**ANNEX**

**BACKGROUND PAPER No. 10**

**ON**

**MARINE BIOTECHNOLOGY**

Disclaimer:

The present document has been elaborated by European Commission services for the purpose of providing background material and information to supplement the Green Paper on Maritime Policy (COM … 2006).

This background document is therefore purely illustrative and is not intended to represent the political views, nor to indicate or announce possible future initiatives of the European Commission.

# TABLE OF CONTENTS

## 1. INTRODUCTION AND SCOPE

Marine (or blue) biotechnology encompasses the applications of biotechnology tools on marine resources. While this type of application is not new, the concept of marine biotechnology per se is relatively young. This is mainly due to the fact that marine resources have been explored to a significantly smaller extent as compared to their terrestrial counterparts. The field is thus characterized by fewer R&D and commercial activities and knowledge on the marine biotechnology "sector" in general is currently limited. The purpose of this working paper is to serve as a brief overview for any potential discussions on the topic. Therefore, it should not be seen as a detailed and comprehensive background paper on marine biotechnology.

### 1.1. What is marine biotechnology?

The clear understanding of what marine biotechnology is and what it encompasses is a prerequisite for assessing its development, prospects and potential impacts in the EU, and for proposing specific measures for support. The most commonly used definition of biotechnology (OECD statistical definition[1]) states that Biotechnology is:

"The application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services".

In the case of marine biotechnology, the living organisms derive from marine sources. Marine biotechnology may include techniques such as bioprocessing, bioharvesting; bioprospecting, bioremediation, using bioreactors etc (so called "process biotechnology techniques"); aquaculture/fisheries; gene, protein, or other molecule based techniques; while applications may include: health, food, cosmetics, aquaculture & agriculture, fisheries, manufacturing, environmental remediation, biofilms and corrosion, biomaterials, research tools etc.

Therefore, marine biotechnology has a horizontal scope encompassing very different applications, for all of which the marine environment is providing the resources.

This contrasts the "conventional" characterization of biotechnology as red (health care sector), green (agro-food sector) and white (industrial sector), according to the application sector. In fact, marine biotechnology may be applied in all of the above sectors.

### 1.2. What is the marine biotechnology sector?

While the general definitions of biotechnology and marine biotechnology are common among different users, a complication arises in the scope (inclusiveness) that is used when addressing the marine biotechnology "sector". In this sense, the sector has ranged from including companies that develop and use bioprospecting and process biotechnology techniques, to including aquaculture and raw material

[1] http://www.oecd.org/document/42/0,2340,en_2649_37437_1933994_1_1_1_37437,00.html. The broad single definition presented here is often accompanied by a list-based definition to narrow down the scope.

extraction from harvest fisheries. An agreement on the scope of the marine biotechnology sector is necessary for the collection of statistical information, and care should be taken when making comparisons among different studies, statistical databases, and any published information in general.

While there is no clear definition of the biotechnology sector, OECD has proposed[2] that for statistical purposes the sector itself should include the developers and users of biotechnology techniques for the production of knowledge, products and/or services (e.g. pharmaceutical company developing drugs using biotechnology), but not the downstream users (i.e. a farmer growing GM crops). A similar approach may be used for the marine biotechnology sector. This is very important in collecting statistical information for further analysis, but also for assessing the prospects of marine biotechnology. On the other hand, any analysis of the potential costs and benefits of marine biotechnology needs to include the impacts to the users of the products and/or services (e.g. a final consumer taking biotechnology-produced therapeutic drugs or a consumer buying seafood checked for safety/quality through biotechnology-based diagnostics).

## 2. MARINE BIOTECHNOLOGY IN THE EU

### 2.1. Introduction

There has been a significant amount of recent activity in the EU aiming at increasing the awareness of the potential of marine biotechnology and marine science in general. A significant activity was the eurOCEAN 2004 conference which was held under the auspices of the Irish Presidency in 2004 (Galway, Ireland). This conference culminated in the Galway declaration[3] and emphasized the need to recognise the importance of marine science for meeting European objectives (such as found in the Lisbon strategy) and the need to strengthen related activities of support. The European Science Foundation (ESF) has in turn published several position papers on Marine Science in Europe, including a specific one on a European Strategy for Marine Biotechnology, with the objective of enhancing an EU wide collaboration.[4] Similar activities have taken place in a number of Member States and associated countries (such as in the UK, Germany, Spain, Norway[5]), that see marine biotechnology as one of the major technologies for the future of the marine sectors. The high expectations from marine biotechnology can also be found in a number of EU activities aiming at developing collaborations, clusters and in general R&D and technology transfer capabilities in this area.[6] The interest in marine biotechnology stems partly from the great expectations on biotechnology and life sciences in general, as a response to which the EU published its Strategy for Life Sciences and Biotechnology[7]. A recent study "Opportunities for Marine Biotechnology

[2] http://www.oecd.org/dataoecd/5/48/34935605.pdf
[3] May 13, 2004. http://www.eurocean2004.com/pdf/galway_declaration.pdf
[4] ESF Marine Board Position Paper 4, 2001
[5] Examples: Cordia, Biotechnology Convention 2005, London, UK. Session: Solutions from the Deep Blue Sea: Emerging Opportunities in Marine Biotechnology.; www.bio-pro.de; seminar "Marine Biotechnology – the next chapter, Tromso, Norway, 2004.
[6] Examples: Blue Bio Net Platform for European Blue Biotechnology funded the framework of the programme "Regions of Knowledge",, http://www.blue-bio.net/index_en.html; www.bluemicrobe.com,
[7] COM (2002) 27 final. Life sciences and biotechnology – A Strategy for Europe (and progress reports)

Application in Ireland" provides a rather comprehensive review of current activities in the EU and in selected competing countries.[8]

Biotechnology development programmes have been initiated in most EU countries, focusing on investment in biotechnology R&D, and related human capital and infrastructures, as well as on supporting measures for the industry (e.g. capital, regulatory environment etc). The interest in Marine Biotechnology seems to be highly supported by maritime regions, and especially those that have traditional strengths in conventional biotechnology (e.g. Germany, France, UK, Spain and others). Nevertheless, as marine biotechnology may also encompass lower-tech activities (such as the extraction of raw materials through harvesting) as well as "conventional" aquaculture, all maritime regions with interests in the exploitation of marine resources are concerned. The marine environment is particularly interesting for biotechnology development in view of its unexplored nature in comparison to the terrestrial counterpart, as the harvest fisheries sector is declining, and as aquaculture production (traditionally based on biotechnology) has increased in importance, being the fastest growing food producing sector with long term prospects for further growth, albeit at lower growth rates.

Marine biotechnology has not been traditionally a major area of application of investment worldwide (in comparison to terrestrial biotechnology), the major investors being Japan and the US. An explanation to this may be the fact that commercial success stories are less obvious, especially as the knowledge base is relatively smaller.

## 2.2. Illustrative research activities

Overall, marine biotechnology projects within the EU are widely conducted, but there are few formal nationally developed R&D programmes[9]. Similarly, while the EC has funded a large number of projects in marine biotechnology, this has taken place under the various broader sub-programmes.

Competence within the EU seems to be high in terms of marine science expertise, R&D and commercial activities, human capital, and infrastructure, although the main R&D investors seem to be the US and Japan[17].

Some examples of relevant and recent marine biotechnology R&D activities in Europe are listed below. This list is not meant to be exclusive but is provided only for illustrative purposes.[10] A more comprehensive listing of relevant research activities as well as other information on marine science and technology is available from the European Centre for Information on Marine Science and Technology (EurOcean)[11]

[8] Opportunities for Marine Biotechnology Application in Ireland. The Circa Group Europe Ltd., 2005.
[9] Opportunities for Marine Biotechnology Application in Ireland. The Circa Group Europe Ltd., 2005
[10] A more comprehensive listing of relevant research activities as well as other information on marine science and technology is available from the European Centre for Information on Marine Science and Technology (EurOcean) http://www.eurocean.org/
[11] www.eurocean.org

- Marine Genomics(EU, FP6): Network of Excellence Implementation of high-throughput genomic approaches to investigate the functioning of marine ecosystems and the biology of marine organisms

- EADGENE (EU, FP6): European animal disease genomics network of excellence for animal health and food safety

- AQUAFIRST (EU, FP6): Combined genetic and functional genomic approaches for stress and disease resistance marker assisted selection in fish and shellfish

- DETECTOX (EU, FP6): Development of an SPR-based biosensor for the detection of lipophilic phycotoxins in shellfish residues

- BIOECOTOX (EU, FP6): Biomarkers: the early warning sentinel of chemical pollution risk assessment

- MARBEF (EU, FP6): Marine Biodiversity and Ecosystem Functioning

- SWORDGEN (EU, FP5): Fine genetic structure of swordfish (Xiphias gladius) in the Mediterranean and the Atlantic: Study by means of individual genetic tagging, using microsatellite DNA markers.

- BRIDGE-MAP(EU, FP5): Bridging Genomes: An integrated Genomic approach for genetic improvement of Aquacultured fish species.

- BASS-MAP(EU, FP5): Tools for the genetic improvement of sea bass. Construction and preliminary application of a medium density linkage and synteny map.

- France: “Genomique Marine” (2003+4 years)

- UK: Salmon traits (2003-2007)

- Norway: FUGE – Functional Genomics, with a strong marine focus (2002 + 10 years)

- Norway: Salmon Genome Project (2000-2005)

## 2.3. Commercial applications

There seem to be four main areas of marine biotechnology applications:

– -Bio-prospecting

– -Improving the production of marine organisms

– -Production of novel products, particularly food and feed products

– -Diagnostics and biosensors

**Bioprospecting:**

high-throughput screening for novel compounds, especially drugs (other uses includes in foodstuffs, nutraceuticals, adhesives, paints, cosmetics, environmental remediation, research etc). It includes biotechnology use in whole drug/molecule development process, i.e. screening, identification, efficacy testing, safety testing, large scale commercial production. Traditionally only 1 out of 10,000-20,000 molecules extracted from terrestrial micro-organisms, plants or animals finally reached the market, which may take 10-15 years and cost up to $800m[12],[13]. This has resulted in large pharmaceutical groups abandoning their search for new drugs derived from natural substances. Evidence of complexity in this process is the relatively empty pipeline of pharmaceutical companies. However, marine biota present a better opportunity for encountering successful candidates in view of the large biodiversity, lack of current knowledge and extreme environments. Ara-C and Ara-A (estimated annual worth $50-100 million) drugs were developed from sponges in the early 50s and proved to be commercial success stories. Anti-cancer agents from marine organisms have an estimated value of $ 1 billion a year. Another good example includes Vent-DNA polymerase which is used as a basic constituent in Polymerase Chain Reaction (PCR). Bioprospecting is applied to all animal and plant phyla living in shallow as well as in deep seabed ecosystems. The advantages of the first include less technical complexity and better economic viability whereas for the latter a larger and perhaps more interesting natural resource base. In general, it is thought that the pace of discovery of new species and products that are potentially useful to pharmacology is higher for marine and microbial than for terrestrial organisms.[14]

A review of patents related to deep seabed genetic resources bioprospecting has revealed that several deep seabed organisms have been used for commercial application, while many are still in the R&D phase. A study conducted on bioprospecting on resources from Antarctica indicated that 18 companies have applied for patents, the majority from Japan and Germany. Important barriers for the development of this sector are technical difficulties, especially in difficult to access environments (and which are often based on public-private collaboration), high costs, and the uncertain IPR situation. There are a limited number of institutions worldwide that can operate vehicles to reach areas of great depths, several of them found in the EU (especially Ifremer in France).

Pharmamar (1986, a subsidiary of Zeltia Group) Spain, is world leader in bioprospecting for anti-cancer compounds from marine organisms which collaborates with fisheries group (Pescanova) which owns fishing vessels and screening centres in all oceans. Over 500 patent applications submitted and/or granted, 10 compounds in pre-clinical development, 3 in clinical trials (two in phase 2, one in phase 1). Only half a dozen companies worldwide are involved in this activity. Staff increased from 70 to 300 between 2000-2002, while new facilities required investment of €22-million. One of few Spanish countries funding its R&D with money collected in the stock market (common practise in the US)

[12] Bioprospecting of Genetic Resources in the Deep Seabed: Scientific, Legal and Policy Aspects, UNU-IAS, 2005

[13] Biotechnologies: current achievements and prospects, Albert Sasson, 2004

[14] Chapter 10:New products and industries from biodiversity. Millennium Ecosystem Assessment – Condition and Trends Assessment, (in press) Island Press, 54 pp.

In total 7 related companies in the EU (UK, Norway, France, Germany, Spain, not exhaustive list) were reported in the study by the Circa Group Ltd.[15]. Furthermore, it was reported that all the major pharmaceutical firms (including Merck, Lilly, Pfizer, Hoffman-Laroche and Bristol-Myers Squibb) have marine biology departments.

**Improving the production of marine organisms:** culture and management of marine organisms. Main applications include the development and the production of healthcare products for farmed fish (preventives and therapeutics), the development of new and/or improved breeds of farmed fish and biotechnology based reproduction technologies.

**Fish health:** the development of fish vaccines and molecular diagnostics for diseases are probably the most promising applications in this field. The international market for fish vaccines has been estimated at €60 million, dominated now by large healthcare companies who bought out the smaller start ups that originally developed the early vaccines. Major companies include Intervet (NL) which owns Norbio (Norway); Novartis which owns Aquahealth (Canada), Schering Plough (US) which owns Aquaculture Vaccines Ltd., and Alpharma (US) which has its production in Norway[12].

**Fish breeding and stock management:** Selective breeding is a recent activity in aquaculture (fish and molluscs) which therefore holds great promise for genetic enhancement programmes. The use of molecular markers for enhancing selective breeding is an even newer activity, which is expected to be crucial for the development of disease resistant strains, strains with improved feed efficiency and strains with improved product quality. Major companies active in this field include Marine Harvest/Genomar (Norway), SalmoBreed as (Norway), Aquagen (Norway), LandCatch (UK) and AQUABounty (Canada, for genetic engineering)[12].

**Production of novel products** (marine raw materials): extraction from harvesting or through culture in bioreactors (food, healthcare, cosmetics, agriculture, medical devices/biomaterials etc): a wide range of companies are involved in the extraction of marine compounds for food and other purposes such as:

– chitin and related compounds from shellfish waste

– omega 3 and other fatty acids from fish oils

– carotenoids, pigments and flavourings

– alginates, carageenans and other compounds from marine algae

– other nutritional supplements such as salts etc.

Although no extensive survey on such companies is available, there seem to be a significant number of companies active in this field within Europe mainly in Norway and Iceland and some activity in the UK, France, and Germany[12].

[15] Opportunities for Marine Biotechnology Application in Ireland. The Circa Group Europe Ltd., 2005.

**Diagnostics and Biosensors:** for use in health management, environmental monitoring, product safety and quality, traceability, antifraud, fisheries management, and monitoring and compliance by government agencies in all of these areas. While there is no comprehensive information on the extent of use of these applications at an EU-wide basis, this field is likely to be among the widest and largest commercially active application areas. Example companies include Biosense (Norway), Aquatic diagnostics (UK), Diagxotics (USA), Genomar (Norway), Jellet Rapid Testing (Canada), etc[12]. European biotechnology-based diagnostics companies reached about €1 billion in 2002[16].

## 2.4. Value and growth perspectives

Estimations on the value and growth perspectives of marine biotechnology should be treated with caution as we have not been able to trace their exact origin neither the methods of calculation and as the definition and scope of biotechnology differs among different countries, statistical databases and studies. Marine biotechnology was globally valued at €2.2 billion in 2004 without counting aquaculture, seaweed and processing related industries which should also be partially attributed to marine biotechnology[17]. Therefore, value is likely to be underestimated. As biotechnology activities are dispersed in various sectors it is really difficult to obtain robust estimations. An often cited example of its large potential is the US Sea Grant Programme that with small investments developed five drugs with market potential of $2billion p.a. According to a study by the United Nations University "Bioprospecting of genetic resources in the deep seabed: scientific, legal and policy aspects" (2005), "estimates put worldwide sales of marine biotechnology-related products at 100 billion US $ for the year 2000". Most probably, this huge difference with the previous estimate is due to differences in inclusiveness of different sectors within the scope of marine biotechnology. For example, it is likely that the latter value includes activities from other sectors that the Marine Industries Global Market Analysis placed to sectors such as aquaculture, fisheries, seaweeds, fish/seafood processing etc.

Marine biotechnology has been considered as one of the most exciting emerging technology sectors[18], with an estimated annual average growth rate at 3.8% (2005-2009) and a total growth rate of 24%. Long term potential is considered to be very large; larger than non-marine biotechnology activity which generated $35.8 billion of revenues in 2002-2005. The global marine biotechnology market is projected to surpass €2.6 billion by 2009 with the non-US segment comprising the bulk of the market[19]. The UK foresight report gives a predicted growth rate exceeding 10% per annum over the next three years (from 2002), while BCC research in 2003 estimated average growth from 1999-2007 as USA(4.7%), Rest of World (6.4%) total (5.9%).

## 2.5. Potential Sectoral Impact

Estimations of the value and growth perspectives of marine biotechnology should also take into account the impacts to a number of sectors such as:

[16] Surviving uncertainty: The Pan-European Mediscience Review 2002, Deloitte & Touche
[17] Marine Industries Global Market Analysis, Douglas-Westwood Limited, March 2005
[18] Report to the UK Foresight Marine Panel, January 05
[19] http://www.bccresearch.com/biotech/C184R.html

*R&D:* this is by far the sector with the most impact, especially in the short term. The impacts include the generation of new knowledge per se, as well as the use of commercialised products (e.g. enzymes, probes etc) for the generation of new knowledge. However, it is difficult to put monetary value to such impacts.

*Fisheries*: the harvest fisheries sector already benefits from diagnostic tools used in stock management as well as in monitoring and compliance.

*Aquaculture:* aquaculture production per se does not seem to form part of the marine biotechnology statistics reported, while it may be argued that the sector as a whole is part of marine biotechnology activities (if the classic biotechnology definition is followed). The impact of diagnostics, new and/or improved breeds, and biotech based health products and services are unquestionably very significant. The potential value of marine biotechnology reported in the UK foresight study and the marine industries global market analysis may therefore be underestimated. The EU aquaculture sector has seen a tremendous growth in the last 20 years (largely based on advances in biotechnology) and is expected to continue, albeit at a lower rate (between 3-4% annual growth rate) which is an indicator of the potential value of biotechnology in this sector (European marine aquaculture valued at approximately €3.5 billion in 2004).

*Agriculture:* the impact in the agriculture sector will mainly depend on the use of marine derived inputs and products (eg as fertilisers, new agrochemicals etc). Some activity has already been reported.

*Health and Cosmetics:* The impacts to these sectors was described earlier and is mainly related to the development of diagnostics, new products and processes mainly based on bioprospecting

*Food:* Impacts to the food sector are likely to be significant, especially in terms of nutraceuticals and feed supplements from bioprospecting and/or through harvesting and extraction and/or through the culture of marine organisms and extraction. As important is the use of diagnostics for food safety, traceability, anti-fraud etc.

*Other Industrial (Manufacturing, Processing, Environmental, Energy):* Important industrial uses are also based on bioprospecting, especially for the production of enzymes, micro-organisms and other compounds. An additional prospective application is the use of marine biomass as an energy resource.

### 2.6. Development potential of marine biotechnology

Against this background, there seem to be two different types of factors that may affect the development of marine biotechnology: 1) those related to the source/environment (the ocean, which is common for all marine biotechnology applications and which may be common to all maritime sectors) and 2) those related to the development of biotechnology in general (which are similar to those that affect red, white, and green biotechnology). It is important that this differentiation takes place, because it may allow better focusing within the framework of the Maritime Policy. While the following is not meant to be an exhaustive analysis, some of these factors (drivers/barriers) seem to be:

*Marine biotechnology-specific / Maritime-related factors*

- geographical location

– remoteness - improvements in accessibility to and internal mobility (also for accessing the resources)

– lack of infrastructure and appropriate coverage of general interest services (health, education, water and energy supply, telephone, post, Internet, waste water and waste treatment)

– available workforce – quantity/quality

- space competition: i.e. competition with other users (tourism, energy, shipping); integrated coastal zone management.

- knowledge base: generally lower, less advanced, at the exploratory phase; stronger in production of knowledge than products/services (compared to non-marine-based biotechnology)

- European funding: EU funds for diversifying the coastal economy and for the development of clusters, collaborations of regions with high prospects

- Other EU/member state relevant policies

*Biotechnology related factors*

These factors have been already analysed and are readily available from the literature, and therefore will not be exposed herein[20]. Mainly they deal with strengthening the capabilities of the biotechnology sector and enabling the transfer from the R&D phase to commercialisation.

As with biotechnology in general, the expectations for job creation and economic development are high but remain to be proven. To this end, and following a request from the European Parliament, the JRC-IPTS has engaged in a study on the: "Consequences, opportunities and challenges of modern biotechnology for Europe" which includes as objectives: to assess the state of biotechnology in the EU, to evaluate the adoption of biotechnology applications in different sectors (health, agro-food and industrial), and to assess the contribution of modern biotechnology to major EU policy objectives.

A marine biotechnology or maritime sector per se is not mentioned as they are covered by other development and application sectors: i.e. general biotechnology sector, human and animal health sector (drug development, vaccines, biopharmaceuticals etc), primary production and agro-food sector (agriculture, forestry, fisheries, and food processing and retail etc.), and industry, environment and energy sector (manufacturing, industrial processing etc.).

Although it is clear that this exercise may have some value in the context of the maritime policy, it will not specifically deal with the question of "the prospects of

[20] Biotechnology for Sustainable Growth and Development. OECD. http://www.oecd.org/dataoecd/43/2/33784888.PDF

marine biotechnology for job creation and economic development" nor with the specific issues that may be unique to marine biotechnology. Such detailed information would ideally be obtained through a specific study on the field.

## 2.7. Measures which may be useful to support the development of the marine biotechnology sector

*1) Measures aimed towards better understanding the marine biotechnology sector.*

Information on marine biotechnology is very scarce, and there are many issues that need clarification. While there are several studies (also cited within the text) available on marine biotechnology, information is still scarce and data are highly questionable. As a result, a logical first step is to engage in activities to better understand the sector and its applications, its environment, its specificities and its needs. It should also be noted, however, that this is a young and emerging sector, whose main impacts are likely to be seen in the future.

*2) Measures aimed towards dealing with the location related specificities of marine biotechnology.*[21]

– - making coastal regions attractive places to live, work and invest

– - identifying and supporting the activities having a future

3) Measures aimed towards strengthening biotechnology capabilities in these regions.

– learn from previous work on biotechnology[22] and adapt to specific requirements

– support RTD, innovation, and technology transfer; the great promise of marine biotechnology is based on the enormous and unexplored diversity of the oceans; as marine biotechnology is at an early phase of development, support should be also stronger for the production of knowledge, on which the production of goods and services will be based. A particular issue with bioprospecting is IPRs and the exploitation of genetic resources in areas beyond national jurisdiction.

[21] There is at least one relevant project funded by the Regions of Knowledge pilot action: BlueBioNet – Conversion of Traditionally Structured Maritime Regions into European Knowledge Regions for Applied Biotechnology

[22] COM (2002) 27 final. Life sciences and biotechnology – A Strategy for Europe (and progress reports)