Blue Growth

Scenarios and Drivers for Sustainable Growth from the Oceans, Seas and Coasts

Maritime Sub-Function Profile Report
Blue Biotechnology (2.4)

Call for tenders No. MARE/2010/01

Client: European Commission, DG MARE

Brest/Utrecht/Brussels, 14th August 2012

The research for this profile report was carried out in the period April – August 2011. This report has served as an input to the main study findings and these have been validated by an Expert meeting held on 9/10th November 2011 in Brussels. The current report serves as a background to the Final Report on Blue Growth.

Content

1 State of Play

1.1 Summary description of the nature of the subfunction

Developing new usages of marine living resources consists in using wild and farmed aquatic living resources as precursors of bio-molecules used for high value products. This subfunction covers the transformation of raw material by biotechnological processes, here called "Blue biotechnology". The growing of aquatic products – especially the growing of micro- and macro algae – is covered in the subfunction profile on "Marine aquatic products".

The OECD (2004)[1] suggests that biotechnology can be defined as "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". Querellou (2010) defines the marine biotechnology (also called blue biotech) as "efforts that involve marine bioresources, either as the source or the target of biotechnology applications".

The blue biotech is the only biotechnological sector defined by the part of the biosphere explored rather than by the process targeted, such as (but not limited to) the white biotechnology (industrial processes), the green biotechnology (agricultural processes), the yellow biotechnology (environmental processes: monitoring, depollution...) and the red biotechnology (health and medical processes). Blue biotech applications can fit into any of the four other coloured biotechnologies.

Current research focuses on a high diversity of applications including but not limited to: anti-oxidants and anti-inflammatory molecules; artificial blood; antifouling molecules; biosourced plastics and polymers; glue active in wet environments; biomarkers, etc.

When describing this subfunction, the main issue is the limit we impose onto the sectors: which activities can we consider in or out of the blue biotech sphere. It is often proposed that the biotech sector should include developers and intermediate users of biotechnology techniques (pharmaceutical firms, cosmetic producers...) but not the downstream and end-users (farmers, fish farmers...) (OECD 2004). Estimating the costs and benefits of the blue biotech sector should nevertheless also include end-users to assess the full impact of the sector on the wider economy (EC 2006).

The distinction becomes complicated when dealing with groups that source their molecules in various biosphere compartments. All the major pharmaceutical firms (including Merck, Lilly, Pfizer, Hoffman-Laroche and Bristol-Myers Squibb) have marine biology departments (EC 2006). Many major cosmetic companies use marine bio-sourced molecules in their products. However, only their marine activities (which size is seldom identifiable) should be accounted in the blue biotech sector.

The key sector of this subfunction is "Marine Services", in its Research and Development dimension. "Fishing" and "Aquaculture" provide some of the raw materials on which the R&D will perform its research. Due to its wide definition, this subfunction covers various industries which could benefit directly from marine biotechnological advances. Some sectors are already under the spotlights for including blue biosourced molecules in their products such as:

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[1] OECD, 2004: Use and Development of Biotechnology. Accessible under: http://www.oecd.org/sti/biotechnologypolicies/biotechnologystatistics-belgium.htm

- The cosmetic sector, investing in the marine biotechnologies genuinely for sourcing new molecules but also for marketing purposes[2], as the "marine" label can suggest a positive image to customers.
- The pharmaceutical sector, looking for new drugs developments based on active molecules derived from marine organisms, and already using marine compounds in its production processes[3].
- The food and nutrition sector, incorporating new ingredients issued from blue biotechnologies: gums (like the guar gum), specific fatty acids (omega-3...) or other functional ingredients[4].

Other sectors benefit also from marine biotech products such as (not limited to):
- The oil industry which can improve its crude oil extraction yield by using specific biopolymers and other marine derived products (in processes called "Enhanced Oil Recovery" and "Microbial Enhanced Oil Recovery").
- The plastics industry, benefiting from new biosourced polymers synthesised from marine bacteria.
- The environmental protection and depollution sector using various properties of environmental remediation: metal fixation, hydrocarbons degradation...

1.2 Description of the current structures

According to interviewees, blue biotechnology takes place in four types of environments, each with various levels of interconnections at the European level:
- An active group of universities and public research institutes is disseminated all over Europe and is covering a wide range of potential sectors: fundamental research (biodiscovery, biology, physiology...) and applied research (drugs, polymers, enzymes, biocides...).
- Numerous start-up and small companies are concentrating their development on niche markets: marine cosmetics, enzymes development, new bioplastics... Interviewees mentioned that in Europe, these companies seem to be predominantly research laboratories spin-off, because there are very few large company keen to develop and market the ideas emerging from the research group and especially produce the proofs of concept.
- Very few medium-size companies (more than 50 employees) dedicated to marine biotechnology development have been identified at the European level. For several interviewees, the lack of medium-size firms is due to the combination of two main factors: a relatively young sector coupled with difficulties to access venture capital.
- Some large companies which have internally developed competencies in marine biotechnology or have acquired promising small blue biotechnological companies to reinforce their activities. Several cosmetic and pharmaceutical companies can be cited as example.

In terms of economic importance, it is very difficult to extract any meaningful information from the available data, as most of the firms involved in the blue biotechnology sector are included either in a category which encompasses all research and development in natural sciences and engineering or are part from a larger sector (pharmaceutics, cosmetics, industrial chemistry...). Estimations of the size of the marine biotechnology sector vary widely depending on publications: Lloyd-Evans estimated the global market for marine biotechnology products and processes to be US$2.4 billion in 2002 (1/3 in the USA and 2/3 elsewhere) with an upwards trend (Lloyd-Evans 2005a) while a US publication put worldwide sales of marine biotechnology-related products at US$100 billion for the

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[2] Some cosmetics companies have even branded themselves as "marine" without using any marine compounds.
[3] An extract from the Horseshoe crab (the Limulus amebocyte lysate or LAL) is used by the pharmaceutical industry to ensure that some of their products (intravenous drugs, vaccines and medical devices) are free of bacterial contamination.
[4] Ingredients that have health improving or disease risk reduction properties.

year 2000 (Arico & Salpin 2005). More recently, the Marine Board of the ESF evaluated the global market for biotechnology products and processes at €2.8 billion in 2010 (Querellou 2010) while a consultancy estimated that "the global market for Marine Biotechnology is forecast to reach US$4.1 billion by the year 2015" (Global Industry Analysts, 2011). Several difficulties arise when considering these figures, among which the lack of clarity in the definition and the scope of the sector considered and in the methodology employed (as highlighted by EC 2006).

1.3 Regulatory environment

In the framework of this study, it has been decided to concentrate only on international and EU wide regulations which affect the subfunction.

The Convention on Biological Diversity is of key importance for the sector as it regulates some of the activities of the blue biotech sector. The Cartagena protocol[5] regulates how genetically modified organisms can be transported between countries, which have an effect on businesses adapting genetic material found in marine organism into well-studied hosts (bacteria, yeast...) through transgenesis. The Nagoya protocol[6], once ratified, will clarify the rules to access genetic resources from foreign countries and to share the benefits arising from their utilisation. There is however a lack of clarity concerning the intellectual property arising from discoveries achieved in the international waters (Arico & Salpin 2005, Schröder 2010).

At the European level, several key regulations and initiatives are affecting directly the "blue biotech" sector:

- The blue biotech is at the crossroads of the EU Integrated Maritime Policy[7] and the EU biotech strategy[8].
- The Lead Market Initiative[9] focused on the bio-based products market among five other promising sectors at the EU level. Specific measures such as "encouraging green public procurement for bio-based products" were designed. Repeating such initiatives will not only maintain biosourced products in the spotlight, it will also help the bio-based producers to reach critical levels of production.
- REACH[10] requires manufacturer to submit a registration dossier documenting the properties (physicochemical, health and environmental) of the chemical substances they produce or import. However, according to interviewees, this regulation does not affect most blue biosourced molecules currently under development as they do not reach the registration threshold (an annual production of 1 tonne).
- The Biocide Directive[11] (currently under revision[12]) regulates the placing of biocide products on the European market. Several marine applications are covered by this regulation such as anti-fouling molecules, pesticides, disinfectants... irrespectively of the quantity placed on the market.
- The new Cosmetic Directive[13], which will enter into force in June 2013, set a positive list for colorants, preservatives and UV-filters which can be used in cosmetic products. Any new blue

[5] The "Cartagena Protocol on Biosafety to the Convention on Biological Diversity" was adopted on 29 January 2000 and entered into force on 11 September 2003.
[6] The "Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity" was adopted on 29 October 2010 and has still to be ratified.
[7] "An Integrated Maritime Policy for the European Union" COM(2007) 575 final.
[8] "Life sciences and biotechnology – A Strategy for Europe" COM(2002) 27 final.
[9] "A lead market initiative for Europe" COM(2007) 860 final.
[10] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency
[11] Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market
[12] COM(2009) 267 final - "Proposal for a regulation of the European Parliament and of the Council concerning the placing on the market and use of biocidal products".
[13] Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products

biosourced molecule which principal function corresponds to one of these three categories should be added to the corresponding annex before being incorporated to any cosmetic.

1.4 Strengths and weaknesses for the subfunction

This subfunction can be characterised by several strengths (S) and weaknesses (W):

- Discovering new molecules:
  - (S) Marine organisms are in their vast majority not known and are potential source for new interesting molecules. Depending on sources, it is estimated that only a few percent of the marine biodiversity has been identified.
  - (S) Numerous unidentified organisms ca be found easily along the European coastlines and in European inshore waters
  - (W) Specific and atypical habitats (deep-sea, mid-ocean ridge…) may be difficult and very costly to explore. Only few players have the technical capabilities to search for new species at great depths.
- Technologies:
  - (S) The ‘Omics revolution[14] is benefiting the sector by offering cost effective methods to sequence DNA of marine organisms, replicate it but also study promising proteins. Second generation technologies enable faster and cheaper procedures.
  - (W) According to interviewees, Europe is less competitive than China and India in offering the best cost-effective sequencing solutions. There are concerns that competencies may be lost in medium to long term if the European sector does not react and leave all the sequencing to be achieved by Asian companies.
- Market:
  - (S) Marine labelled products have a strong appeal for final consumers, especially in the cosmetic and the nutritional sectors.
  - (W) “Blue technology” is a coherent appellation from a marketing perspective. However it does not encompass a structured sector, but various branches with different potential applications.
- Businesses:
  - (W) There seem to be a gap between the research community and associated start up companies, and the large companies which could be interested by blue biosourced products. According to interviewees, small companies have difficulties to reach the critical size, mainly due to difficulties to attract investors during second and third-round funding stages.

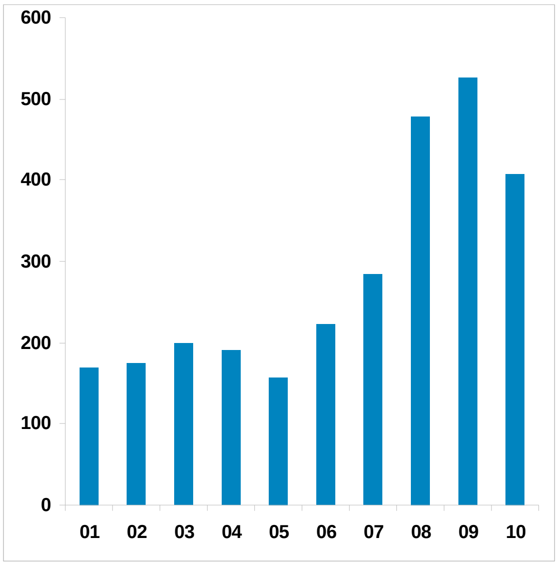
[14] The ‘omics revolution is defined by the simultaneous development of several technologies related to : genomics, transcriptomics, proteomics

2 Research and technology

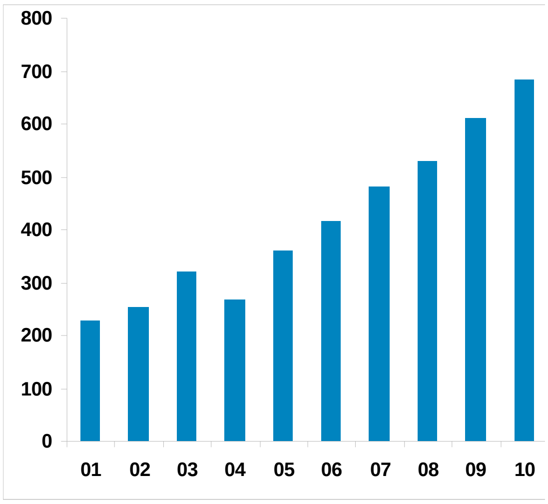
2.1 Research and technology mining

Table 2.1: Below tables compare the total number of global inventions and publications related to Blue Biotechnology (2001 – 2010):

Inventions



Publications



Source: Thomson Reuters

The rising number of global inventions in the past two years and more so of the publications in the course of the last decade gives a clear outlook of the increasing importance of Research and Technology in this function.

The table below compares EU-27 countries in terms of patents filed on their grounds, with competing countries (2001–2010). Priority country means the place where the invention was invented and filed. [15]

Table 2.2: Country score in inventions related to Blue Biotechnology

Priority countries	Total inventions (2001 - 2011)	% of global
Japan	1181	28%
China	570	13%
US	563	13%
EU-27	537	13%
South Korea	269	6%
Global	4227	

Source: Thomson Reuters

[15] Priority country is used in the absence of an inventor county within the patent data. The particular field is not present across a good amount of authorities

Table 2.3: Country score in scientific citations related to Blue Biotechnology

Priority countries	Total citations (2001 - 2011)	% of global
EU-27	20043	41%
US	12915	27%
China	1180	2%
Japan	917	2%
South Korea	585	1%
Global	48693	

Source: Thomson Reuters

Table 2.4: Country score in published papers related to Blue Biotechnology

Priority countries	Total published papers (2001 - 2011	% of global
EU-27	2179	36%
US	1461	24%
China	249	4%
Japan	236	4%
South Korea	140	2%
Global	5995	

Source: Thomson Reuters

The positive positioning of the EU-27 countries is also championed in terms of the number of scientific citations. This is mirrored also by the percentage of published papers.

Table 2.5: Top 20 global patent assignees - organizations or individual owners of the patent's invention - are presented in the table below in Blue Biotechnology

Top assignees	Total number of patents filed (2001- 2011)
UNIV KANGNUNG WONJU	28
L'OREAL SA	21
NOEVIR KK	21
NESTLE SA	18
DOKURITSU GYOSEI HOJIN SANGYO GI	17
HUMAN GENOME SCI INC	17
KAO CORP	16
LION CORP	14
ASAHI KASEI KK	12
GUANGZHOU TIANBAO SONGYUAN BIO	12
DAINIPPON INK & CHEM INC	11
FUJI FILM CORP	10
MITSUBISHI GROUP OF COMPANIES	10
TOYO SHINYAKU KK	10
BASF	9
IAMS CO	9
ICHIMARU PHARCOS INC	9
KANEKA CORP	9
NIZHEGOROD EPIDEMICS MICROBIOLO	9
UNIV PUKYONG NAT	9

Source: Thomson Reuters

2.2 Assessment of R&D patterns

Over the last ten years, *scientific publications* on the discovery and the usage of new marine molecules have constantly risen. Patent publications were stable between 200 and 2005 (between 160 and 200 patents published every year) and constantly rose since 2006 (from 220 patents in 2006 to over 400 patents in 2010).

Europe generates almost a third of the scientific publications (in particular the United Kingdom, France and Germany) when the USA publish approximately a quarter of the scientific papers related to this field. Taken individually, other countries produce far less publications: according to our data, the first two followers, Canada and China, publish only 4% of the identified material.

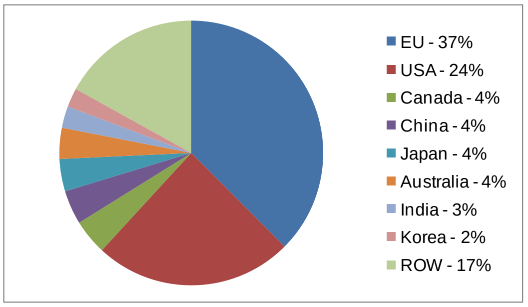


Figure 1: Scientific publications

When comparing this scientific activity to the trend in *patents publications*, the difference is striking: Europe only represents 13% of patents filled in relation to new marine molecules, at the same level than the USA. Japan (28%) and China (13%) seem far more active in patent publications than in scientific publications.

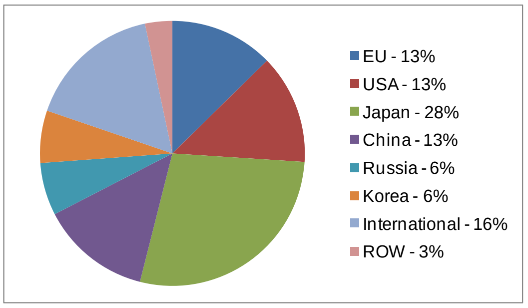


Figure 2: Patents

Top authors in this field are seldom listed as top patent assignees, either when considering referring institutions or individual researchers. These differences in publication pattern can be explained by possible differences in procedure to fill and grant patents between countries.

However, the main reason for such differences seems to be the fierce competition for commercial applications, especially in the cosmetics and chemical sectors. It has been mentioned by some interviewees that companies were more prone to fill a patent than publishing in scientific journals to keep interesting findings away from competitors. Leading companies in patent publishing are mainly from the cosmetic sector (L'Oreal in Europe and Noevir, Kao Corp, Lion Corp in Japan), the chemical sector (in Japan: Asahi Kasei, Dainippon Ink & Chem Inc and Fuji Film Corp) and the food sector (in Europe: Nestle)Interviewees stress the fact that sourcing new molecules from the marine environment to the benefit of specific market applications is a staged process which consists in 1-discovering new organisms, 2- identifying interesting molecules for their marketable properties and 3- defining a cost-effective production process. At each stage, important research activities have to be undertaken.

2.3 Assessment of R&D patterns

The discovery stage is of key importance. Currently, several compartments of the marine environment are explored to find new interesting molecules:

- Nearby waters: Europe is surrounded by several seas and benefit also from regions outside Europe (mainly French territories). Some interviewees mentioned that the European coastal biodiversity would give them interesting material to be investigated for decades.

- Atypical environments (sometimes called extreme environments): hot waters (hydrothermal sources), cold waters (Arctic and Antarctic), under high pressure (abysses). Heat-stable or heat-labile molecules can be derived from organisms found in these atypical environments.
- Open seas: Craig Venter's Global Ocean Sampling Expedition and Tara Oceans are two major projects dealing with the identification of the marine biodiversity at a global scale. Other less exposed projects pursue the same objectives.

The discovery process is extremely time-consuming and requires expensive equipment, especially for atypical environments and open seas. Very few industrial actors consider the time and effort involved in this search to be worthwhile. As a result, the major part of marine compounds isolated and analysed so far were discovered by researchers from scientific institutes (Schröder 2010).

The identification of new molecules in marine samples benefits from recent technical developments allowing research teams to focus more effectively on interesting organisms and interesting molecules. Over the last 20 years, the 'omics revolution has allowed researchers to used computer assisted techniques to identify genomes, proteins and other metabolites more effectively.
Second generation sequencing technologies (also called 'deep' sequencing) enable 10 to 100 times faster automated procedures. High-throughput screening techniques allow researchers to quickly perform multiple chemical, genetic or pharmacological tests. Identification of interesting molecules or genes is therefore accelerated, allowing new molecules to be discovered at a lower cost.

Once the molecules are identified, the definition of cost effective production pathway is the last technical conundrum to be overcome. Two major routes can be explored by developers: either the extraction of the interesting molecule from the organism it was discovered in or its synthesis by biochemical pathways.

Extraction processes face several key challenges linked to the production of the interesting organism: Is the harvest phase sustainable and profitable? Can the organism be domesticated and grown as a new aquaculture species (fish, algae, crustacean...) or in specific closed systems (bacteria...)? In some cases, there are issues related to the purification of the molecule and to cross-contamination that have to be overcome as they are detrimental for several applications (health, cosmetic, nutrition). The extraction phase is also technically and economically challenging: in some cases, the molecule of interest is only present at a 1 per million ratio in the parent organism (ie to extract 1g, the company would need to harvest 1 tonne of live animal) which imply high extraction costs and need for a high volume of harvested or produced organism. Moreover, natural variability can seriously impact production yields: an interviewee mentioned that he had a blank production year due to low levels of active molecules in the organisms he was harvesting.
The biochemical pathway faces other challenges, among which the necessity to adapt the interesting genetic sequences to usual hosts through transgenesis (bacteria: *Escherichia spp*, *Bacillus subtilis...;* yeast: *Saccharomyces cerevisiae*...), which is one of the main technological barriers the sector is currently facing. There is also a need for new hosts' identification allowing researchers to exploit more genetic sequences.

2.4 Underlying R&D processes and trends

Apart of sourcing new molecules, biotech advances can be realised by the in depth study of "model organisms" which have several applications for fundamental research but also for cancer research and neurodegenerative disorders as some of them are "more closely related to humans than other major invertebrate model in use" (Querellou 2010).

Internationally, the main competitors in terms of research are the USA, which is the leading player in the biotechnology sector, China and India, where sequencing facilities are flourishing, Japan and Brazil (Querellou 2010).

There are key technical developments to be achieved for the blue biotechnological sector:

- Fundamental research in biology, physiology and ecology is needed to understand how the discovered organisms (bacteria, sponges, crustaceans...) grow and live, to understand how to cultivate/grow them for research purposes but also for production.
  - It has been mentioned by interviewees that only a small fraction of identified bacteria (less than 5%) can be cultivated with current techniques. As bacteria can only be fully studied when cultivated, progress in cultivation techniques will unlock huge potential.
  - Understanding the influence of natural variations on wild population is important to assess more precisely the productive potential of marine organisms. For example, Stengel, Connan & Popper (2011) explore the implications of natural variability on the concentration of interesting molecules in natural populations of algae.
  - It is also important to assess if harvesting can be sustainable or if the interesting organisms can be grown by the aquaculture sector (fish, crustaceans...).
- Although metagenomics techniques allow researchers to avoid looking at individual organisms when searching for promising molecules, the complete sequencing of individual genome remains fundamental from a research perspective, especially to identify new biotech hosts and model species.
- There is a need for continuous research in the biotechnological adaptation of interesting genes into well known bacteria or yeast for production in controlled environment. Refinement in transgenesis techniques and identification of new strains of host bacteria and yeast will also allow more genetic material to be exploited by the sector. According to interviewees, current techniques are more empirical than systematic and a serious research investment is needed to streamline the techniques.

3 Future developments

3.1 External drivers affecting the performance of the cluster

Crude oil price is a strong driver for petrochemicals prices (polymers and fibres, lubricants, inks, dyes, agrochemicals...) and has therefore an impact on biosourced equivalents competitiveness. Marine bio-sourced polyethylene can currently be produced at $3 to $5 per kg when petrochemical equivalent are produced at $1 per kg. Higher crude oil prices will help to close the commercial gap between the different production technologies and foster the development of bio-sourced products competing with petrochemicals.

There is an increasing demand for bioactive compounds by the pharmaceutical industry. However finding a bioactive molecule is just the beginning from a pharmaceutical perspective, as there are several important steps to validate before being able to register a new drug, among which proving the stability, the safety and the quality of the molecule, testing it through various clinical trials... This process is long (between 15 and 20 years) and expensive (various estimates place the cost between US$ 500 million and US$ 1 billion) (de la Calle 2007).

Access to finance is also a key issue for this sector: It has been commented that few investors are keen to take risks in these new technological developments. Interviewees mentioned that businesses may access financial through various national funds in Europe at the initial stage. However, according to interviewees, businesses seem to struggle during the second and third rounds of funding, lowering their growth potential. Some interviewees commented that SMEs struggle to reach a certain critical mass, making them less attractive for investment by large established companies of their sector[16]:

Case: Clinical trial performed with the help of Innovation Norway.

Why this Case is important: This case shows how the implication of specific and targeted public funding can accompany small companies at key development stages.

Key description of the case: Ten years ago, a university professor in molecular biology from the University of Bergen identified interesting molecules with skin regenerating properties in fish eggs. After looking for potential commercial applications, it was decided to enter the cosmetic market, seen as more accessible than the pharmaceutical sector. In order to scientifically ascertain the molecule properties, a clinical trial was performed by a leading US laboratory, which would not have been possible without the financial support of Innovation Norway, an important Norwegian governmental fund supporting innovation.

Future developments: With the positive results of the clinical trials, the company was able to sign a partnership with a large cosmetic company to incorporate the new molecules into future cosmetic products.

Impacts on blue growth: Focusing specific funding at key stages for SMEs (proof of concept, second round of financing…) will allow them to grow and to reach the critical mass needed for their survival.

Some interviewees consider that current interests for algae biofuel developments are diverting investors' attention from other marine applications and especially blue biotech. It has been mentioned that the algae biofuel sector could suffer from a speculative bubble which could be detrimental to the aquaculture sector but also to the biotechnological sector.

[16] Some interviewees commented that they had to increase their turnover from €5 million to €50 million before large companies would be interested in investing in their company.

3.2 Assessment of response capacity and commercialisation potential

The blue biotechnology sector is highly focused on integrating the latest R&D developments. There is however a lack of knowledge-sharing between companies which are very closed and secretive, and do not share information easily. This is especially true for cosmetic and pharmaceutical companies for whom new developments are seen as important market opportunities which cannot be shared with competitors. This leads to an overall slow learning process, which is hampering knowledge development in this sector significantly.

The blue biotechnology sector is a relatively new sector in Europe. According to some interviewees, the sector suffers from a lack of entrepreneurial culture in Europe: there are numerous fresh ideas and new molecules in the research community, but the industrialisation phase is weak. Some start up businesses seem to be too technologically oriented and not enough market-focused, which does not serve their development.

This sector is already supplying niche markets but also some specific mass-market (marine cosmetics sourced from algae for example). Most interviewees commented that the blue biotech sector will not grow as a separate sector but promising companies will be progressively integrated in the demanding various sector (health, cosmetics, chemicals...). However, from a development perspective, some interviewees felt that increasing the blue biotech products awareness among potential customers would benefit to the whole sector as it will generate a momentum in the industry. Several groups of molecules can be destined to a wide range of market: chitin derived from crustacean shell can be incorporated by various sectors: cosmetic, pharmaceutical, water treatment, bioplastics... (Ifremer 2010). Other examples are biopolymers sourced from marine bacteria which can be used to produce bioplastics, drug encapsulation or water treatment membranes.

Some interviewees mentioned that due to the marine biodiversity richness, identifying interesting molecules will almost always be successful and will not constitute the major technical hurdle for the sector, although the discovery step is expected to be time-consuming and expensive. From their perspective, finding cost-effective solutions to produce end-products that fit a market need will be the real challenge for the industry.

Overall the response capacity is rather low due to:
- the widespread range of potential applications,
- the highly specialized production processes,
- the lack of communication between companies from the sector,
- the lack of entrepreneurial skills in the sector.

3.3 Most likely future developments (the Micro-future)

Interviewees agree in considering that the “high value marine product” sector has limited chances to grow over the next 20 years as a structured and independent sector, but numerous blue biotech applications will be adopted by other sectors. They also consider that it is not the supply of marine products that will structure the sector but the demand for specific applications.

The sector presents a high diversity of potential applications, covering all sorts of industries. Interviewees believe that major applications will reach the market, among which new medical molecules, bioplastics, enzymes or biocides. Applications that have the potential to reach critical mass will certainly be coveted by large players: cosmetic companies (L’Oreal, Estée Lauder...), pharmaceutical companies (Merck, Lilly, Pfizer...) but also large chemical players (Novozymes, BASF...).

Pharmaceutical demand will be driven by an increasing ageing population, with age-related conditions to be treated: cancer, neurodegenerative disorders, osteoporosis... Pain relief and antibiotic resistance are also two areas where marine molecules may be relevant (Schröder 2010). Marine active molecules have already been identified for major conditions but they have to be adapted before entering the validation process to reach the pharmaceutical market.
The combination of declining crude oil production and increasing awareness for "green" products will push for the development of biosourced plastics benefiting the whole packaging industry (food, cosmetics...). Medical applications can also been derived from these polymers: they can be exploited as a new generation of degradable prosthesis allowing bones reconstruction but also as a new type of drug encapsulation.

Depending on sectors, new molecules will be sourced either directly from marine organisms (cosmetics, nutraceuticals) or through biotechnology (pharmaceutical, bioplastics…). For some sectors (cosmetics, nutraceuticals…), customers express their choices towards molecules from natural sources (ie extracts from plants and animals) which have to be exploited sustainably. This trend will lead to the exploitation of marine organisms and co-products of the fishing and aquaculture sectors for the extraction of interesting molecules. Those molecules can only be economically viable if harvesting can be achieved at a sustainable level and that issues related to natural variability could be overcome.

Case: Marine biosourced plastics.

Why this Case is important: This case shows how raising the awareness of industrials on a specific marine product may unravel more interesting applications.

Key description of the case: Several species of bacteria present the ability to synthetise polyesters under stressed conditions. These polyesters, called PHA, are fully biodegrable and compostable in a few weeks by bacterial activity. IFREMER biotech team has specialised in the identification of these specific bacteria but also in the development of potential applications. They are currently exploring how to incorporate these PHA in food packaging.

Future developments:

Potential applications for PHA are diverse: biodegradable plastic bottles, drug capsules, surgical suture...
Researchers are confident that there will be enough momentum and awareness generated by a first PHA product reaching the market to allow other applications to

However, most interviewees believe that the largest part of marine molecules will be sourced through biotechnology and will not be extracted from wild material: original molecules will be sourced in marine organisms but final compounds will be optimised and produced through biotechnology. The end-product would therefore only be linked to the marine biodiversity by the original organism it was derived from. This trend is expected to be followed by mass market applications (bioplastics…) but also by sectors which use marine molecules as intermediate products (pharmaceutical, cosmetics…)

Interviewees indicate that the positive evolution of the "high value use of marine resources" subfunction mainly depends on few key drivers which are:

- The major hurdle for the sector resides in its ability to find effective solutions to produce biosourced products at a competitive cost.
- The increase in oil price which will impact the price of petrochemicals and close the commercial gap with biosourced products. Policies that stimulate "green" consumption such as increasing costs of GHG emission rights which will increase the price for petrochemical plastics and will have a stimulating effect on the biosourced plastics. The high production costs will remain an obstacle if demand for bioplastics is low.

- The capacity of the European sector to avoid key competencies to be concentrated by competing countries (China, India, South East Asia...): some interviewees believe that Asian countries' biotechnology sectors are progressing rapidly and will soon become very competitive to attract high skilled workers, which will be mostly trained in these countries. Some interviewees believe that European universities will have to develop more specific marine training and education to raise the awareness of marine biosourced products among future European scientists and managers.
- The ability for SMEs to raise funding enabling them to grow after initial stages are completed.

3.4 Impacts, synergies and tensions

Most interviewees believe that the growth of the sector will lead to the creation of numerous small biotechnological companies at the European level which will integrate larger groups once the proof of concept and the initial market developments are achieved. Most interviewees do not see a new sector of blue biotechnological firms emerging as a separate sector.

In term of job creation, interviewees do not see the sector as a large employer at the European level. This is coherent with a recent analysis published by the JRC which stated that "biotechnology contributes to employment, mainly in the form of 'better jobs' (more higher-qualified jobs). [...] The effect in terms of 'more jobs' is unclear because of lack of data and replacement effects" (Zika et al. 2007).

Considering potential environmental impacts, it has been mentioned that biotechnological developments will help reducing energy and water requirements, recycling costs of chemical products and greenhouse gas emissions. For example bio-sourced polymers can be designed to be biodegradable and compostable in just a few weeks, which would be an important improvement compared to currently available petrochemical polymers which are not biodegradable.

Hotspots of start-up and SMEs are expected to appear close to Universities and research centres where specific interests for marine applications are growing. In Bretagne for example, several SMEs focusing on marine cosmetics, marine biopolymers and other applications have emerged close to public research institutes (IFREMER, Roscoff laboratory from Université Pierre et Marie Curie). Several public initiatives have been engaged to improve the communication between these different actors such as the Pole Mer Bretagne. Recent developments show that a close link to the coastline may not be necessary for this process to happen.

In general, interviewees foresee few tensions between this subfunction and other marine activities. There are general concerns about biodiversity loss and pollution (especially in coastal waters) for businesses sourcing their products from wild plants and animals (mainly in the cosmetic and nutraceutical sector). Strong synergies are expected as blue biotech products can answer to key needs:
- 1.1 Deepsea shipping, 1.2 Shortsea shipping (incl. RoRo), 1.3 Passenger ferry services, 1.4 Inland waterway transport: Synergy – These subfunctions may benefit from marine bio-sourced products such as coating with anti-fouling or anticorrosive properties.
- 2.1 and 2.2 Catching fish for human consumption: Synergy – Catching sector may provide useful raw material (crustacean chitin, fish bones...) for research and new molecule production, marine bacteriological progresses may generate shelf life improvements. Tension – overfishing may reduce the volume of raw material delivered to the blue biotech sector (cosmetic and nutraceutical).
- 2.3 Growing marine aquatic products: Synergy – Aquaculture sector may provide useful raw material (algae by products, fish bones...) for research and new molecule production. It would

benefit from advances in fish medications but also benefit from shelf life improvements achieved through marine bacteriological progress.

- 2.5 Agriculture on saline soils: Synergy – Development of biosourced pesticides and reinforcing treatments.
- 3.1 Oil, gas and methane hydrates: Synergy – Specific applications may provide solutions to improve the extraction yield of oil (“Enhanced Oil Recovery”). Tension – accidental spills may reduce locally marine biodiversity.
- 3.3 Marine renewables (wave, tidal, OTEC, thermal, biofuels, etc.): Synergy - underwater construction could benefit from marine biosourced coatings with anti-fouling or anticorrosive properties.
- 3.6 Mineral raw materials: Synergy – recent developments show that mineral nodules may partly be of biogenic origin (Wang & Werner 2010). Unlocking the metal fixating properties of selected bacteria could improve the potential of this function.
- 3.7 Securing fresh water supply (desalination): Synergy – development of specific biopolymers and bio membranes could improve the overall efficiency of the desalination process.
- 4.2 Yachting and marinas and 4.3 Cruise including port cities: Synergy – as for the shipping sector, provision of marine bio-sourced coatings with anti-fouling or anticorrosive properties. Tension – development of marinas and port cities may reduce biodiversity in coastal areas.
- 5.3 Protection of habitats: Synergy – bio stimulation can be used to foster bioremediation after important pollutions (as for the Exxon Valdez oil spill when bacteria were stimulated to degrade hydrocarbons)
- 6.3 Environmental monitoring: Synergy – bio-discovery activities can improve the knowledge of specific biomarkers for environmental monitoring.

4 Role of policy

4.1 Policy and political relevance

Several countries have decided to implement policies aiming at fostering the biotechnology sector as a whole (USA, India, Japan...). The main objectives are related to the development of a profitable bio economy which would not only generate growth and employment, but also which will improve energy efficiency and reduce the dependence to crude oil of the chemical production sector. However, few countries seem to have defined specific strategic vision for marine biotechnology development (Ireland, Norway).

It is believed by most interviewees that EU is well placed to send useful signals either to the research community or to end-users to increase the general awareness for marine biosourced products which will participate to the growth of the sector. Moreover, some interviewees felt that it is in the remit of the EU to ensure that marine natural resources are exploited in a sustainable manner.

4.2 Domains for EU policy

There are mainly two levels of intervention 1- continuing and fostering the support for the public research sector and 2- improving the support for SMEs in their development towards profitable and innovative applications fulfilling specific market demands.

It should be noted that some interviewees felt that public intervention has been more directed on supply-oriented policies (R&D funding) and should lean towards more demand-oriented measures, fostering the uptake of blue biotech innovations by industries (cosmetics, pharmaceutics, packaging...) and end-users.

- Funding of biodiscovery projects and fundamental research in biology, physiology or ecology is of key importance as marine organisms are widely unknown. Focusing some part of future framework programs (but also other funding systems: Marie Curie, INTERREG...) towards maritime projects will help securing this.
- Improving the awareness for marine bio-sourced products is believed to be important for the growth of the sector, either at the educational stage (such as specific topics on marine sciences in scientific and managerial curricular) or at the end-user level (like incentives to switch to bio-sourced material, such as the Lead Market Initiative).
- Seed investment initiatives should encourage start-up and small businesses to improve the market competencies of their workforce (either by training existing staff or by recruiting new competencies).
- It has been mentioned by interviewees that SMEs will benefit from the creation of a specific public-private investment fund (an interviewee mentioned a “European Marine Biotechnology coinvestment fund), which could partly be inspired by the Innovative Medicines Initiative. It would aim at participating in the second-round financing of promising SMEs, which would help to structure the sector. It would grant loans or take shares in promising SMEs and would also help reinforcing the business structure of these companies. This fund could also act as a catalyst to pool several small businesses in larger and more coherent firms.

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Annex 1: Stakeholders interviewed

Blue biotechnology

Interviewee	Organisation	City/country
Dr Hordur G. Kristinsson	Matís ltd	Iceland
Dr Xavier Briand	BiotechMarine (high tech lab from Groupe Roullier)	France
Dr Catherine Boyen	Station Biologique de Roscoff	France
Dr Jan Buch Andersen	ArcticZymes AS	Norway
Dr Werner Müller	BIOTEC marin Gmbh	Germany
Luis Mora	Pharmamar	Spain
Christine Bodeau	Laboratoire Sciences et Mer	France
Dr Charlie Bavington	GlycoMar Limited	UK
Dominique Pradines or Benoit Sirop	Thalgo	France

Annex 2: Impact matrix of the medium-term and longer-term developments

Table: Impact matrix of the medium-term and longer-term developments

Function	Indicators	Bal-tic	North Sea	Medi-terr.	Black Sea	Atlan-tic	Arc-tic	Outer most
1. Economic impacts	Market value GVA	+ +	+ +	+ +	+ +	+ +	+ +	+ +
2. Employment impacts	Employment	0/+	0/+	0/+	0/+	0/+	0/+	0/+
3. Environmental impacts	CO_2 levels Nutrient / water quality Energy requirement Water requirement	+ 0/+ + +	+ 0/+ + +	+ 0/+ + +	+ 0/+ + +	+ 0/+ + +	+ 0/+ + +	+ 0/+ + +
4. Other impacts								

Explanation:

++ = *Strong positive impact expected*

+ = *Considerable positive impact expected*

0 = Negligible impact expected

- = *Considerable negative impact expected*

-- = *Strong negative impact expected*

Annex 3: Impact, synergies and tensions matrix

Function affected	Sub-function affected	General	Bal-tic	North Sea	Medi-terr.	Black Sea	Atlan-tic	Arc-tic	Outer most
1. Maritime transport and shipbuilding	1.1 Deepsea shipping	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-
	1.2 Shortsea shipping (incl. RoRo)	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-
	1.3 Passenger ferry services	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-
	1.4 Inland waterway transport.	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-
2. Food, nutrition, 99health and eco-system services	2.1 Catching fish for human consumption	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-
	2.2 Catching fish for animal feeding	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-
	2.3 Growing aquatic products	+	0/+	+	+	+	+	0/+	+
	2.4 High value use of marine resources (health, cosmetics, well-being, etc.)								
	2.5 Agriculture on saline soils	0/+	0/+	0/+	0/+	0/+	0/+	0/+	0/+
3. Energy and raw materials	3.1 Oil, gas and methane hydrates	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-
	3.2 Offshore wind energy	0	0	0	0	0	0	0	0
	3.3 Marine renewables (wave, tidal, OTEC, thermal, biofuels, etc.)	+	+	+	+	+	+	+	+
	3.4 Carbon capture and storage	0	0	0	0	0	0	0	0
	3.5 Aggregates mining (sand, gravel, etc.)	0	0	0	0	0	0	0	0
	3.6 Mineral raw materials	+	+	+	+	+	+	+	+
	3.7 Securing fresh water supply (desalination)	+	+	+	+	+	+	+	+
4. Leisure, working and living	4.1 Coastline tourism	0	0	0	0	0	0	0	0
	4.2 Yachting and marinas	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-
	4.3 Cruise including port cities	+/-	+/-	+/-	+/-	+/-	+/-	+/-	+/-

Function affected	Sub-function affected	General	Bal-tic	North Sea	Medi-terr.	Black Sea	Atlan-tic	Arc-tic	Outer most
	4.4 Working	0	0	0	0	0	0	0	0
	4.5 Living	0	0	0	0	0	0	0	0
5. Coastal protection	5.1 Protection against flooding and erosion	0	0	0	0	0	0	0	0
	5.2 Preventing salt water intrusion and water quality protection	0	0	0	0	0	0	0	0
	5.3 Protection of habitats	+	+	+	+	+	+	+	+
6. Maritime monitoring and surveillance	6.1 Traceability and security of goods supply chains	0	0	0	0	0	0	0	0
	6.2 Prevent and protect against illegal movement of people and goods	0	0	0	0	0	0	0	0
	6.3 Environmental monitoring	+	+	+	+	+	+	+	+

Explanation:

++ = Strong positive impact on other subfunctions/sea basins expected

+ = Considerable positive impact on other subfunctions expected

0 = Negligible impact on other subfunctions/sea basins expected

- = Considerable negative impact on other subfunctions expected

-- = Strong negative impact on other subfunctions expected

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