventis Animal Nutrition, GSK, Invitrogen and Dow Chemical Company; it has an exclusive licence to exploit new enzymes and bioactives from hot-vent microbes north of Iceland.

TABLE 81: CONT

COMPANY	COMMENTS
Embiosis Pharmaceuticals	La Jolla-based, this under-capitalised company, previously known as MicroGenomics, announced it was for sale in August 2003, in spite of an impressive array of technologies and partnerships. Proprietary technologies EmbioVersity™, a way of investigating unculturable environmental microorganisms from a wide variety of habitats, including marine microbial biofilms: gene clusters are isolated, transferred to proprietary broad host-range plasmid vectors and then expressed in engineered laboratory bacteria, reproducing the chemical and enzymatic diversity; and EmbioScreen-Micro™, a proprietary high throughput phenotypic screening technology, which simultaneously identifies active compounds and their advantageous molecular targets, to narrow down the screening focus. Looking for new treatments for human bacterial and fungal infections. Alliances included Genencor, Eastman Chemical Company and the Electrosynthesis Company.
Genencor	Involved in a biosilicon collaboration with Dow Corning and in exploitation of Antarctic microbes for new enzymes (the MICROMAT consortium)
Kosan Biosciences	Founded in 1995 in Hayward, California, Kosan is focused on polyketide discovery and synthesis, specifically epothilones, from natural sources including marine organisms; Kosan has an agreement with Roche for epothilone R&D, in which Kosan may receive payments of up to $220 million and royalties based on sales. The company's KOS-862 (Epothilone D) is in Phase II studies as a treatment for breast cancer, non small cell lung cancer and colorectal cancer. Kosan is also developing geldanamycins from *Streptomyces*, with 1t-AAG in phase I studies with the National Cancer Institute, has a development agreement with Johnson & Johnson for ketolides, and is producing analogues to discodermolide.
Martek	Established in 1985, with HQ in Columbia Maryland and manufacturing in Kentucky and South Carolina, develops and sells products from microalgae. The Nutritional Products Group manufactures and sells two nutritional fatty acids, docosahexaenoic acid (DHA) and arachidonic acid (ARA) and a patented DHA ARA blend sold as Formulaid® for infant formula worldwide. The DHA oil is sold as Neuromins® to nutritional supplement manufacturers and received approval as a novel food in the EU in June 2003, as a DHA-rich oil from *Schizotrychium* spp. The Fluorescent Products Group has developed proprietary fluorescent markers for use in drug discovery and research. The company maintains a library of more than 3,300 live microalgal species and a related database. Martek's first profits were made in 2002.
Mera Pharmaceuticals	Began as Aquasearch, replaced by merger with Mera after constructive bankruptcy in 1998; based in Kona, Hawai'i, produces microalgal materials in bioreactor modules, including AstaFactor™ astaxanthin, positioned as an anti-inflammatory and anti-oxidant as well as a feed colorant; during 2003 the company continued to work to reduce accumulated losses
MSD Inc	A partner in the MICROMAT consortium, exploiting Antarctic microbes for new molecules of therapeutic interest

TABLE 81: CONT

COMPANY	COMMENTS
Nereus Pharmaceuticals	A start-up established to commercialise discoveries made at the Scripps Institution of Oceanography, has raised $32 million in venture capital since 2000 and has 4 lead compounds in pre-clinical development for treatment of cancers and fungal infections. Nereus is moving ahead with synthetic compounds identical or analogous to the marine bioactives isolated from sponges, tunicates and other organisms. The company will also develop a line of anti-tubulin agents which inhibit normal internal cell processes.
Neurex Corporation	Based in Menlo Park, California, and owned since 1998 by elan corporation of Ireland, Neurex is the developer of *Conus* toxin as the pain-reliever ziconitide, in partnership with Pfizer and Warner-Lambert; Neurex also had deals with American Home Products and Medtronics for agrochemical and drug delivery..
PSD Inc.	Based in Sandy, Oregon, and selling a concentrated extract of Russian-origin Pacific *Laminaria japonica*. for a variety of uses that are very close to medicinal claims. The alginates and fucoidan in the product are claimed as the effective components.
Wyeth Ayerst	Wyeth Research has had a long-standing programme of screening natural bioactives from a variety of sources including marine; the Wyeth collection contains >3000 organisms, including spiroxin-producing fungi, namenamicin-producing ascidian and maiviticins-producing *Micromonospora* actinomycete; Wyeth is also working on hemiasterlins from *Cymbastella* sponge.

Aphios Corporation appears to be an important up-and-coming company with a strong focus on marine bioactives. It is developing antiviral (HIV, influenza, smallpox, herpes and SARS) and antimicrobial therapeutics from a library of unique marine micro-organisms and other marine sources, from normal to extremophilic environments, including:

- bryozoans, sponges, corals and tunicates
- shark and fish
- hydrothermal vents
- hypersaline ponds
- deep-sea sediments via submersibles
- shallow mangrove swamps and other near shore locations
- tropical and temperate oceans

Aphios's technology base includes 29 issued U.S. and international patents, and several pending patent applications for products, microbial cell disruption and fractionation technologies for the rapid and selective isolation of semi-purified marine molecules and formulation technologies for drug delivery. It uses supercritical fluid extraction to obtain bioactives. Aphios's R&D portfolio includes anti-HIV and anti-influenza marine bioactives and a marine antimicrobial compound, Asterias™, aimed at dental plaque and gingivitis. The company is producing drug delivery formulations of natural anticancer agents such as generic paclitaxel and bryostatin-1 using its patented supercritical technology and is in clinical trials with two natural-origin products for quality of life of cancer patients, *Zindol*™ for nausea, based on ginger, and cannabinoids for pain and cachexia.

TABLE 82: APHIOS'S MARINE-RELATED GRANTS

SOURCE	PROJECT
NCCAM (National Center for Complementary & Alternative Medicine)	Anti-Smallpox Therapeutics from Marine Micro-organisms
NIAID (National Institute of Allergy and Infectious Diseases)	Development of Novel Anti-Influenza Agents
NCI	*SuperFluids*™ Isolation of Natural Anti-Cancer Products
NIDCR (National Institute of Dental and Craniofacial Research)	Development of a Marine Anti-Plaque Compound
NIAID	Novel Anti-HIV Chemotypes from Marine Micro-organisms
NCI	*SuperFluids*™ *CXP* of Bryostatin 1
NSF (National Science Foundation)	Crystallization of Natural Products
NIST (National Institute of Standards and Technology)	Marine Microorganisms and Saline Fermentation, ATP
NCI	Improved Isolation of Bryostatin 1

Corporate collaborators include Novartis, Bayer, Bristol-Myers Squibb, Eli Lilly and the Gillette Company.

Wyeth Ayerst has had a marine bioactives product for many years. Its culture collection includes fungi, actinomycetes and eubacteria, some from marine sources, as well as marine invertebrates. A total synthetic analogue of hemiasterlin A has been in clinical studies for cancer. Namenamicin, isolated from *Polysyncraton*, a Fijian ascidian, has superb activity in screens but was present at less than 0.01% in harvested samples.

California

This state has an impressive range of activities based on the different campuses of the University of California. Foremost amongst these is the Scripps Institution of Oceanography[186] at UCSD (San Diego), with a team in the Marine Research Division led by William Fenical[187] and the associated Center for Marine Biotechnology and Biomedicine, with a team led until recently by the late John Faulkner[188], both high-achievers in the marine biology and biotechnology arena. UCSD's Center for Marine Biotechnology and Biomedicine CMBB is based in the Scripps Institution of Oceanography in collaboration with UCSD School of Medicine. Research programs focus on marine biomedicine and marine drug discovery, with an emphasis on cancer and both infectious and inflammatory diseases. CMBB and Marine Research Division scientists investigate a wide range of biotechnologies, from the special properties of deep-sea marine microbes to the genetic engineering of commercially viable marine animals.

186 see http://www.sio.ucsd.edu/

187 see http://fenical.ucsd.edu/index.htm

188 see http://www.mrd.ucsd.edu/jf/

Fenical's group[189] in the Marine Research Division is supported by the National Cancer Institute (National Institutes of Health) and several local and international pharmaceutical companies including Bristol-Myers Squibb, as well as a recent BioStar-funded project with AgraQuest for pesticides. Bill Fenical is founder and scientific adviser of Nereus Pharmaceuticals Inc, a young San Diego-based company established to develop the Scripps Institution's marine bioactives into medical products in the anti-cancer, anti-fungal and dermatological areas.

TABLE 83: UNIVERSITY OF CALIFORNIA SAN DIEGO ACTIVITIES

	ACTIVITIES
Center for Marine Biotechnology and Biomedicine CMBB	Study of marine sponges, tunicates, soft corals, gorgonians, nudibranchs and sea hares, and their associated symbiotic micro-organisms. Biomedical interests include anti-cancer, anti-fungal and anti-bacterial agents, inhibitors of HIV-1 integrase (with the Salk Institute), anti-inflammatory agents, such as pseudopterosins (with UC Santa Barbara), and agents to treat tropical diseases such as leishmaniasis (with Universidad Central de Venezuela)' CMBB is also active in establishing marine organisms as models for mammalian toxicology and research
Marine Research Division, Scripps Institution for Oceanography	Anti-cancer bioactives from sponges, coral and tunicates: eleutherobin, discovered in 1995 in a soft coral, active against ovarian, breast, pancreatic and colon cancer cells and apparently identical to taxol; mitotic inhibitors from tunicates, diazonamide A and tamandarin A, active against HCT-116 human colon carcinoma cells; sargassamide, halimide and avrainvillamide, potential anti-cancer agents produced by marine fungi growing on algal surfaces; cyclomarin A, exumolides, and avrainamide, which inhibit swelling and control pain in experimental inflammation; antimicrobials and 'salinosporamide-A', a cytotoxic agent, from novel isolates of the actinomycete *Salinospora*

CMBB and MBD scientists have also discovered anti inflammatory agents, including pseudopterosin, already being used in Esteé Lauder's internationally marketed skin-care product that reduces swelling and retards degeneration of the skin. Another target is AIDS and other viral diseases, and new antiviral bioactives, halovirs, have been discovered that have *in vitro* action against herpes simplex and human immunodeficiency virus. Antimicrobial focus includes screening for methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus and amphoterocin-resistant Candida albicans.

In addition to the 'classical' search for bioactives from marine invertebrates, Fenical's group looks in oceanic sediments for microbes that might contain new molecules. The SIO has constructed a miniaturised sampling device and collected bottom sediments from more than 1,000 m deep in the Atlantic and Pacific Oceans, the Red Sea and the Gulf of California. In addition to the support organisations mentioned above, funds have been received from the Khaled Bin Sultan Living Oceans Foundation.

There is also a research focus on signalling and activating molecules in marine microbes. A recent discovery with the Dept of Pharmacology UCSD is that

[189] see http://www.sioadm.ucsd.edu/rab/

adociasulfate-2, produced by a marine sponge, inhibits the transport of proteins along the microtubule network within the cell. Adociasulfate-2 also causes apoptosis in *Drosophila melanogaster* embryos, which may be promising for cancer treatment. Other areas include the defensive mechanisms of marine organisms and the relative roles of invertebrates and symbionts as sources of bioactives. The sea hare *Aplysia californica* stores compounds from red algae that make it distasteful to predators. Nudibranchs obtain similar protection from defensive chemicals in their diet of sponges, bryozoans or tunicates, which they preferentially absorb. Many marine natural products, particularly those from sponges, have been attributed to "symbionts" rather than the host organism. It is difficult if not impossible to investigate this using conventional isolation and culture techniques because virtually no symbiont can be grown independently and, if culture is successful, there is no guarantee that the bioactive output will be the same. CMBB therefore localises specific target chemicals in the cells using physicochemical methods and demonstrates presence or absence of symbionts from these cells, rather than attempting to culture the symbionts.

There is an MD/PhD degree offered in conjunction with the UCSD School of Medicine and PhDs through the Scripps Institution's marine sciences curricula. When fully developed, CMBB will provide laboratory and office space for approximately 30 graduate students and is working with the local biotech industry to develop fellowship support and industrial internships.

Dr Jane Burns of the UCSD School of Medicine discovered and developed the Pantropic Retroviral Expression System, originally to help with transgenesis of shellfish such as oysters, abalone and mussels to protect against disease and in striped bass to improve growth rate. The Dept of Food Science and Technology at UCD (Davis) has interests in novel enzymes from marine sources and their use in food processing.

The State of California also supports marine research through its California BioSTAR Program, established in July 1996 to bring California businesses into research partnerships with University of California researchers and students. The goals of the programme are to build businesses and markets based on new products and technologies coming out of R&D in California, which itself has been accelerated by the programme. By 1998, 46 research partnerships had been established, costing $12 million in collaborative funding. In 2001, the programme changed its operating name to the UC Discovery Grant. By 2003, BioSTAR/UCDG has awarded almost $23 million to University of California researchers at the nine campuses and the three UC-associated national laboratories and more than $2.3 million for UCLA research projects. BY 2004, 595 matching grants had been made for a range of projects.

Of over 310 projects in biotechnology, only 5 have a marine biotechnology focus and 4 of these are Bill Fenical's. AgraQuest received funds to work with Bill Fenical's laboratory for agrochemical uses of marine bioactives, and some of the work has benefited Nereus Pharmaceuticals, the spin-out for which Fenical is founding scientist and member of the advisory board.

Phillip Crews of the Chemistry department at University of California Santa Cruz, in Baja California, has been a pioneer in the field of sponge chemistry since the mid-1970s. The Marine Natural Products Laboratory has a collection of 800 pure marine bioactives and thousands of uncharacterised extracts. His team's collecting efforts extend to the South Pacific islands of Fiji, the Solomon Islands, and Papua New Guinea. The most promising drug lead has come from the bengamides, isolated from a *Jaspis* sponge collected in the Benga Lagoon in the Fiji Islands. The licensee Novartis has developed a total synthesis for a bengamide analogue that is now in clinical trials for breast cancer. Other interesting leads include manzamines from sponges collected in Papua New Guinea, which are potential anti-malarials, and lipoxygenases found in recent high throughput screening of Crews's bioactives and extracts collection, which could have potential in stroke and heart attack therapy.

TABLE 84: BIOSTAR MARINE BIOTECHNOLOGY PROJECTS

TITLE	AWARD	PERIOD	COMMENTS
Investigation of deep marine sediment microbes for the development of crop protection products (Fenical)	$135,802	01.2002 – 01.2004	This programme is for the screening and development of fermentable natural product pesticides from unique marine actinomycetes collected in sediments from water depths between 30 and 300 m, using a recently developed grab device; it is part of a collaborative research program with the University of Guam. Pure cultures and fermentation broths will be sent to AgraQuest, the corporate sponsor, for isolation and characterisation, with technical assistance from Scripps
Marine actinomycetes as a resource for drug discovery (Fenical)	$840,278	08.2001 – 08.2003, renewed to 08.2005	The funding is to isolate large numbers of new actinomycetes from diverse marine sediments and to thoroughly explore their biomedical potential; they will be cultured and extracted at Scripps Institution of Oceanography and the extracts tested in sophisticated biomedical assays performed at Nereus Pharmaceuticals, Inc., the corporate sponsor. The renewal is for continued development of sampling equipment that will allow for the rapid collection of high quality sediment cores from deep-sea locations.
Large-scale saline fermentation for the discovery and development of marine microbial drugs (Fenical)	total $840,712	06.1999 – 06.2000; renewed twice to 08.2003	Funding is to develop and optimise pilot-scale (500 L) saline fermentation techniques to produce gram-quantities of three novel marine drug candidates and provide them to collaborators for advanced pre-clinical testing.
Equipment Support for a Developing Program in Marine Microbial Biotechnology (Fenical)	$195,370	06.1998 – 06.1999	Modern instrumentation is needed for the recently dedicated Charmaine and Maurice Kaplan Laboratory at CMBB, to investigate the unique microbial resources present in deep-sea sediments as a source of new anti-viral agents, to bring the facility to modern standards and to establish CMBB as a world`s leader in the discovery and development of marine pharmaceuticals. SeaTech Inc., a California-based biotechnology company, is the corporate sponsor.

TABLE 84: CONT

TITLE	AWARD	PERIOD	COMMENTS
Plasmids from Marine Sediment Bacteria as a Source of Genes Encoding Novel Traits (Helinski)	$314,718	06.1998 – 05.2000	a library of large plasmids found in both culturable and non-culturable bacteria will be prepared for probing for genes of interest expected to be useful in engineering plants and microorganisms to produce high value chemicals or pharmaceuticals and/or to find direct use in agriculture; potentially improve the agronomic properties of strawberries and tomatoes and lead to the production of high value lipids that will be grown in control plots in California

That all is not plain sailing in California can be seen from the history of CalBioMarine technologies Inc[190], founded in 1986 to cultivate marine invertebrates and extract bioactives. During the 1990s, CBM was working with UCSD to grow the bryozoan *Bugula neritina* in aquaculture to harvest the anti-cancer agents bryostatins. CBM then signed an exclusive licence in 1999 to bryostatin genetic technologies from the Haygood lab of the Scripps Institution, with the intention of altering cloned genes to generate bryostatin analogues. CBM was also working on the production of ecteinascidin 743 (ET-743), from the sea-squirt *Ecteinascidia turbinata*, and on the design of new bioreactors for hot spring *Cyanobacteria* spp., from which CBM had created a library of over 600 extracts with interesting bioactivities. After failing to raise funds in 2003-2003, CBM folded its operations, with the founder maintaining activities only to keep the intellectual property alive, and try to continue offering the marine extracts library for industrial screening contracts.

Pacific Standard Distributors, Inc is based in California and imports Modifilan®, a concentrated extract of *Laminaria japonica* harvested in the Russian waters of the North West Pacific, for health and food supplement use as a cancer support, in the treatment of autoimmune diseases, for the reduction of cholesterol and balancing of blood sugar levels. Modifilan is also used a chelator for the treatment of human heavy metal and radioactive isotope contamination.

Florida

Harbor Branch Oceanographic Institution[191] in Fort Pierce is another important site for marine biotechnology and bioactives research. In the Division of Biomedical Marine Research, work includes characterisation of compounds from marine plants, invertebrates and associated microorganisms using bioassay guided purification, production of un-natural natural products through the manipulation of biosynthetic genes and development of micro-analytical methods for monitoring aqua and cell cultures used in the production of therapeutically important marine natural products. Last year, HBOI hit the news when, after 20 years of searching, it rediscovered a sponge that produced a potent anti-cancer bioactive. HBOI has nearly a hundred patents on bioactives, from

[190] see http://www.calbiomarine.com/sys-tmpl/door/
[191] see http://www.hboi.edu

tens of thousands of organisms collected since the 1980s, including discodermolide, currently in clinical trials.

The Center of Excellence in Biomedical and Marine Biotechnology[192] is a virtual institute involving Florida Atlantic University, Florida International University, Harbor Branch Oceanographic Institution, Nova Southeastern University and the Smithsonian Marine Station at Fort Pierce, Florida. There are also industrial partners in the Center, including Custom Biologicals, Edgetech, Ixion Biotechnology, Nabi Biopharmaceuticals and Sunol Molecular.

The aim of the Center is to provide a sustainable and stronger biotechnology sector in Florida based on marine biotechnology, with the support of local economic development agencies such as the Business Development Board of Palm Springs and the Enterprise Development Corporation of South Florida. There is a strong training element in the Center's targets, as well as a focus on new medicines and novel diagnostics as products, and new technologies for exploration.

The Center will use the research vessels and submersibles of the academic partners to explore the waters round Florida and the Bahamas, with the aim of collecting sponges, soft corals, tunicates and algae and sampling organisms from several compartments including the sea itself, sediments and surfaces of organisms. Bioactives that might be detected will be screened for anti-cancer, anti-inflammatory, anti-oxidant, anti-ageing, anti-alcoholism and CNS-supportive activity.

In addition to culture methods for 'difficult' organisms, the Center will also work on identifying relevant genes and expressing them efficiently in conventional bioreactor organisms. Since previous work by Florida Atlantic University and Harbor Branch has revealed that not all bioactives from sponges and tunicates come from their microbial symbionts, the Center will also develop invertebrate cell culture systems.

Hawai'i

The state is very active in aquaculture and mariculture but its main focus is on fish, shell-fish and crustacea. The industry consists of more than 80 companies with revenues of more than US$20 million p.a.[193] In addition, there is existing cultivation and harvesting of macroalgae, including *Gracilaria* spp., and several companies growing microalgae such as *Spirulina* and *Haematococcus* for nutraceutical and food or feed additive use.

Apart from Guam, Hawai'i is the only part of the USA with genuinely tropical waters, and thermal vents are also heavily-concentrated here as a result of the continuing volcanic activity in and around the islands. This has stimulated interest in bioactives and novel enzymes from extremophilic organisms. The cultivation of microalgae and the potential for products from marine micro-organisms is also supported by skills in bioprocess engineering.

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[192] see http://www.floridabiotech.org/about.html

[193] *Key Business Sectors Marine Biotechnology*, Enterprise Honolulu 12.03, www.enterprisehonolulu.com

TABLE 85: HAWAI'IAN COMPANIES INVOLVED IN PRODUCING MARINE MICROALGAE

COMPANY	COMMENTS
Cyanotech	astaxanthins for human nutraceuticals, animal and aquaculture feeds and therapeutic use for humans; marine phycobiliproteins for diagnostics
Mera Pharmaceuticals	astaxanthins for human nutraceuticals and feed use; Mera is also a leader in photobioreactor technology, with a proprietary closed system, the 'Mera Growth Module', for continuous commercial production of astaxanthin from *Haematococcus* for up to 9 months and experimental and pilot production of any other culturable organism; Mera completed a $3m expansion of culture operations in 1999. Founded with input from Scripps Institution
Micro Gaia Inc	microalgal constituents for nutraceuticals, foods and drinks, infant formulae, cosmetics, aquaculture feed; Micro Gaia has also developed a closed bioreactor system, the Bio-Dome

Work at the University of Hawai'i' in the Dept of Chemistry includes cloning and analysis of genes and gene clusters from marine microalgae such as *Scytonema ocellatum*, which produces scyophycins, powerful antimicrofilament macrolides with solid tumor selectivity but non-specific toxicity. This might be counteracted by transferring the genes to conventional *Streptomyces*, which can then be engineered to produce analogues, thus there is a programme on isolating genes from cyanobacteria and expressing them in *Streptomyces*. There is also a research programme on new antibiotics from marine sources.

MarBEC was set up especially to research, develop and exploit Hawai'i's marine biota, with a focus on the chemical, pharmaceutical, cosmetics and life sciences industries. The University of Hawai'i at Manoa and University of California Berkeley established MarBEC in 1998, using grant from the US National Science Foundation of US$12.4 million over 5 years. Industry founders of MarBEC included Monsanto, Eastman Chemical, Hawaiian Electrical and Aquasearch Inc. (a microalgal food supplement manufacturer later bought by Mera). The University of Hawai'i' at Manoa hosts MarBEC's research ship R/V Kaimakai-O-Kanaloa and Pisces V submersible. MarBEC capitalises on the existing activities in microalgal fatty acids, novel enzymes and anti-sunlight compounds.

MarBEC is also involved in genetic engineering of conventional host organisms using genes identified in or isolated from marine organisms, for bioreactor production of bioactives of interest.

Maine

The Mount Desert Island Biological Laboratory (MDIBL), Bar Harbor, Maine, established in 1921, which contains the Center for Marine Functional Genomic Studies, the first sequencing centre in the world dedicated to marine organisms. A major focus of the Center is on fish and their genetics, especially as models for human disease and development and test models for the study of carcinogenesis, mutagenesis, and endocrine disruption. Fish such as *Fundulus heteroclitus* are sensitive and useful test systems for environmental pollutants. The Center has also established cell lines from fish and marine mammals. One marine bioactive discovered here is squalamine, the anti-inflammatory, anti-cancer, anti-angiogenesis molecule from sharks. The Center is also developing a genome bank for sharks.

Maryland

There is an alliance between Maryland's biotechnology association and Scotland's biotechnology community, mediated through BIA Scotland. There has been liaison and collaboration in the past[194] between Dunstaffnage Marine Laboratory and the main biotechnology centre in Maryland, COMB.

COMB was established in 1985 as one of the centres within the University of Maryland's Biotechnology Institute (UMBI). COMB absorbed some of the existing activities of the University, including a focus on the Chesapeake Bay Blue Crab, and added an impressive range of additional activities and skills in marine biotechnology and bioengineering that now makes it one of the world-leading institutions in this sector[195].

The Columbus Center in which COMB is based is dedicated to marine bioscience and biotechnology and is a US$160 million purpose-built development in Baltimore's Inner Harbour. COMB has about 150 staff and facilities for transgenic research, extremophile bioreactor cultivation, genome analysis, laboratory and tank cultivation of marine and freshwater biota, advanced analytics, advanced breeding and hatchery research. The research, training and development programmes are multidisciplinary, across the themes of aquaculture and fisheries biotechnology, marine environmental biotechnology, microbial and extremophile processes, marine natural products and functional genomics.

COMB's research funding in 2002 reached US$4.8 million, of a total including establishment costs, of US$8.6M. Of the total, 8% came from foundations, 3% from industry and the balance from the Federal and State governments, about equally.

TABLE 86: RECENT RESEARCH AND DEVELOPMENT RESULTS AT COMB

MICROALGAE	discovery of a new algal toxin responsible for fish deaths; patent application filed
SHELLFISH	a new, sensitive, diagnostic for 'Dermo' in the Eastern Oyster; patent issued
MARINE VIRUSES	mapping viral communities in Chesapeake Bay
SYMBIONTA	isolation of a marine sponge-associated microbe that produces anti-malarial drugs; patent application filed
ENVIRONMENT	progress in the isolation and identification of Chesapeake Bay bacteria that bioremediate PCBs; two patent applications

COMB is a world leader in Blue Crab research. It has also established, according to the Center itself, the world's strongest program in extremophile research and adaptation to life in extreme environments. Other teaching and research programmes include Marine Functional Genomics, including bioinformatics and extremophile functional genomics, and Marine Environmental Biotechnology, with areas of microbial bioremediation, biofilms, biofouling, biosensors, microbial consortia and microbial symbiosis.

UMBI's centres include:

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194 *Marine Science Review, Report of Visit to Maryland & Virginia*, New Park Management June 2001

195 see www.umbi.umd.edu/~comb/welcome/welcome.html

TABLE 87: ACTIVITIES WITHIN THE UNIVERSITY OF MARYLAND BIOTECHNOLOGY INSTITUTE[196]

CENTER OF MARINE BIOTECHNOLOGY (COMB)	Basic and applied research in marine biosciences including biotechnology; applied aquacultural and maricultural research, advanced breeding techniques, development of monitoring and diagnostic tests
CENTER FOR ADVANCED RESEARCH IN BIOTECHNOLOGY (CARB)	Characterisation of bioactives and other molecules from marine sources
CENTER FOR AGRICULTURAL BIOTECHNOLOGY (CAB)	Involvement in marine by-product bioprocessing
INSTITUTE OF HUMAN VIROLOGY (IHV)	Able to test promising marine bioactives against viruses
MEDICAL BIOTECHNOLOGY CENTER (MBC)	Applied cellular studies that can define the activity of marine molecules

COMB is responsible for some industrial applications of marine-origin compounds, including bioadhesives, productivity enhancers in oyster culture and surfactants for manufacturing processes. CAB has developed an improved bioprocess for generating chitosans from crab-waste, aimed at the oil industry.

Maryland is also the home of the Natural Products Branch of the National Cancer Institute. Based in Frederick, the NPB-NCI possesses an unparalleled collection of organisms, including over 10,000 from marine sources, mainly tropical, and a high-power screening capability for anti-cancer and anti-HIV activity. The Australian Institute for Marine Science has a large-scale agreement with NPB-NCI to screen extracts from marine organisms. Some use of this is made by UK-based researchers[197]. NPB-NCI has been responsible for isolating and synthesising analogues to bryostatin 1 and ecteinascidin 743.

New Jersey

Rutgers University at New Brunswick New Jersey contains the important Institute of Marine and Coastal Sciences, IMCS. This is responsible for education, research, and service activities in marine science, including biotechnology and ecology, in estuarine, coastal, and ocean environments. 12 laboratories and groups contribute to different aspects of marine biotechnology, with the main relevant activities within the Center for Deep-Sea Ecology & Biotechnology CDSEB and the Deep Sea Microbiology Laboratory. CDSEB is responsible for an intensive programme of molecular genetic analyses of deep-sea and other marine organisms and has the world's largest collection of ultra-low frozen organisms from deep-sea hydrothermal vents and cold-water sulphide methane seeps. IMCS's Deep Sea Microbiology laboratory investigates thermophilic Archaea and bacteria and their community dynamics, using cultures and isolations, molecular

[196] source: adapted from *Marine Science Review, Report of Visit to Maryland & Virginia*, New Park Management June 2001

[197] For example, Dr M Jaspars of the Marine Natural Products Laboratory University of Aberdeen, see *ibid.*

ecological approaches, genetic engineering and biochemical approaches, combined with comparative protein structure modelling.

IMCS at Rutgers has also developed and hosts the Ocean Biogeographic Information System (OBIS). This is an on-line database of global marine animal and plant distributions, for use in oceanography, resource mapping and investigation of global biodiversity. IMCS is a co-founder of the Mid-Atlantic Bight (MAB) National Undersea Research Center, a joint-venture with the Marine Sciences Research Center at Stony Brook University. This is the result of a regional competition in 1992 and focuses on understanding the natural and man-made factors behind change and stability in the New York Bight south of Long Island down into Chesapeake Bay. The MAB Center operates undersea research platforms and sensors, including the LEO-15 Observatory, a REMUS Autonomous Underwater Vehicle, other submersibles and remotely operated vehicles. LEO-15 is a Long-term Ecosystem Observatory established at a 15 meter inner shelf site offshore from the Rutgers University Marine Field Station at Tuckerton, New Jersey.

Rhode Island

Activities at the University of Rhode Island URI are based around the work of Yuzuru Shimizu, Professor of Biomedical Sciences. He has worked on red-tide microalgae, dinoflagellates, developing methods of sampling and large-scale culture. His work has been funded by the National Sea Grant College Program, notably in 1994 with the project Large-scale Culturing Key to Drugs from Sea, which looked at the possibility of developing continuous culture methods for microalgae as well as single-batch culture in large fermenters. He has continued with two consecutive $1 million 5-year grants from the National Cancer Institute, as part of the National Cooperative Natural Products Drug Discovery Group. This work is a collaboration between URI, William Fenical's and John Faulkner's groups at the Scripps Institution of Oceanography San Diego and Bristol-Myers Squibb Pharmaceutical Research Institute, and is on-going, looking for marine bioactives as anti-cancer agents and building on Shimizu's isolation and patenting of caribenolide I from *Amphidinium*, a dinoflagellate. Many of the organisms are collected from Hawaii, the Caribbean and in the Salton Sea, inland in California.

Shimizu's recent and current research interests include the chemistry of red-tide toxins and other microalgal toxins and the structure-activity relationship and biosynthetic mechanism of the toxins; the isolation and structural determination of anti-tumour and antiviral compounds from marine organisms; cyclic peptides in blue-green algae; biosynthesis of saxitoxin and brevitoxins; and conformational analysis of neurotoxins with respect to receptors.[198]

URI also houses the Marine Ecosystem Research Laboratory MERL, which has 15,000 litre culture tanks for marine organisms.

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198 source: University of Rhode Island web-site www.uri.edu and *Scientist seeks cancer drugs in the sea*, Article May 2001 from URI 'Pacer' – http://advance.uri.edu/pacer/may2001/story15.htm

Other activities

TABLE 88: SOME OTHER UNIVERSITIES AND INSTITUTIONS IN USA WITH RELEVANT PROGRAMMES

ORGANISATION	ACTIVITIES
American Type Culture Collection	Based in Manassas Virginia, the ATCC is a patent depository and micro-organism maintenance institution with approaching 100,000 micro-organisms, over 500,000 gene clones and a growing stem cells collection. ATCC's Bacteriology Laboratory received a National Science Foundation grant 1999-2002 to take part in a biodiversity survey of mid-Atlantic estuarine micro-organisms.
University of Arizona	The Moore group in the College of Pharmacy has a symbiont project, in collaboration with other centres such as the Scripps – swinholide, theopalauamide, enterocin from *Aplydium*; also isolating bioactives such as salinamides, anti-inflammatories, and mixed polyketide-terpene molecules from marine *Streptomyces*;
Biotechnology Center of Excellence Corporation	BCEC is a private, non-profit organisation, providing technical assistance, policy support and technology transfer facilitation for a wide range of biotechnological application in life sciences, on an international scale. It is or has been active in/with North Hokkaido, Quebec, the University of Ulster, the BioMinas Foundation in Minas Gerais, Brazil, Cagliari in Sardinia, Italy, UNIDO in Vienna, Austria, and the Fundación Chile in Santiago, Chile. BCEC has strong associations with South America, including Chile, Venezuela and the United Nations Economic Commission for Latin America, partly through the BioAmericas programme. BCEC was the founding Secretariat for the Pan American Marine Biotechnology Association.
University of Delaware	Center for the Study of Marine Policy – active in assessing impacts of new technologies and activities such as marine biotechnology; involved in the assessment of benefits from the US NOAA Sea Grant Research program with respect to outreach on marine biotechnology and in establishing international network on oceanic ecological governance
Oregon State University	Dept of Pharmaceutical Sciences has a research programme in bioactives from marine sources; cloning, sequencing and biochemically characterising genes and gene clusters from cyanobacteria; investigating the effects of gene mutation; using bioactives as research reagents (eg antillatoxin as sodium channel probe); Astoria Seafood Lab researches impact of marine bio[techno]logy on food industry
University of Pennsylvania	discodermolide (licensed to Kosan) and spongistatins; Prof Smith has a long-standing collaboration on natural products with the Kitasato Institute
Rockefeller University	The Laboratories of Molecular and Cellular Neuroscience and Molecular Vertebrate Embryology have collaborated with researchers from the Marine Biology Station Roscoff France and the University of Athens Greece on applications of a marine mollusc extract, 6-bromoindirubin-3'-oxime, to stabilise and differentiate stem cells for research and tissue engineering use
University of South Alabama & Clemson University South Carolina	Donlar Corporation was established in 1990 to commercialise and further develop the technology, marketing the biopolymers for water treatment and agricultural use, with a market of \$m 10^2s and royalties to the universities.
University of Utah	Asst Prof E Schmidt, Medicinal Chemistry, provides graduate study in biosynthesis in marine invertebrates, including polyketides, peptidases, terpenes and alkaloids, with use of terrestrial gene probes to isolate homologues in marine organisms, clone them and express in conventional organisms; gene cluster studies and identification of novel products such as enzymes – has worked on microsclerodermins from sponges, the symbiont *Entotheonella* and theopalauamide from *Theonella* sponges

Support Organisations

The Pew Charitable Trusts form an independent non-profit organisation established between 1948 and 1979 by children of the Sun Oil Company founder Joseph N. Pew and his wife, Mary Anderson Pew. Based in Philadelphia, the Pew trusts fund provision of information, policy solutions and support for civic life. In 2003, with approximately $4.1 billion in dedicated assets, more than $143 million was available for new and ongoing projects. $19 million was used for 13 grants on public policy and $42 million for 23 grants on the environment, including several for marine and biological conservation studies. Marine biotechnology has not been a specific focus of the Pew studies, except for one on the possible impacts of transgenic salmon.

The Gordon Research Conferences provide an international forum for the presentation and discussion of frontier research in the biological, chemical, and physical sciences, and their related technologies. Founded in 1931, they commemorate the insight and the years of work by Neil Gordon in establishing meetings. The first Gordon Conference outside the USA took place in Volterra in 1990. In 2004, two marine conferences are scheduled, on marine natural products and marine micro-organisms.

CANADA

Canada's waters are temperate, cold and arctic. Canada already has well-established aquaculture, marine products and ocean technologies industries. Because it has the largest coastline in the world, it would make sense to make the best use of this. In the case of Labrador and Nova Scotia in particular, there is a strong focus on the seas, since 90% of the population lives in coastal areas.

There is research into marine bioactives at the University of Winnipeg, Manitoba. The Department of Chemistry is involved in isolation of new pharmaceutical agents from marine organisms, microorganisms and traditional medicinal plants, biosynthesis of natural products and microbial transformations of bioactive natural products; characterisation using high-performance analytical techniques and biological screening, biosynthesis and biotransformation. Recent discoveries include elisabethamine and 12-acetoxypseudopterolide, diterpene analogues of pseudopterosin from *Pseudopterogorgia elisabethae*.

The strongest applications of marine bio[techno]logy are in Newfoundland and Labrador. The state is benefiting from the Federal Government's Can$300m Atlantic Innovation Fund initiative, and had received $45m by 2002. The Canadian Center for Fisheries Innovation is in St John's. Oceans Advance, specifically aimed at broad ocean technologies, is the regional revival programme based on St John's, funded by the Canadian National Research Council as a national technology clustering initiative and established in 2001. St John's will host the 7th International Marine Biotechnology Conference in 2005, with significant involvement from **Bio-East**, a division of the GENESIS Group, the commercialisation arm of Memorial University of Newfoundland. Bio-East is a network of over 50 commercial, academic and government organisation actively involved in the biotechnology industry. Bio-East is encouraging activities in marine biotechnology, pharmaceutical and nutraceutical research and genomics, and building up N&L as an international centre for marine biotechnology, with companies such as A/F Protein Canada, NovaLipids, Newfoundland Aqua products and Atlantic Marine Products.

Most output to date of activity in N&L is in added-value products from fish and shellfish by-products, such as omega-3 fatty acids (Atlantic Marine Products, Catalina and

Gateway Maritime, Brigus) and chitin-chitosan (AquaShell Processing, Badger's Quay), and soil conditioners and fertilisers from composted fish and plant wastes (Genesis Organic, Wild Cove).

The longest established true biotechnology company is A/F Protein Canada, based in St John's, working on anti-freeze genes, the potential for anti-freeze proteins in food, transplant organ preservation and stabilisation of pharmaceuticals and faster-growing transgenic salmon. Their technology and products are based on discoveries at Memorial University.

The Institute for Marine Biosciences is based in Halifax, Nova Scotia, and is a National Research Council of Canada institute. Although there is no directly-named biotechnology programme here, there are individual activities such as investigation of fish C-type lectins, new processes for value-added products from fish waste, antibacterial peptides from fish and marine pathogen genomics that are relevant.

In 1999, the Federal Government established AquaNet, a C$27m programme for the support of aquaculture[199]. This is one of 21 Networks of Centres of Excellence, established by the Natural Sciences and Engineering Research Council (NSERC), the Canadian Institutes of Health Research (CIHR) and the Social Sciences and Humanities Research Council (SSHRC), in partnership with Industry Canada. The administrative centre is at the Ocean Sciences Centre, Memorial University of Newfoundland and the Office of the Executive Scientific Director is at the Centre for Aquaculture and the Environment of the University of British Columbia in West Vancouver. AquaNet is currently planning a research forum on Non-Food Aquaculture Products, although to-date, most of the funded research projects have not addressed this topic. One project looking at integrated aquaculture is using seaweed and mussel farming with salmon, to make better use of nutrients and reduce the impact of salmon cages on the environment. The commercial partner in the project concerned with seaweeds is Acadian Seaplants Ltd of Dartmouth, Nova Scotia.

The North Pacific Marine Science Organization (PICES)[200] is co-ordinated by the Institute of Ocean Sciences in Sidney, British Columbia. It is an intergovernmental scientific organisation, established in 1992 to promote and coordinate marine research in the northern North Pacific and adjacent seas, with Canada, Japan, the People's Republic of China, the Republic of Korea, the Russian Federation, and the United States of America as members. PICES is developing a North Pacific Ecosystem Status Report that will periodically review and summarise the status and trends of the marine ecosystems in the North Pacific. PICES is a partner with NOAA in a project to develop the North Pacific Ecosystem Metadatabase, an inventory of the extensive biological and physical data collected on the ecosystem. PICES also conducts a Continuous Plankton Recorder Survey of the North Pacific, using funding from the Exxon Valdez Oil Spill (EVOS) Trust Fund's Gulf Ecosystem Monitoring (GEM) programme and the North Pacific Research Board.

[199] see http://www.aquanet.ca/English/

[200] see http://www.pices.int/default.aspx

Projects in the US Microbial Observatories Programme 1999-2008

TABLE 89: GRANTS YEAR ON YEAR

2003 GRANTS			
TOPIC	**ORGANISATIONS**	**FUNDING**	**YRS**
Linking Microbial Discovery to Biogeochemical Processes: An Oligotrophic Oceanic Microbial Observatory	**University of California-Santa Barbara** **Oregon State University**	**$592,198** **$306,102**	**5**
Kamchatka, a Geothermal Microbial Observatory	**University of Georgia Research Foundation Inc** **University of Maryland – COMB** **Portland State University**	**$748,070** **$160,000** **$98,106**	**4**
Microbial Diversity and Function in the Permanently Ice-Covered Lakes of the McMurdo Dry Valleys, Antarctica	**Montana State University** **University of California- Riverside** **Southern Illinois University** **Oregon State University**	**$348,184** **$247,362** **$359,998** **$100,000**	**5** **5** **5** **3**
Analysis of Novel Archaeal and Bacterial Diversity Associated with Iguanas Across Environmental Gradients	**University of Illinois at Urbana-Champaign**	**$200,000**	**5**
Sponges of the Class Demospongiae	**University of Maryland- COMB & Indiana University**		**4**
Exploration of Eukaryotic Microbes in Sulfide-Enriched Sediments at Redox Boundaries in the Black Sea	**University of South Carolina** **Woods Hole Oceanographic Institute**		**1**
Initiation of a Microbial Observatory for Anaerobic Electrophiles in Marine Sediments	**Michigan State University**	**$100,000**	
Characterization of Novel Anaerobic Microorganisms from a Sulfide Spring	*University of Oklahoma Norman Campus* *Woods Hole Oceanographic Institute*	*$550,151* *$281,000*	*3*
A Longitudinal and Molecular Diversity and Chemical Survey of Red Layer Microbial Communities in Yellowstone National Park	*Western Oregon University*	*$532,414*	*4*
Eukaryotic Microbial Communities of the Old Woman Creek National Estuarine Research Reserve	University of Akron	$220,574	3
Diversity of Plant-Associated Diazotrophic Bacteria and Their Distributions Within Specific Vegetation Zones Along an Environmental Gradient	University of South Carolina	$768,750	2
Characterization of the Microbial Community of Hirudo medicinalis	University of Connecticut	$100,000	
		6,426,713	

TABLE 89: CONT

2002 GRANTS			
TOPIC	ORGANISATIONS	FUNDING	
Diversity of Halophilic Bacteria and Geochemical Signatures in a Tropical Solar Saltern	**University of Puerto Rico at Humacao**	**$556,432**	**3**
Evolution and Diversity of Biochemical Pathways: A Methylotrophic Microbial Observatory	**University of Washington**	**$899,996**	**5**
Anhydrophilic, Halotolerant Microbial Mats of San Salvador Island, Bahamas	**University of North Carolina at Chapel Hill** **University of South Carolina** **Texas A&M University**	**$853,720**	**5**
Intra-annual Diversity and Dynamics of Chesapeake Bay Virioplankton	**University of Delaware Center of Marine Biotechnology** **Smithsonian Environmental Research Center**	**$989,663**	**5**
Salt Plains Microbial Observatory	*Oklahoma State University* *Wichita State University* *University of Tulsa*	 *$198,480* *$254,860*	*4*
Linking Phylogeny and Biogeochemistry for the Discovery of Novel Chemolithotrophs Inhabiting Geothermal Gradients in Yellowstone National Park	*Montana State University*	*$569,362*	*4*
Microbial Observatory at Soap Lake: Biogeochemistry, Microbial Diversity, and Productivity of Anaerobic Haloalkaliphilic Bacterial Communities	*Central Washington University* *Washington State University* *University of Missouri-Rolla*	*$840,461*	*3*
Viruses from Yellowstone Thermal Acidic Environments	*Montana State University* *Idaho National Engineering & Environmental Laboratory* *Portland State University*	*$569,362*	
Collaborative Research in an Alaskan Boreal Forest Soil	University of Wisconsin-Madison University of Alaska University of Illinois at Urbana-Champaign University of California-Berkeley	$512,484 $55,166 $200,934	4
Microbial Nitrogen Transformations in Suboxic Environments	University of Washington	$634,761	3
Function in Contaminated Aquifers	University of California-Davis	$200,160	2
Anaerobic Bacteria and Methanogens in Northern Peatland Ecosystems	Cornell University	$837,558	4
		5,475,395	

TABLE 89: CONT

2000/2001 GRANTS			
TOPIC	**ORGANISATIONS**		**YRS**
Undergraduate Research in the Molecular Diversity of Hot Spring Bacteria		**$222,953**	**3**
Discovery and Characterization of Uncultivated Bacteria, Archaea and Protista from the San Pedro Channel Time Series	**University of Southern California**	**$1,259,677**	**4**
Environmental Genomics and Microbial Observatories: Analysis of Genetic Variability, Gene Content, and Genomic Potential in Uncultivated Marine Picoplankton	**Institute for Genomic Research, Monterey Bay Aquarium Research Institute**	**$1,290,074**	**3**
Prokaryotic Diversity of a Salt Marsh/Estuarine Complex at the University of Georgia Marine Institute, Sapleo Island	**University of Georgia Research Foundation Inc**	**$1,002,179**	**4**
Microbial Diversity in Lakes of the Hawaiian Archipelago	University of Hawaii	$206,873	3
Species Discovery and Population Dynamics of coccoid Algae in Itasca State Park, Minnesota	North Dakota State University Fargo University of North Carolina at Wilmington	$400,000 $60,195	3
Collaborative Research on Microbial Diversity in Caterpillars	University of Wisconsin-Madison Portland State University	$838,049 $638,702	4
Observing Microbial Diversity and Horizontal Gene Transfer in a Shallow Contaminated Aquifer	Cornell University	$499,598	3
Microbial Biogeochemistry and Functional Diversity across the Forest-Tundra Ecotone in the Rocky Mountains		$1,000,000	4
Duke Forest: Exploring Fungal Diversity in Response to Environmental Change	Duke University	$411,854	3
		7,830,154	
1999 GRANTS			
TOPIC	**ORGANISATIONS**	**FUNDING**	**YRS**
Analysis of a Eukaryotic Microbial Mat Community Across Environmental Gradients in a Thermal, Acidic Stream	**Montana State University**	**$860,454**	**5**
Bacterioplankton Biology and Biogeochemistry at the Bermuda Atlantic Time-series Station: An Oceanic Microbial Observatory	**University of California- Santa Barbara** **Oregon State University**	**$298,318** **$299,990**	**3**
Salt Marsh Microbes and Microbial Processes: Sulfur and Nitrogen	*Marine Biological Laboratory*	*$1,165,771*	*4*
An Alkaline, Hypersaline, Meromictic Lake (Mono Lake, California)	*University of Georgia Research Foundation Inc* *University of California Santa Barbara* *University of California Santa Cruz*	*$737,651* *$202,077* *$248,164*	*5*
Spatial Scales of Genetic and Phenotypic Diversity Among Streptomycetes in Native Soils	University of Minnesota-Twin Cities	$989,992	4

TABLE 88: CONT

1999 GRANTS			
TOPIC	**ORGANISATIONS**	**FUNDING**	**YRS**
Diversity of Nitrogen-Cycling Microorganisms at the H.J. Andrews LTER	Oregon State University	$561,431	3
Northern Temperate Lakes Long Term Ecological Research Site	University of Wisconsin-Madison	$1,174,501	5
Observing Patterns of Prokaryotic Diversity along Land use Gradients of the CAP LTER	Louisiana State University & Agricultural and Mechanical College	$481,170	4
Linking Resource and Stress Gradients to Microbial Community Composition and Function through the Soil Profile of a California Annual Grassland at the Sedgwick Reserve	University of California Santa Barbara	$778,672	
		7,798,191	

Note: **bold** *entries are marine biotech; italic entries are freshwater biotech; others are land- or organism-based*

APPENDIX 12: REST OF THE WORLD

UNESCO

The Biotechnology Action Council of the Paris-based United Nations organisation UNESCO has established a number of BETCENs – Biotechnology Education and Training Centres, throughout the world. The Marine Biotechnology BETCEN[201] is based at the College of Marine Sciences, Ocean University of Qingdao, People's Republic of China. The activities of the BETCEN focus on research and training, mainly in aquaculture of fish and shellfish, but also algal farming. Visiting students and fellows include nationals from China, the Special Territory of Hong Kong, Indonesia, The Republic of Korea, Malaysia, the Philippines, Thailand and Vietnam.

CENTRAL & SOUTH AMERICA

The main focus of marine resource management in Central and South America is on aquaculture of trout, salmon, crustacea and molluscs, with production beginning in earnest during the 1980s. By 1997, the region provided over 2 percent of the volume of world aquaculture output and 5.1 percent of value, at US$2.7 billion. Six countries contributed over 90% of the total output - Chile (48 percent), Ecuador (17 percent), Brazil (11 percent), Colombia (6 percent), Cuba (6 percent) and Mexico (5 percent). For countries such as Chile, with its salmonids and *Gracilaria* seaweed, and Ecuador, Mexico, Honduras, Colombia Peru, Panama and Belize, whose major produce is shrimp and prawn, aquaculture is a very important export earner, with 90% of output being sold abroad[202]. Tilapia culture in Colombia, Brazil, Mexico, Cuba, Costa Rica and Jamaica has the highest growth rate of any sector and is the most important part of the freshwater sector, worth >US$500 million in 1998. The remaining sector of importance is the farming of scallops, oysters and other shell-fish.

However, in the mid-1990s, increasing interest led to the establishment of the Pan American Marine Biotechnology Association PAMBA, based in Framingham Massachusetts, one of the two US-based organisations with a cohesive and networking role in Latin America. The other is The Biotechnology Center of Excellence Corporation BCEC, based in Waltham Massachusetts. BCEC is an important actor in Latin America, through its BioAmericas programme with Chile and project support work in other Latin American countries, and because it provided the first Secretariat of PAMBA.

Given the importance of aquaculture to the region, it is realistic to assume that marine biotechnology will also be of importance, and that the countries involved, with the necessary national resources to develop this will generally follow the ranking for aquaculture – Argentina being an addition to the above list.

Targets might include:

- better detection and prevention of disease, including White Spot and 'Taura' syndromes, in penaeid shrimps and prawns, and for diseases of salmonids;
- bioremediation of the impact of mariculture and aquaculture;

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201 see http://mirror.eschina.bnu.edu.cn/Mirror2/unesco/www.unesco.org/science/life/ bac_programme.html

202 Hernández-Rodríguez A, Alceste-Oliviero C *et al.* (2001) *Aquaculture Development Trends in Latin America and the Caribbean* – a very useful reference from which much of the background information in this section is taken

- evaluation of microalgae and microalgal constituents as feeds and feed ingredients for aquaculture;
- advanced broodstock technology including gene probes for selection and genetic modification for enhancement;
- cultivation of microalgae; and bioactives from marine organisms.

The freshwater sector is perhaps less of a target for biotechnology, since output is often from semi-intensive systems or for sport fishing. Nevertheless, the use of biotechnology in stock improvement of *Tilapia* and in feed enhancement might be an important target. Finally, there will be applications for marine biotechnology and marine-derived outputs in the mollusc sector, for selection and improvement of stock, disease control, feed enhancement and bioremediation.

Bioactives from marine sources has started to be addressed. The Spanish Government department CYTED, Science and Technology for Development, operates the network projects within the Cooperación Iberoamerica programme. The Iberoamerican Network of Search and Development of New Bioactive Substances of Marine Origin (**RIBUSDEMAR**) ran from 1998-2001 under the co-ordination of Dr. Agustín Pérez Aranda, of Instituto Biomar, Leon and Madrid.

TABLE 90: COUNTRIES AND UNIVERSITIES INVOLVED IN THE RIBUSDEMAR IBEROAMERICAN NETWORK ON MARINE BIOACTIVES 1998-2001

ARGENTINA	Grupos de Productos Marinos, Universidad de Buenos Aires
CHILE	Dep.de Química, Universidad de Chile Dep.de Química, Universidad de Lagos Instituto de Química de Recursos Naturales, Universidad de Talca
COLOMBIA	Dep.de Química, Universidad Nacional de Colombia
COSTA RICA	CIPRONA, Universidad de Costa Rica
CUBA	CEBIMAR, Centro de Productos Bioactivos Marinos
DOMINICAN REP	CIBIMA, Facultad de Ciencias, Universidad Autónoma Santo Domingo
	Investigación Farmacológica, Universidad de la Baja California
PANAMÁ	Dep.de Biología Acuática, Universidad de Panamá y Smithsonian T. Research
PANAMÁ	
SPAINo	Dep.de Química Orgánica, Facultad de Química, Universidad de Santiago de Compostela Instituto Biomar S. A Instituto Universitario "Antonio González", Universidad de La Laguna Instituto de Productos Naturales, Consejo Superior de Investigaciones Científicas Dep.de Productos Naturales Marinos, Universidad de Cádiz Dep.de Fisiología Animal, Facultad de Biológicas, Universidad de Sevilla Dep.de Química Orgánica, Facultad de Farmacia, Universidad de Salamanca Dep.de Química Fundamental, Facultad de Ciencias, Universidad de A Coruña Dep.de Química-Física y Orgánica, Facultad de Ciencias, Universidad de Vigo
URUGUAY	Química Farmacéutica, Facultad de Química, Universidad Mayor República Oriental

Marine Bioactives network was a sub-theme within an overall and very large network for investigation of natural substances. This network is interesting because there is a very strong co-operation between different institutes for identifying, characterising and screening bioactives. Samples are assigned to different institutes accompanied by a standardised identification protocol, so that results can be correlated accurately afterwards. In this way, distributed expertise and resources can be efficiently harnessed.

Brazil

The foremost site of research is the Laboratório de Química Bio-Orgânica e de Produtos Naturais do Mar of the Universidade Federal Fluminense in Niterói (Rio de Janeiro). This is intensively involved in isolation and characterisation of marine bioactives, under Professor Alphonse Kelecom. Sources that are studied include benthonic algae and invertebrates (sponges, fan corals, tunicates, anemones and sea cucumbers), as well as those from terrestrial plants. Work also includes derivatisation and development of synthetic and semi-synthetic processes, and structure-activity analyses, and studies of marine chemical ecology. Work has already resulted in isolation of a number of interesting and novel compounds, including fatty acids, lignans, polypeptides, terpenes and dibromotyrosines.

There is research into marine resource management and exploitation at the Instituto Oceanográfico of the Universidade de São Paolo. Work in the Department of Biological Oceanography includes ecology and biodiversity in coastal and EEZ waters and algal aquaculture.

Bioactives from marine and other sources are being used in cancer treatment studies headed up by Fundaçao SOAD para Pesquisa do Câncer in Porto Alegre, by Professor Gilberto Schwartsmann at the Hospital of the Universidade Federal do Rio Grande do Sul.

Caribbean

The emphasis here is on aquaculture of lower-value species – although the Caribbean produces 6% of Latin America's aquaculture output, it is only 2% of overall value[203]. Cuba is the major producer, with 92% of output. Cuba and the Dominican Republic are both involved in the IberoAmerica Network.

Chile

Although the commercial and technological emphasis in Chile is on aquaculture, there is some activity in marine biotechnology. Chile is the second largest producer of cultured salmonids in the world (after Norway), the primary supplier of salmonids to Japan, and the second largest supplier to the United States (after Canada). The value of the salmonid exports is >US$700 million, with Atlantic salmon representing 43% and rainbow trout about 27%.

The University of Antofagasta, Centro de Biotecnología y Biología Molecular (CBBM) has been set up to focus on marine and freshwater microorganisms, fish, shell-fish, aquaculture industrial processes, marine pollution and bioremediation, and especially to aim for practical application of the research findings. A current project concerns the

[203] Hernández-Rodríguez A, Alceste-Oliviero C *et al.* (2001) *Aquaculture Development Trends in Latin America and the Caribbean*

transport of copper in marine micro-organisms isolated from the Pacific Ocean off North Chile and the potential for using them for bioremediation. CBBM's facilities include an analytical laboratory and resources for bioinformatics, microbiology and molecular biology. CBBM is also the recipient of a national grant to use marine biotechnology in marine invertebrate mariculture, including establishment of microbiological protocols for scallop and abalone culture, use of microbes as feed, development of new techniques for disinfecting seawater for hatchery circulation and training programmes for young aquaculturists.[204]

Plancton Andino Ltda, based in Puerto Varas in the X. Region of Chile, was established to provide hydrography services to aquaculture and monitor toxic-bloom microalgae. PAL has a joint venture with the German company Coastal Research and Management, of Kiel, on the EU-supported project "Aquatoxsal" and the Lighthouse-Foundation project on sustainable development off Chile's coast in the Archipelago of Isla Chiloé.

Mexico

Since 1977, the Mexican private sector has sponsored a research project to domesticate and genetically select wild broodstock of *Litopenaeus vannamei* prawn to enhance the shrimp-farming industry.

CICESE at Universidad de Ensenada is the most important centre for marine biotechnology in Mexico. There are three main themes: Environmental Marine Biotechnology, Marine Natural Products and Food and Aquaculture.

TABLE 91: MARINE BIOTECHNOLOGY AND AQUACULTURE ACTIVITIES AT CICESE, ENSENADA MEXICO[205]

THEME	RESEARCH
Environmental Marine Biotechnology	• Biodiversity and Phylogenetics of Marine Microorganisms • Bioremediation of Marine Effluents • Ecotoxicology and Molecular Biomarkers • Infectious diseases from marine organisms and environments • Fermentative processes and biocatalysis of marine resources, metabolites, and fisheries by-products
	• Bioprospection of Bioactive Marine Metabolites - anticancer agents, antibiotics, biotoxins, nutraceuticals • High Throughput Screening in marine organisms • Bioactivity and High Value Chemicals • Metabolic Pathway Engineering • Marine Bioprocess Engineering • Functional Genomics of Marine Natural Resources
	• Functional Foods and Nutrition – nutraceuticals and probiotics • Environmental physiology of aquatic organisms • Endocrinology of Marine organisms • Immunology of Marine organisms • Genetic Engineering of Marine Organisms for bioactives • Functional Genomics in Marine organisms • Fisheries by-products – chemical and food products

[204] source: CBBM's website
[205] source: CICESE web-site

Other Latin American states

Colombia has established a US$5.8 million genetic research programme on Litopenaeus vannamei, partly Government-funded and partly supported by the shrimp-farming industry. The goals are to improve the survival and growth rate in the presence of now-endemic diseases such as Taura syndrome virus by 12 and 15 percent, respectively.

In Ecuador, there is a research programme between the National Chamber of Aquaculture and national research centres to identify the molecular markers for the immunological stages of development in prawn and shrimp, to help establish levels of disease tolerance in specific strains.

In Venezuela, the introduction of disease when penaeids were imported in 1989 resulted in the need for kill-out and re-stocking using indigenous strains. The use of specific breeding programmes and selection has resulted in a virus-resistant *Litopenaeus stylirostris* line, which is the mainstay of the indigenous shrimp-farming sector and has been successfully exported to Mexico, Honduras, Ecuador and Colombia.

Support Organisations

PAMBA is specifically focused on marine biotechnology in the Americas. The main goals are to sponsor exchanges of people, facilitate knowledge transfer, sponsor conferences and workshops, create specialist advanced courses in marine biotechnology, publish proceedings and encourage commercial activities. PAMBA was created in 1999. Although much of its focus is on Central and South America, it includes members from USA and Canada and has an international organising committee with members from Australia, France, Germany, Italy, Japan, Norway and South Africa. The secretariat is based in Framingham, Massachusetts.

The IberoAmerican Network programme operated by CYTED, a branch of CICYT, the Spanish Government's science and technology agency, is also of very great importance in creating cohesion and synergy across Latin America.

AUSTRALIA-PACIFIC

Australia

Outside USA, Europe collectively and Japan, Australia has the biggest marine biotechnology and exploitation activities. In Australia, the main effector of the Oceans Policy in biosciences is the **Australian Institute for Marine Science** (AIMS). The Oceans Policy is explicit that sustainable aquaculture and novel compounds from the sea are 'key generators' of national wealth and social and environmental benefits.

AIMS is a statutory authority established in 1972. Its total budget for 2004-2005 including capital projects and establishment costs is over A$29.3 million **(£11 million**([206]), of which A$22 million (£8.5 million) is provided by Government and A$6.9 million (£2.65 million) is expected to be provided by sale of goods and services.[207] The 2003-2004 budget was A$34.4 million **(£13.3 million**).

[206] At Aus$2.59 = £1.00, exchange rate July 2004

[207] see http://www.dest.gov.au/budget/PBS/2004/pdf/2004-2005_dest_pbs_07_part_c_aims.pdf [April 2004] – AIMS overview, appropriations and budget measures summary

The marine biotechnology group includes three teams, for bioactive molecule discovery, bio-innovation and tropical aquaculture, whose expenditure in 2003-2004 was A$7 million (**£2.67million**).[208] By focusing on specific topics with clear economic targets, the group is enabled to draw in commercial collaboration. The targets include prawn farming, new bioactives for human health, plant health and bioremediation, and platform technologies for environmental monitoring and diagnostics (including shellfish toxin assays).

Focus is clearly an important part of success. AIMS has the advantage that its targets are the use of research to support economic growth and commercial activities; its Mission Statement and Vision are

To generate and transfer theknowledge to support the sustainable use and protection of the marine environment through innovative, world-class scientific and technological research

To lead marine research in ourchosen fields and to deliver greater benefits to Government our partners, our customers, our people and the general public than they can obtain from others

The commitment to transfer of knowledge and delivery of benefits to partners and customers is a prerequisite for the commercially-focused activities undertaken by AIMS. In the UK context, such activities might be more appropriately undertaken by an organisation that is not primarily academic or within an HEI. The European Centre for Marine Biotechnology or an institute comprising the resources of the Plymouth Marine Laboratory, the MBA Plymouth and the University of Southampton might provide the foundation for such a market-driven organisation.

Research activity

AIMS has its headquarters in Townsville Queensland and two other branches at Fremantle Western Australia and Casuarina, Darwin Northern Territory. It is the largest marine biotechnology and sciences establishment in the Pacific region, with about 150 people, two-thirds in research. It has extensive collaborative international liaisons with research organisations and universities (see **Table 83** below).

AIMS strongly promotes its library of more than10,000 marine invertebrate and plant species and 7,000 marine microorganism species, the AIMS Biodiversity Collection. This is made available to pharmaceutical, cosmetics, environmental and contract research companies for R&D and screening programmes. Extracts are being screened for their anti-fungal and anti-infective activities and for potential use in agriculture, as well as human therapeutic potential in other areas. A major achievement was the AIMS-US National Cancer Institute agreement in July 2002, in which extracts from the Biodiversity

[208] see http://www.aims.gov.au/pages/research/research-capability/capability-03.html [June 2004] and related pages summarising activities of the groups at AIMS

Collection are tested in NCI's cancer screen. The results, including any identified anti-cancer compounds, remain AIMS's property for exploitation.

The main marine biotechnology facility at the Townsville site was commissioned in 2001/2002 at a cost of **A$6m**, about half the cost of the total refurbishment programme AIMS has undergone recently. It includes facilities for DNA analysis, microbiology, cell culture, physical and chemical analyses, bioactive isolation and fermentation, with biochemistry, molecular genetics and ecology laboratories nearby. The advanced analytical equipment alone cost A$2.5m and includes an NMR facility. AIMS also runs a number of research vessels, including 24m and 27m floating laboratories and 12m and 7m collection vessels.

The Federal Government is funding a collaboration between AIMS and the Australian National University, the Arafura-Timor Research Facility, part of the remit of which is to improve "the national capacity to describe, benefit from and control the use of Australia's biodiversity resources"[209], especially in the Timor Sea coastal area. AIMS also has a Memorandum of Understanding in place with the US National Ocean and Atmospheric Administration, dating from 2001, for joint work on reef ecology, water quality and climate change.

TABLE 92: AIMS'S INTERNATIONAL PARTNERS IN RESEARCH PROJECTS, INCLUDING INDUSTRY-FUNDED

EUROPE	National Environmental Institute, Denmark IFREMER, France University of Bremen, Germany
ASIA-PACIFIC	Angiogen Pharmaceuticals, Australia Nufarm Australia SunScreen Technologies, Australia ToxiTech, Australia Xiamen University, China University of Guam LIPI, Indonesia Hokkaido Tokai University, Japan KEPCO Japan Osaka City University Medical School, Japan Tokyo University, Japan University of Malaysia University of Canterbury, New Zealand Chulalongkorn University, Thailand
USA	NASA State University of New York Cornell University University of Maine University of South Carolina University of Washington National Cancer Institute Woods Hole Oceanographic Institute

209 *AIMS Research Plan 2003-2006*, Australian Institute for Marine Research p10

Two strategic themes of AIMS's Research Plan are Bio-Innovation and Bioactive Molecule Discovery, feeding into the Federal Government's themes of Frontier Technologies for Building and Transforming Australian Industries and Promoting and Maintaining Good Health. Current-year funding of the Marine Biotechnology Group totals A$6.91 million, split between the Bioactive Molecule Discovery team (c. 25%), Bio-innovation team (c. 30%) and Tropical Aquaculture team (c. 45%). The Marine Bioproducts team works with organisms from the Great Barrier Reef, all of Australia's tropical and temperate waters, and others harvested from New Zealand, Papua New Guinea, Thailand, the Philippines, and Antarctica in international collaborations. Once the bioactives in an organism are isolated, AIMS is able to screen for a wide range of activity, including agrochemicals, neurological mediators, antimicrobials, anticancer, antiviral and immunological agents, as well as technical and industrial potential such as anti-fouling, food-processing and cosmetic ingredients.

A more precise anti-cancer screen is available through the strategic liaison with the US National Cancer Institute. AIMS also provides purification, structural confirmation, and biochemical characterisation. AIMS has also isolated novel DNA-modifying enzymes, proteases, lipases, and chitinases with enhanced activity and stability in extreme conditions, and is investigating the bioremediation capabilities of marine microbes.

Current-period activities of the Bioactive Molecules Team include:

- continuing analysis and screening of marine macro-organisms and micro-organisms for useful compounds for medicine, industry and the environment
- agrochemical sector bioassay development and identification of new pesticides that overcome the problem of resistance
- marine natural products chemistry
- development of environmental and food quality biosensors
- further work on the anti-oxidant properties of marine microbes in the field of anti-ageing and cancer prevention
- development of new aquaculture species that can provide materials for the global biomedicines sector.

Current-period activities of the Bio-innovation team include a responsibility for developing and applying practical and policy-supporting environmental assessment techniques and development of new molecular healthcare approaches based on the adaptive mechanisms of marine organisms. The Bio-Innovation team will also work with the Bioactive Molecules team in developing biosensors for seafood toxins and molecular techniques for the production of bioactives, as well as provide technical assistance to the AIMS spin-out ToxiTech, which provides assay-based services in food and water quality. The molecular techniques for bioactives focus on understanding the relationship between host invertebrates and symbiont microorganisms, to optimise bioactive production.

AIMS scientists have been looking at antioxidants from seaweeds and other marine organisms for over 20 years, including isolation and investigation of chemical synthesis, until 1992 in collaboration with ICI Australia. AIMS has applied for patents and has been exploring applications with the Japanese companies Shiseido and Toyo Suisan Kaisha, and with Pan Australia Labs and the Heart Research Institute of Australia.

These antioxidants belong to the family of mycosporine-like amino-acids (MAAs), similar to those originally found in terrestrial fungal spores. They are found in macroalgae, microalgae and a variety of invertebrate organisms, including crustacea, that live in shallow-water or inter-tidal zones or float freely in the oceans, and act as protectants against UV damage. MAAs are also found in the tissues and eggs of tropical and temperate fishes. *Vibrio harveyi* and *Pseudoalteromonas* spp. found in marine invertebrates metabolise mycosporines and generate more-active molecules such as 4-deoxygadusol in sea urchins, asterina-330 in sea cucumbers and mycosporine-glycine in corals. Toyo Suisan is interested in 4-deoxygadusol as a natural antioxidant for food-processing and cosmetic applications and, because of their potential for anti-inflammatory use and as anti-ageing compounds. AIMS has focused on sun-screen applications of MAAs, as well as testing them in neurodegenerative and cardiovascular diseases.

Other activities within AIMS also have some relevance for marine biotechnology and resource exploitation. The Conservation and Biodiversity Group is focused on tropical biodiversity but is also researching new methods of deeper-water non-destructive sampling methods that might be relevant in UK contexts. New species of marine organisms are processed through the biotechnology group, to identify new bioactives and exploit them where possible.

The Risk and Recovery Group is examining, through general ecology of mixed populations and through a specific focus on corals, the factors responsible for ecological resilience, which may be of interest in the context of exploitation of mixed marine resources. The Coastal Processes Group aims to discriminate between natural adverse impacts on coastal ecosystems and those created by human impact and pollution, to work out how to mitigate human-induced effects. The Tropical Aquaculture Group is investigating ways of culturing sponges for the extraction of bioactives and biomaterials.

AIMS has recently appointed a Commercialisation Officer to capitalise on the change in rules concerning technology transfer from federal research agencies.

An interesting activity is a joint exploratory project with the University of Canterbury New Zealand on marine sponges of Antarctic waters. AIMS has so far isolated several hundred novel symbiotic organisms and a number of bioactives from 5 species of sponge. AIMS is also working with Nufarm Australia Ltd on selective herbicides from marine sources and with Sunscreen Technologies Pty on a bioactive from coral. Other contacts and potential collaborations are with Faustus Forschungs Compagnie (a Leipzig, Germany-based drug discovery and development company), PharmaMar (Spain), Diversa and Cerylid.

In other areas, AIMS has spun out and 50%-owns ToxiTech Pty Ltd, a vehicle for saxitoxin detection technology. Angiogen Pharmaceuticals Pty Ltd, a recent start-up in Australia, is looking to fight cancer, multiple sclerosis and CNS disorders by attacking angiogenesis. AIMS has licensed its underwater computing technology to WetPC Pty Ltd. It is also working with three international groups, Westernhigh Pty Ltd, Greenfields Resources Holdings (a Japanese company) and Pennington Seeds Inc on an economic development project in China, for agricultural water remediation.

The CSIRO, the federal government's research organisation, operates a Microalgae Research Centre (CMARC) in Hobart, Tasmania. CMARC maintains the CSIRO Collection of Living Microalgae and supplies microalgae for research and as aquaculture larval feeds in Australia and Asia-Pacific. The culture collection contains over 750 strains, including representatives from all classes of marine microalgae, some freshwater microalgae, and unusual marine fungi. CMARC researches new microalgae and nutritional ingredients, including reference cultures for pigment standards, PUFAs and other novel fatty acids and lipids. CMARC is collaborating with the University of Florence on bioreactor technology for economic land-based culture of marine microalgae.

Macquarie University in New South Wales has a strong interest in marine natural products, their biological activity, ecological roles, biosynthesis and their modes of action as drugs. They are using phage display technology to directly couple biologically active natural products to the gene of their cellular target, identifying the target of marine extracts and defining their actions at an early stage.

A two-week intensive programme in Marine Biotechnology is taught jointly by the University of Sydney, the University of Queensland, James Cook University and the Australian Museum, and uses the Heron Island Tropical Research Station in the Great Barrier Reef as its base. It is part of the National Degree in Marine Science. Aspects covered include abilities of corals and other reef life to protect themselves against sunlight and repel other organisms, and molecular and genetic techniques to separate and identify useful proteins. There is a stated aim to develop skills for identifying biological molecules from marine sources with potential commercial application.

Corporate activity

Amrad Corporation, based in Richmond Victoria, has supported a collaborative programme at the University of Queensland on cone snail toxins, resulting in an analogue of zicotinide, AM336, for control of severe pain. Although it has to be given by direct intrathecal injection into the brain, it does not stimulate tolerance and has good efficacy in morphine-tolerant patients. After a financial crisis and refocusing in 2003, Amrad is now seeking to licence out AM336.

Cerylid Biosciences Ltd is a Victoria-based company that has focused on building a library of over 600,000 natural product extracts and working in-house or with partners using high-throughput screens to establish therapeutic uses. Cerylid claims its library is one of the world's most extensive collections of natural chemical diversity; though mainly focused on extracts from Australian plants, marine organisms and microbes (80%), it includes contributions from Asia (12%) and marine samples from Antarctica (8%). Cerylid was founded in January 2000 by an investment consortium led by Rothschild Bioscience Managers (now The Australian Bioscience Trust). So far, it has raised A$23m, and current investors include JAFCO Investment (Asia Pacific) Ltd, Amrad Corporation Ltd, Development Australia Fund and The Australian Bioscience Trust. AIMS has supplied samples from the AIMS Biodiversity Collection to Cerylid for evaluation.

One other area in which Australia, like Hawai'i, has excelled is in the production of carotenoids from marine algae. *Dunaliella salina* grows very well in open culture in Australia, making it relatively inexpensive to produce microalgal carotenoids. Major companies in Australia include Cognis Australia Pty Ltd, owned until 2001 by Henkel KgaA of Düsseldorf, which had acquired the Betatene company in 1995 and Western Biotechnology in 1997. In 2001, Henkel sold the entire Cognis business, including the Health and Nutrition section, to a consortium of funds advised by Permira (formerly known as Schroder Ventures Europe), GS Capital Partners (the private equity arm of Goldman Sachs) and Schroder Ventures Life Sciences, for about € 3.0 billion, close to its annual turnover. The Australian company now reports to the Roermond, Netherlands, based Cognis BV. Another company selling microalgal carotenoids is the Western Australia-based independent, AquaCarotene Ltd, which grows *Dunaliella* in Karratha and extracts and packs in Perth.

New Zealand

The most active centre for marine biotechnology in New Zealand is the University of Canterbury's Marine Chemistry group. Discoveries include cytotoxic bioactives from sponges, including variolin B from the Antarctic *Kirkpatrickia varialosa*, pateamine from a New Zealand *Mycale*, isohomohalichondrin B, an antitumour polyether macrolide, from the New Zealand deep-water sponge *Lissodendoryx* and the mycalamides, antiviral and cytotoxic agents from *Stylinos* spp. Screening work on novel bioactives is carried out in the Green Products & Processes group, funded by the Spanish companies PharmaMar and Instituto BioMar for medical targets.

The Marine Chemistry group[210] has been working on marine bioactives for 30 years, accumulating over 5000 samples. 17 of the marine compounds found by the university's chemistry lab have been patented, at a cost of US$50,000 each, for their anticancer properties. Variolin and isohomohalichondrin B are now in pre-clinical development with PharmaMar, with whom the lab began working in the late 1980s. The agreement with Instituto BioMar is more recent. Variolin, a potent apoptosis (cell death)-inducing agent originally isolated in 1993 from an Antarctic sponge collected from under the ice near Scott Base, looks particularly promising. Isohomohalichondrin B was found in a yellow sponge found 100m underwater on the sea floor off Kaikoura, New Zealand. Both compounds are now made synthetically. The group is also conducting separation and production of optically pure compounds for the pharmaceutical and fine chemical industries using marine fungal enzymes. The group collaborates with the US National Cancer Institute, the Danish Technical University, the London School of Pharmacy, the Centre for Polymer Therapeutics Cardiff and, locally, with Canterbury Health Laboratories and Canterbury Development Corporation in the BioCaNZ project, specifically on natural products.

Battershill, at the National Institute of Water & Atmospheric Research of New Zealand (NIWA) in Wellington, has devised methods of growing the deepwater sponge *Lissodendoryx* in shallower water in order to harvest and extract anti-cancer halichondrins from the sponge. NIWA is farming *Mycale hentscheli* in pilot aquaculture units, to produce viable quantities of anti-cancer agents including mycalamides, pateamine and peloruside. NIWA also maintains a culture collection of marine organisms within its Marine Biotechnology Programme, which it tests for actives.

Industrial Research Ltd, ex-government research institute, is involved in screening marine organisms and plants as well as terrestrial plants and food processing waste streams for useful bioactives and materials for functional foods.

New Zealand has one of the largest underwater geothermal systems in the world. The Institute of Geological and Nuclear Sciences (IGNS), based in Wellington, carries out

[210] see *Sea Sickness Pills*, Lynette Hartley 2.6.2003 http://www.unlimited.co.nz/unlimited.nsf and *Bioprospecting in New Zealand, discussing the options*, Ministry of Economic Development November 2002 p9

marine exploration. IGNS has a research collaboration with the University of Hawai'i and Victoria University in Wellington and there has been an exchange of top posts between the three institutions, with the director of Hawai'i Undersea Research Laboratory (HURL) becoming chief executive of IGNS and the new University of Hawai'i at Manoa chancellor coming from IGNS. One aim of the collaboration is to use HURL's two submersibles and mother research ship for deepwater investigations round New Zealand, to collect marine micro-organisms from thermal vents.

The Philippines

These islands have a well-established seaweed industry, exporting raw materials and processed ingredients such as agar and carrageenans.

The University of the Philippines, Diliman, has a Marine Science Institute; researchers here work on new products from seaweed for the higher-value food ingredients sectors, including sucrose-reactive agars for confectionery and high-sulphated and high-methylated agars for increased lipophilicity. One of the foremost researchers on conopeptides and neurotoxins from marine molluscs also works here, Dr Lourdes Cruz; she is also researching anti-TB bioactives and added-value biochemicals from Spirulina.

GeneSeas Asia Inc is a collaboration between researchers at the University of Utah and at the University of the Philippines, including Lourdes Cruz, led by Gisela Concepcion. GeneSeas works on bioactives from extracts of marine organisms collected around the Philippine Islands. The company has over 1000 organisms in its collection and has isolated a number of antibacterial, antifungal and cytotoxic compounds including adociaquinone B from *Xestospongia*, bistratamide D from *Lissoclinum bistyratum*, makaluvamine N from *Zyzzya fuliginosa* and tubericidins from *Didemnum voeltzkowi*.

Other oceanic islands

Researchers at the University of Guam were responsible for isolating and characterising the bioactive manoalide. The University is also involved in the US Microbial Observatories project. and in the Fenical-AgraQuest project on bioactives from marine actinomycetes as agrochemicals. Aims is also a collaborator on testing new bioactives.

The Marine Studies Programme at the University of the South Pacific, Republic of Fiji focuses on bioactives from novel Pacific organisms. Earlier discoveries in the region include jaspamide and the bengamides, isolated from *Jaspis* sponges by Philip Crews of the University of California Santa Cruz. Jaspamide is a cyclodepsipeptide, with antifungal, anthelmintic, insecticidal, and ichthyotoxic activity and the bengamides are anti-cancer agents which, as a synthetic analogue, is in clinical development by Novartis for the treatment of breast cancer. The USP aims to develop indigenous capacity to gain benefit from such discoveries. There are international research links to aid identification and characterisation, but USP is also building cancer-screening capacity as well as developing a chitinase inhibitor assay to study anti-fouling chemicals. The Marine Studies Programme also researches marine algae in Fiji, Samoa and French Polynesia, with molecular studies on specific families of red algae. There is also research on bioactive compound derivatives from marine algae, and aquaculture for human consumption and commercial harvesting for export.

EAST AND SOUTH-EAST ASIA

Japan

The Japanese government is aiming to create a 25 trillion ¥ (approx. € 325 billion) market for new biotechnology products by 2010:

TABLE 93: BIOTECHNOLOGY STRATEGY IN JAPAN[211]

SECTOR	TARGET TRILLION ¥
medical care	8.4
foods	6.3
tools and IT	5.3
environment and energy	4.2
miscellaneous other	0.8

The degree of expenditure on Japan's marine research and infrastructure is considerable, estimated at over £600 million. The Marine Science and Technology Center and the Marine Biotechnology Institute are the most important drivers of marine biotechnology and related bioengineering and oceanic engineering in Japan, with individual centres of activity in universities in Tokyo, Hokkaido, Kitasato, Fukuyama and Saga.

The **Marine Science and Technology Center** JAMSTEC was founded in 1971 and was renamed the Japan Agency for Marine-Earth Science and Technology in April 2004 after amalgamation with geological and earthquake sciences. Its marine activities are physical sciences and engineering, and it is responsible for the design and building of Japan's submersibles and hyperbaric research facilities. Its budget was approx. £215 million in 2001 and **£190 million** in 2002, the difference due to exchange rate movements.[212]

The **Marine Biotechnology Institute** MBI was established in 1988 and is an early example of public-private partnership, with a total investment of about **£123 million** (approx ¥28 billion), 50% from 24 companies and banks, the remainder from MITI, for the period 1988-1998. The MBI also received a significant share of MITI's 1988-1996 programme 'Fine Chemicals from Marine Organisms', with funding of almost **£27 million** over the three years 1993-1995, for example.

[211] source: *Invest in Japan Special Edition* Vol 2.2003, JETRO

[212] 1988: ¥228 = £1.00; 2000: ¥163 = £1.00; 2001: ¥175 = £1.00; 2002: ¥188 - £1.00

The shareholders of the MBI include:

Asahi Glass Company	Kajima Corp.	Nippon Suisan Kaisha
Ebara Corp.	JFE Steel Corp.	Sekisui Chemical Company
Fujitsu Ltd.	Kirin Brewery Company	Shimizu Corp.
Hazama Corp.	Kyowa Hakko Kogyo Company	Shiseido Company
Hitachi Zosen Corp.	Japan Energy Corp.	Suntory Ltd.
Idemitsu Kosan Company	Nichirei Corp.	Taisei Corp.
Ihara Chemical Industry Company	Nippon Steel Corp.	Tonen General Sekiyu K.K.
Kansai Paint Company		Tosoh Corp

MBI operates two research stations, at Kamaishi and Shimizu, comprising the Research Centre for Industrial Utilisation of Marine Organisms. These cost approx. **£24 million** to build and equip. The Center has over 75 researchers, plus visiting people. MBI's work is in four main areas:

- management and exploitation of the MBI Culture Collection, MBIC, with over 20,000 strains, including 1000 microalgae, and a database for classification of bacteria based on DNA gyrase B subunit B probes
- applied bio-organic chemistry, isolating and characterising anti-foulant molecules such as tribromomethylgramine, bioactives effective against red tide dinoflagellates, antibacterials and metal chelating compounds; there is also work on cultivating hard-to-isolate microbes
- applied molecular design, isolating genes from marine organisms and expressing them in *Escherichia coli* and plants, harvesting marine microbial secondary metabolites such as enzymes, and working on directed evolutionary engineering
- applied microbiology, focusing on culture techniques and application of marine microbes for environmental remediation, including the use of microbial communities for methane generation
- applied microalgal biology, specifically linking hydrocarbon production and carbon dioxide fixation by cloning and transferring genes from microalgae such as *Botryococcus braunii* and *Chlorococcum littorale*; cell-to-cell signalling is also studied.

MBI also manages the Japanese marine microorganism culture collection and owns a research vessel, the *Sohgen-Maru*, which is used mainly for exploration in sub-littoral zones around Japan and in the Pacific Ocean islands such as Yap, Pohnpei and the Republic of Palau.

The MBI's Culture Collection (MBIC)[213] contains over 30,000 microbial strains, of which over 750 bacterial and 300 microalgal strains are characterised and available via online catalogue. The MBI uses gene and genome analysis to catalogue these, including the pattern of small subunit rDNA sequences and/or type II topoisomerase gene (gyrB) sequences. MBIC distributes live stocks in its catalogue upon request. MBIC has worked on ways to make marine micro-organisms more available for exploitation, and has

[213] contact mbic@mbio.co.jp for further information

developed methods for better isolation of marine micro-organisms, the estimation of microbial diversity, and new culture methods for different marine environments. MBI provides the strains for research purposes only, under Materials Use Agreements (MUA) that establish the rights and obligations of the users. Because of the Convention on Biological Diversity, in some cases an authorisation is needed from relevant governments before supplying strains. MBI can obtain this on behalf of the researcher who wants to use one of these 'Special permission required' strains.

The MBI's Kamaishi laboratory is on the warm-water side of Japan. There is an agreement in place with Kitasato University for extension research at MBI. The building is owned by the Research Center for the Industrial Utilization of Marine Organisms. Research groups are staffed by a mixture of MBI scientists, postdoctoral fellows and researchers from member companies. The research teams are working on environmental as well as marine topics, including biological carbon dioxide fixation by marine organisms, the impact of trichloroethylene, the biological degradation of oil and a project on Integrated Biological Systems. The involvement of an industrial consortium and METI (trade and industry rather than education and science) means that all the research projects have applied goals. However, fundamental research is not ignored, and includes molecular evolution studies, molecular classification, and a combined molecular genetics and structural biology approach to create artificial enzymes.

In 1990, the Japan Marine Sciences and Technology Center, JAMSTEC, was established for a specific deep-water programme, DEEP-STAR, to include marine biology, marine ecology, and engineering of extremophilic bioreactors. JAMSTEC has built or adapted a number of deep ocean submersibles for exploration and recovery, including the *Shinkai 2000* and the *Shinkai 6500*.

The Tokyo University of Agriculture & Technology Department of Biotechnology has activity in marine biotechnology headed up by Dr. Haruko Takeyama, chair of the IMBC's 2005 International Program Committee.

The Kitasato Institute, Tokyo, has a continuing programme of research into natural bioactives, including marine-origin. The Institute also has a long-standing collaboration with Professor A Smith of the University of Pennsylvania.

There is a Cooperative International Research Project on Marine and Coastal Environment, which involves institutes in Japan including the Department of Fisheries Science at the University of Kitasato, Iwate.

Saga University is also active in investigating novel bioactives from marine organisms, under the leadership of Yuto Kamei[214], see table below.

[214] *Seaweed essence fights type-A flu virus better*, Kyodo News October 22, 2003, and web-site search on 'Yuto Kamei'

TABLE 94: NOVEL BIOACTIVES PRODUCED AT SAGA UNIVERSITY, JAPAN

extract of a *Rhodophyceae* (red seaweed)	activity against influenzavirus
MC21-T, active against methicillin-resistant *Staphylococcus aureus*	a new species of *Pseudoalteromonas* bacterium
protease inhibitors	
bioactives with anti-cancer activity	seaweeds (47 of 336 indigenous species) including green *Cladophoropsis vaucheriaeformis* and *Halimeda discoidea*, red *Laurencia okamurae* and brown *Dictyopteris undulata*
anti-leukaemic palmitic acid	red seaweed *Amphiroa zonata*
antifungal proteins	*Streptomyces* spp.
novel anti-fungal chitinase A	pseudomonad bacterium

The Department of Marine Biotechnology, Faculty of Life Science and Biotechnology at Fukuyama University is also active in education, mainly in fish, offering courses in gene technology, genetics and breeding, aquacultural engineering, defences against fish disease and environmental microbiology for bioremediation. Fukuyama University has an exchange agreement with the University of Queensland, Australia.

Current research activities at the University of Hokkaido's Division of Marine Biosciences include

- cDNA cloning and structural analysis
- protein engineering of muscle proteins and enzymes of marine animals
- exploring useful enzyme inhibitors from marine bioresources
- bioconversion of marine oils to value added products
- microbiology of marine products
- viral and bacterial fish diseases and taxonomy, and ecology and biotechnology of marine microorganisms.

The University operates marine biological stations in Akeshi, Oshoro and Usujiri and a field centre for the Institute of Algological Research in Muroran. The University's Graduate School of Fisheries is based in Hakodate.

The Biotechnology Center of Excellence Corporation USA has a technology assistance agreement with the Northern Regions Center in Hokkaido.

Corporate R&D

Given the strong support of marine biotechnology and bioprocessing over the years in Japan, estimated at over £600 million from the Government and its partners, it would not be surprising if the sector makes a small but significant contribution to achieving this. However, it is rather more difficult to see what products have reached the market as a result of this investment, with the exception of advanced deep-water submersible and remote control vehicles. There are a few bioactives in development, including KRN7000, a synthetic version of agelasphin from *Agelas mauritianus*, with **Kirin Brewery** for cancer treatment, GTS-21, a synthetic analogue of anabaseine from the nereid *Amphiporus lactifloreus*, with **Taisho** for CNS diseases such as Alzheimer's, and UCN-

01, a synthetic derivative of staurosporine, with **Kitasato Institute** as an anti-fungal and anti-hypertensive.

TaKaRa Bio appears to be active in researching marine organisms for bioactives and novel enzymes. The company has investigated fucoidans and fucoidan-hydrolysing enzymes, to find novel bioactives and enzymes from *Pyrococcus furiosus*, a thermophile from hot-vent sediments. Takara Shuzo, the parent company, announced it would spend ¥6 billion in 2000 on a new facility at Dragon Genomics Center, its subsidiary; of this, 20% (approx **£7 million**) would be devoted to marine genomics and the search for useful genes and products.

Fujisawa Pharmaceutical Co. has isolated an anti-cancer agent from *Chromobacterium violaceum*, a depsipeptide, which is now in Phase I and early Phase II studies.

Shiseido and **Toyo Suisan** are reported to be working with Australia's AIMS on anti-oxidants from marine sources.

The Naito Foundation[215] is a privately-funded organisation that has supported symposia and conferences on marine biosciences and biotechnology. It was established in 1969 with personal funding to mark the 80th birthday of Toyoji Naito, President of EISAI Co Ltd. It encourages fundamental research in the natural sciences related to the prevention and treatment of human diseases. Activities notably include presentation of awards for outstanding research achievements, support for research, including inter-institute and foreign exchange, and sponsoring symposia. The 9th conference on bioactive natural products in 1997 focused on bioactives from marine sources, including micro-organisms, symbionts, sponges, mollusca and others, with sessions on characterisation and biochemical effects, as well as food toxins and ecochemistry.

The Japan Society for the Promotion of Science, JSPS, a government agency, supports a multidisciplinary and international programme on Biodiversity Studies in the Coastal Waters of the East and Southeast Asia, "BIODIVERSITY". Within this is the multicentre project 'Exploitation and Application of Novel Functions of Microbial Resources in the Tropics' led by Professor Tadayuki Imanaka of Osaka and Kyoto Universities and co-ordinated by the International Center for Biotechnology at Osaka University and Institute of BioSciences, Universiti Putra Malaysia. There are 26 projects overall, with partners from Japan, Malaysia, Indonesia, the Philippines, Thailand and Vietnam. The projects can be grouped into three areas as shown in **Table 86** below.

[215] see http://www.naito-f.or.jp

TABLE 95: PROJECTS IN THE JSPS-SUPPORTED MICROBIAL RESOURCES REGIONAL PROGRAMME

PROJECTS	ORGANISATIONS
Useful metabolites from microbes	
General screening and application of marine microbes including extremophiles	Hokkaido University & Kyoto University, Japan, Universiti Sains Malaysia & Universiti Malaysia
Production of polyalkenoates from palm oil using microbes	Universiti Putra Malaysia
Organic acid and oligosaccharide producing endophytes	Chiang Mai University, Thailand
Thermostable enzymes	RDCBt, LIPI, Indonesia, Osaka University, Japan, Mahidol University, Thailand
Biosurfactants	Chulalongkorn University & TISTR, Thailand
Research into CO_2- and N_2-fixation	
CO_2-fixing microbes and thermophilic micro-algae	University, Thailand
bacteria, microbial ecosystem analysis, breeding and biomass production	UPD & UPLB, Philippine, Osaka University, Japan, Suranaree University, Thailand, RDCBt, LIPI, Indonesia,
Commercialisation of mixed inoculum for crop enhancement	Universiti Putra Malaysia
Bioremediation	
Survey, molecular cloning and exploitation of halophiles and other microbes for degradation of chitin and petroleum oil	University, Thailand, UPLB, Philippines, Universiti Putra Malaysia

South Korea

MOMAF, the Ministry of Maritime Affairs and Fisheries,[216] is responsible for policy concerning exploitation of South Korea's marine resources. Earlier this year, it was reported that MOMAF is planning to subsidise 20-30 new start-ups and young marine-based firms each year, as part of its Ocean Korea 21 plan.[217] This also envisages establishing 10 incubator laboratories, one per region. For marine biotechnology, the focus is on new materials from marine organisms for pharmaceuticals to treat cancer, diabetes and other diseases, as well as development of biodegradable and environmentally-friendly pesticides and cosmetics. The use of genomics and diversity in marine aquaculture will also be supported, in order to develop new ecosystems in marine farming.

SK Chemicals Co., Ltd, a leading chemical fibres firm established in 1969, is diversifying and its Life Science Institute is looking at marine and other natural-source bioactives as pharmaceuticals. The Institute recently completed a large-scale screening programme of 286 marine microalgae and hundreds of fungi for lead bioactives, identifying new potent enzyme inhibitors and anticancer agents in cyanobacteria. Isolates included forms of aeruginosin, agardhipeptin, oscillopeptin, anabaenopeptin, circinamide and microviridin.

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[216] http://www.momaf.go.kr/eng/main/main.asp

[217] http://www.momaf.go.kr/eng/policy/ocean/b_ocean.asp

In 2002, the Ministry of Commerce, Industry and Energy founded the Gangneung Development Institute for Marine Bioindustry, on the north-east coast of South Korea. The Institute provides business development, joint R&D and technology transfer, training and information exchange and other sector-development services. Companies currently occupying the post-incubator facility produce functional food additives and materials from sea squirt (dietary fibre and colourants), squid cartilage (chitooligosaccharides and chondroitin sulphate), alaskan pollock, shellfish, seafood wastes, seaweeds (polysaccharides), shells and starfish (calcium products). The Institute is one of a number of marine-focused initiatives in the Gangwon area centring on Gangneung, in which Won 16.8 billion (about £80 million) has been invested.

Thailand

Thailand is a world-leader in shrimp biotechnology, for breeding and disease resistance.

The Marine Biotechnology Research Unit (MBRU) is part of the National Center for Genetic Engineering and Biotechnology. It was set up at Chulalongkorn University in 1987 as a consortium between researchers at the National Center, Chulalongkorn University and Srinakharinwirot University. The research fields include marine biotechnology in aquaculture and utilisation of marine organisms and their products. Research facilities at MBRU consist of indoor experimental ponds and aquariums, laboratories for food analysis, molecular biology, microbiology, algal research and analytical chemistry and equipment to produce aquaculture feeds.

Taiwan

The Taiwan Fisheries Research Institute (TFRI) is based in Keelung in northern Taiwan, with five research and application divisions, Marine Fisheries, Aquaculture, Marine Food Technology, Biotechnology and Planning and information. TFRI operates research centres and laboratories in Marine Aquaculture and Marine Biology at Taitung. Penghu and Tungkang. TFRI has six research vessels. Although the main focus of TFRI is on fisheries and aquaculture, it aims to develop applications of biotechnology in this sector.

The Development Center for Biotechnology, based in Taipei, is publicly-funded and carries out a range of biotechnology projects, including recycling of industrial carbon dioxide for the production of docosahexaenoic acid using microalgae.

The National Taiwan Ocean University in Keelung has institutes of Marine Biology and Bioscience and Biotechnology. The Graduate Institute of Marine Biology works on taxonomy and ecology of phytoplankton and zooplankton, benthic marine algae, various groups of invertebrates and fish. The Institute of Bioscience and Biotechnology (IBB) works in a number of relevant areas, including anti-oxidant enzymes, DNA damage-binding proteins, biomolecular engineering of bioactives and lipases for industrial and healthcare use, algae for extraction and stabilisation of metals.

There is a tantalising reference to the E-land Marine Biotechnology Science Park, in I-Lan province, in an on-line regional investment prospectus – address 451, Ho-Ping Road, T: 886-3-9364567, F: 886-3-9354632, with a projected income possibility of T$4 billion (US$1.3 billion), profit margin around 20□-40□ and web co-ordinates http://www.e-land.gov.tw, but no further details accessible at this time.

In 2002, a health supplement company Lytone Enterprise launched a new use for their food ingredient, 'Marine Active', based on dipeptides and proteins derived from deep ocean fish, to treat gout by reducing uric acid levels in blood. The product had been developed for sports support, as a buffer against lactic acid accumulation in muscle. Lytone estimated that the product would enter a world-wide gout treatment market worth over US$2 billion each year. Marine collagen, peptide and amino-acid digests and other added-value products from marine wastes are sold to the food and feed industries. Lytone also markets a chitin-chitosan product ChitoClear® for use in agriculture, to mix with spray pesticides or liquid fertilisers at point of use to form a slow release medium, for reduction in amount needed with increase in efficacy.

Singapore

The Institute of Molecular and Cell Biology at the University of Singapore, set up by Leslie Barnett of Sydney Brenner's team, has been responsible for the Fugu Genome Project[218] since it was set up by Sydney Brenner in 1989. This is an international collaboration with the US Department of Energy Joint Genome Institute at Walnut Creek, the UK Human Genome Mapping Project at Hinxton, the Molecular Science Institute of University of California Berkeley and the Institute for Systems Biology Seattle.

The importance of the genome of the fugu (Japanese pufferfish, *Fugu rubripes*), is that it contains only 390 Mb, eight times smaller than the 3000 Mb human genome, but has about the same number and type of functional genes, in a highly-conserved gene-order. The intergenic regions and introns in the Fugu are highly compressed and have very few repetitive sequences, which accounts for the parsimony.

MAINLAND ASIA

India

In India, the Ministry of Science and Technology's Department of Biotechnology (DBT), has a specific programme on Aquaculture & Marine Biotechnology. This is overseen by an advisory task force with members from the Indian Institute of Chemical Biology, Sambalpur University, the Central Institute of Fisheries Education, the National Institute of Oceanography Goa, the College of Fisheries Mangalore, the Centre for Cellular & Molecular Biology Hyderabad, Cochin University of Science and Technology, IARI Delhi, National Centre for Cell Science Pune and the Department of Zoology Delhi University.

Since the start of the first national biotechnology programme in 1986, state programmes have been started with Gujarat, Rajasthan, Madhya Pradesh, Orissa, West Bengal, Haryana, Punjab, Jammu & Kashmir, Mizoram, Andhra Pradesh and Uttar Pradesh and Biotechnology Application Centres have been established in Madhya Pradesh and West Bengal.

In aquaculture and marine biotechnology, relevant activities include development of recombinant diagnostics and vaccines for fish, genomics & proteomics studies in marine organisms and aquaculture species, bioactive molecules from marine organisms for therapeutic and industrial applications; *in vitro* tissue culture, cell culture system development in various aquaculture species; bioconversion and post harvest aspects in aquaculture waste treatment. Progress so far includes some disease diagnostics and vaccine development for whitespot syndrome virus and Monodon baculovirus in prawns, an rDNA vaccine for *Aeromonas* disease in fish, bio-active compounds including a whole

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218 see http://www.fugu-sg.org/

cell and lipopolysaccharide Vibrio immunostimulant for prawns, a new alkaline protease from deepsea sedimentary fungi for industrial use, and transgenics. New methods for farming seaweeds, including *Eucheuma* and *Gelidiella* have been developed, with high-quality kappa-carrageenan and more efficient bacteriological agar production as a result. For the 10th Research and Development Plan, there will be more emphasis on marine extremophiles and bioactives and other materials from marine organisms.

Annamalai University, Parangipettai in Tamil Nadu, has established the Centre of Advanced Study in Marine Biology, and created a number of postgraduate courses and diplomas in aspects of aquaculture and mariculture, including a 2-year MSc in Marine Biotechnology, sponsored by the Indian Government's Department of Biotechnology in New Delhi. Coastal and oceanic biodiversity is a strong theme, including the ecology, biology and biotechnology of mangroves, the culture of seaweeds, marine algal research and pharmacology and marine tissue culture. There is also an interest in bioinformatics, microbial evolution and halophiles and other extremophiles.

The state of Tamil Nadu has also decided to invest in a marine biotechnology park as a strategic development, given the extent of coastline the state possesses.

Specific Marine Biotechnology MSc courses are also offered by Andhra University in Visakhapatnam, Andhra Pradesh and Goa University, Goa

China

The Ocean University of Qingdao is China's foremost marine bio[techno]logy establishment, and has hosted several important international and regional conferences, as well as being the site of the UNESCO BETCEN in Marine Biotechnology for Asia. Work is on-going on development and production of marine-origin drugs, biomaterials and fine chemicals. Several marine-origin health supplements have been developed at Ocean University, including Hailikiang, containing ß-carotene, phycocyanin and marine algal polysaccharides, for immune maintenance and lipid-lowering, Haifujian, a combination of chitosan polymers and algal polysaccharides, based on sea cucumber and algae, for immunoregulation and tumour inhibition, and Haifukang Healing Derma for skin repair. In the Special Territory of Hong Kong, activities centre on the Chinese University of Hong Kong, in the Department of Biochemistry, and focus on bioactives from marine organisms.

Iran

The Biotechnology Institute of the Iranian Research Organization for Science and Technology (IROST)[219] is based in Tehran. There are five research departments including Bioprocess and Engineering in Biotechnology, Environmental Biotechnology, Food Biotechnology, and Medical Biotechnology. The Institute operates the Persian Gulf Marine Biotechnology Research Center on Queshm Island.

The Institute manages the Persian Type Culture Collection of Industrial and Infectious Microorganisms[220]. Work in the Bioprocess department includes deriving single cell proteins from citrus peel pigments and pectins as well as algae fermented by halophyte microorganisms. Environmental Biotechnology works on biodegradation of pollutants

[219] see http://biotech.irost.net/

[220] see http://database.irost.net/

such as crude oil, high-sulphur fuels coals and textile manufacturing waste water. In Food Biotechnology, one focus is new enzymes for the starch processing, fruit juice, sugar and dairy industries. Medical Biotechnology activities are mainly focused on terrestrial pest control using insecticidal microbes such as *Bacillus thuringiensis* and *B. sphaericus* and on fermentation production of antibiotics.

The Persian Gulf Marine Biotechnology Research Center provides training, research, and production facilities for the:

- Establishment of marine microorganisms and algal culture collection
- Production of implants for bone transplant using corals
- Production of anti-cancer drugs
- Polysaccharide production (agar and alginate)
- Breeding and production of pearl oysters (in conjunction with UNESCO) with the aim of creating a sustainable pearl industry
- Large scale production of SCP and biofertilizer from macroalgae
- Production of beta-carotene from *Dunaliella salina*
- Production of microalgae for aquaculture feed

The Darvag Manufacturing and Industrial Company of Amol, which is a major meat, protein and fish processing company, plans to produce high-value enzyme-processed materials for cosmetics and health use from shrimp waste and fish scales.

AFRICA

East and South Africa

BIO-EARN is the East African Regional Programme and Research Network for Biotechnology, Biosafety and Biotechnology Policy Development[221], established in 1999 by the Department for Research Co-operation of the Swedish International Development Cooperation Agency (Sida). The Network and its projects are given full support by governments of the member countries, Ethiopia, Kenya, Tanzania and Uganda, with assistance from institutions and organisations within Sweden and other European countries, such as Svalöf Weibull AB, Lund University, the University of Agricultural Science Uppsala, Plant Research International, Wageningen and ISNAR The Hague, who take students for training as part of knowledge and technology transfer. Most of the projects are land-based, but there is work underway at the Departments of Botany and Biochemistry of the University of Nairobi, Kenya on the use of extremophiles in bioremediation.

The Department of Botany's project is investigating and establishing organisms from hot springs and soda lakes in the Kenyan Rift valley for bioremediation of easily degradable as well as recalcitrant pollutants, setting up a bioremediation process based on biofilm reactors with monocultures or mixed flora. The Department of Biochemistry's project has isolated and characterised new robust biocatalysts, especially extracellular hydrolases, from the same extreme environments, and will also characterise and set up a collection

[221] see http://www.bio-earn.org/index.html

of extremophile microbes. The host institute for both projects is Lund University, Sweden.

A marine biotechnology programme has recently begun at Rhodes University in Grahamstown, South Africa, in the Pharmaceutical Chemistry lab of D R Beukes. The focus is on isolation and characterisation of bioactives from marine algae, sponges and ascidians collected off the South African coast, culture and isolation of microbial isolates, and synthetic studies on promising bioactives.

POLAR REGIONS

Arctic

There are projects specifically investigating boreal marine organisms, including BOSMAN II, funded by the Federal Ministry of Science, Germany. The EU's most northerly marine station is on the coast of Svalbard, administered by Sweden.

Antarctic

The Antarctic has been the site of a great deal of bioprospecting, not only by countries such as Australia and New Zealand but also by UK and Spanish researchers. There is currently considerable concern that, without a specific code in place for exploitation of Antarctic organisms, the Antarctic environment will be despoiled by bioprospectors. Some exploitation is already taking place as a result of discoveries of unique organisms and bioactives - the source of 12% of the Australian company Cerylid Biosciences' marine organism library is the Antarctic, for example. In the mid-late 1990s, AMRAD Corporation of Melbourne Australia had an agreement with the Antarctic Cooperative Research Centre, Tasmanian, to screen about 1,000 micro-organisms or extracts a year for potential therapeutic use.

A US-European consortium MICROMAT has been involved in bioprospecting in Antarctica, partners given in **Table 87** below. It is noticeable that the commercial partners are US-based and the academic, European. The UK involvement in this is based at the University of Nottingham. It is the activities of this consortium that have stimulated the concern of the United Nations University social-issues researchers who have recently published a report on bioprospecting and patenting of Antarctic marine life[222].

[222] The International Regime for Bioprospecting, Existing Policies and Emerging Issues for Antarctica UNU/IAS Report August 2003

TABLE 96: MEMBERS OF THE MICROMAT CONSORTIUM

University of Bordeaux (FR)
DSMZ Braunschweig (DE)
University of Ghent (BE)
University of Liège (BE)
University of Nottingham (UK)
BioSearch Italia SpA (IT)
Genencor International (USA)
Merck, Sharp and Dohme (USA)

The University of Canterbury New Zealand and AIMS Townsville Australia are currently collaborating on exploitation of Antarctic marine sponges.