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Blue Biotechnology

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2.1 Introduction

Biologists categorise living things into 36 divisions (technically phyla) and members of 34 of these divisions are found in the marine environment. In fact, the marine realm represents 70% of the biosphere. Life forms are estimated to have appeared at the bottom of the world's ocean approximately 3.6 billion years ago, compared to only several hundred million years ago for terrestrial life. Due to the ancient history and diversity of life forms encompassed, the oceans are considered a unique reservoir for a wide variety of potentially useful molecules (Arrieta et al., 2010). However, until recently, marine molecules remained largely unexploited due to difficulties associated with accessing them. Our ability to access remote parts of the ocean has greatly improved over the last century, and particularly in recent decades, as a result of advances in oceanographic technology. The technology used to screen molecules of interest has also improved over the last few decades. Recent estimates show an exponential increase in the use of marine molecules or sequences of nucleic acids extracted from marine organisms in a variety of biotechnological fields. Industries involved encompass a broad range of applications including human health, agriculture, aquaculture, food, cosmetics and bioremediation (Arrieta et al., 2010; Blunt et al., 2011; Leal et al., 2012; Marine Board, 2010). Marine molecules have also been used to develop pharmaceutical drugs such as anti-cancer medication, as well as treatments against HIV and Alzheimer disease which have already been commercialised (Molinski, 2009). The market for such biotechnologies appears to be vast and has been expanding consistently over the past few decades. The market value of a number of commercialised products had already surpassed several billion USD per annum by the year 2010 (Leary, 2009).

2.1.1 Definition of Blue Biotechnology and Marine Biotechnology

Biotechnology is broadly defined by the Organization for Economic Co-operation and Development (OECD, 2005) in the following way:

- **OECD statistical single definition of biotechnology**: 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 (OECD, 2016).
- **OECD list-based definition for biotechnology**: The following list of biotechnology techniques functions as an interpretive guide in using the single definition. The content of the list-based definition is indicative rather than exhaustive and is expected to change over time as data collection and biotechnology activities evolve (OECD, 2016).
    - **DNA/RNA**: Genomics, pharmacogenomics, gene probes, genetic engineering, DNA/RNA sequencing/synthesis/amplification, gene expression profiling, and use of antisense technology.
    - **Proteins and other molecules**: Sequencing/synthesis/engineering of proteins and peptides (including large molecule hormones); improved delivery methods for large-molecule drugs; proteomics, protein isolation and purification, signalling, identification of cell receptors.
    - **Cell and tissue culture and engineering**: Cell/tissue culture, tissue engineering (including tissue scaffolds and biomedical engineering), cellular fusion, vaccine/immune stimulants, embryo manipulation, marker-assisted breeding technologies.
    - **Process biotechnology techniques**: Fermentation using bioreactors, bio-refining, bioprocessing, bioleaching, biopulping, biobleaching, biodesulphurisation, bioremediation, biosensing, biofiltration and phytoremediation, molecular aquaculture.
    - **Gene and RNA vectors**: Gene therapy, viral vectors.

- **Bioinformatics**: Construction of databases on genomes, protein sequences; modelling complex biological processes, including systems biology.
- **Nanobiotechnology**: Applies the tools and processes of nano/ microfabrication to build devices for studying biosystems and applications in drug delivery, diagnostics, etc.

This very clearly shows what is involved in biotechnology in general. There is however no single, official definition of blue biotechnology or marine biotechnology. Blue biotechnology is generally considered the use of marine bioresources as the source of biotechnological applications (Figure 2.1). In other words, marine resources and marine organisms are used to develop products or services for biotechnological gain (ECORYS, 2014). In contrast, marine biotechnology also includes the application of biotechnology developed using any resource (marine, terrestrial, freshwater or a combination) to the marine environment, and human activities therein.

Workshops and questionnaires were conducted in 2013 and 2014 in order to reach an agreement on a common understanding of the term marine

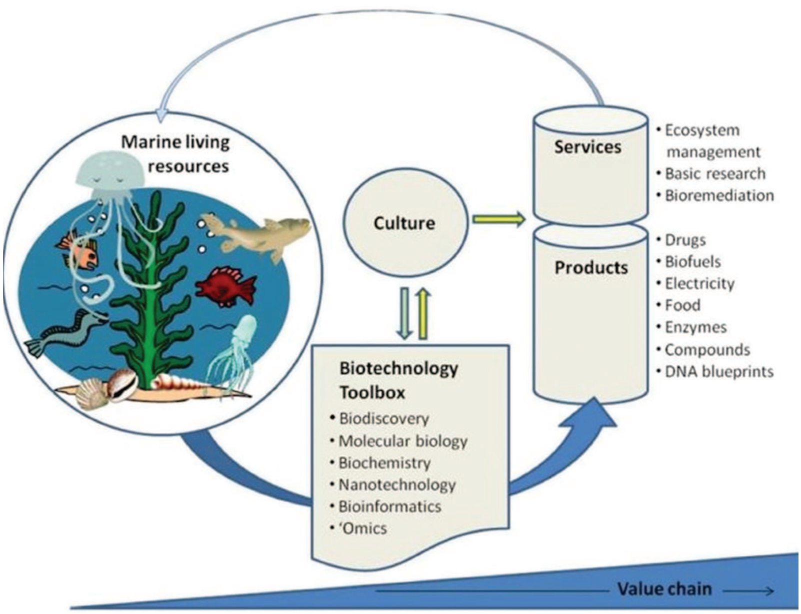

Figure 2.1 Marine biotechnology.

Source: OECD, 2013.

biotechnology. During workshop discussions, the European Commission (EC) highlighted the importance of consensus regarding marine biotechnology's definition for the development of new initiatives and policy options. It became apparent over time that adaptation of the existing OECD definition for biotechnology (single and list-based parts) could be the most straight forward way to reach an overall consensus and definition (OECD, 2016).

International definitions of **(marine) biotechnology**

- **Marine Board definition of marine biotechnology**: Marine biotechnology encompasses those efforts that involve marine bio-resources, as either the source or the target of biotechnology applications (Marine Board, 2010).
- **Mediterranean Science Commission (CIESM) definition for marine biotechnology**: Marine biotechnology is a category of products and/or tools relating to marine bio-resources, as either the source or target of their application. It provides goods and services for innovative industries and/or society as a whole (Not published, presented at an OECD workshop in 2012).

By adding reference to marine organisms or the use of biotechnology in the marine environment, the OECD's broad definition of biotechnology can be applied to define marine biotechnology. The OECD's list-based definition is particularly useful in this regard due to the fact that it can be adapted by adding specific technologies or elements of marine biotechnology (OECD, 2016). The definition for marine biotechnology can therefore be seen to approximate the OECD list-based definition for biotechnology.

The blue biotechnology sector is unique amongst biotechnology sectors in terms of the way that it is defined. For example, whereas red (medical, health and pharmaceutical), green (agricultural), yellow (environmental) and white (industrial) biotechnologies are delineated on the basis of the processes they entail or the markets they serve, blue biotechnology is the only biotechnology sub-sector to be defined by its source material, i.e. marine resources (see Table 2.1) (Kafarski, 2012). Therefore, the characterising feature of blue biotechnology is the first part of the development pipeline: from sampling to discovery and bioprospecting, to research and development (R&D) and initial product development (Figure 2.2). Blue biotechnology has the potential to contribute to a variety of other biotechnology and industry areas. As such, blue biotechnology is not a clear-cut sector. There are important overlaps associated with products of blue biotechnology feeding into other sectors of different colour, such as energy (marine algal biofuels), pharmaceuticals

Table 2.1 Biotechnology sub-sectors, associated colours and basis for delineation (Kafarski, 2012)

Biotechnology Sub-sector	Colour	Basis for Delineation
'Marine' or 'Blue'	Blue	Source of biomaterial
Medical and pharmaceutical	Red	Processes or markets
Agricultural	Green	Processes or markets
Nutritional	Yellow	Processes or markets
Industrial	White	Processes or markets
Environmental protection	Grey	Processes or markets
Management of deserts and arid regions	Brown	Processes or markets
Bioinformatics, computer science and chip technology	Gold	Processes or markets
Law, ethical and philosophical issues	Violet	Processes or markets
Bioterrorism and biological weapons	Dark	Processes or markets

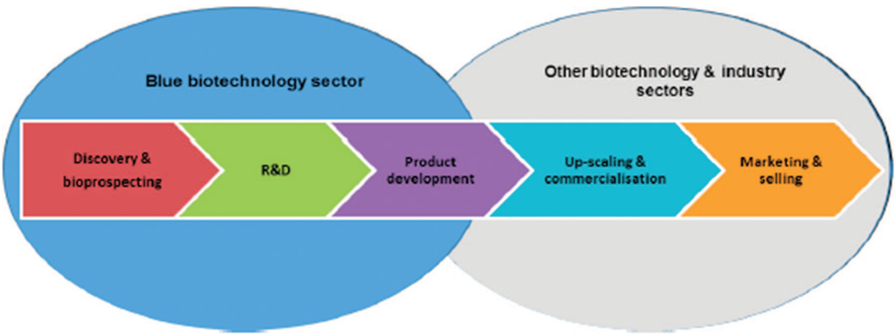

Figure 2.2 Visual representation of the blue biotechnology sector in Europe.
Source: ECORYS, 2014.

(novel antibacterials), cosmetics, aquaculture, food and nutrition, environmental protection and depollution (ECORYS, 2014; OECD, 2013; Marine Board, 2010). Subsequent stages or processes within the value chain become part of the wider biotechnology industry; these are separated from the marine component and should no longer be considered part of the blue biotechnology sector per se, but rather as part of any of the other classical biotechnology sub-sectors (ECORYS, 2014).

It is possible that definitions will change over time and that the distinction between 'blue' and 'marine' biotechnology may disappear. However, within this study, we strictly define blue biotechnology as requiring bio-material sourced from the oceans and define marine biotechnology more broadly as either involving sources from or applications in the marine environment.

2.1.2 Generic Value Chain of Blue Biotechnology

An alternative method for defining the blue biotechnology sector is through analysis of current marine biotechnology stakeholders. Building on the value chain approach, the position of stakeholders within the chain and the variety of activities conducted may then be considered (i.e. R&D, production, services and marketing) (see Figure 2.3) (ECORYS, 2014).

Key components of the generic value chain of blue biotechnology are listed in Figure 2.2 and include sectors such as discovery and bioprospecting. However, steps 2–5 in Figure 2.2 may not always be unique to blue biotechnology:

1. Discovery and bioprospecting: This initial phase of the value chain involves investigating environments and collecting living organisms. Extracts are made from organisms and genes may then be isolated to identify active gene products. Preliminary de-replication may take place at this time, as well as the establishment of preliminary evidence

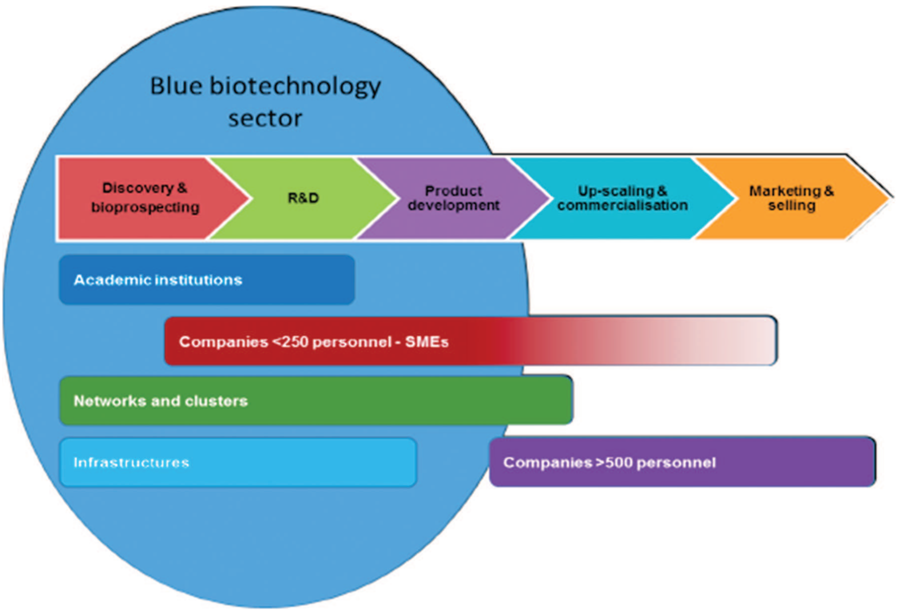

Figure 2.3 The value chain stakeholder composition in the marine biotechnology process. The sector is defined as in Figure 2.2.

Source: ECORYS, 2014.

for activity in lab-bench tests. This stage involves establishing the uniqueness and proprietary position of a particular environment.

2. Research and development: Extracts are taken from organisms during the R&D phase so that molecular components can be identified. Other activities which fall under R&D include: isolation of specific genes and gene products plus identification of their nature; de-replication of molecules and gene sequences/products; molecular characterisation of active molecules; structural identification; confirmation of proprietary position; synthetic strategies; and validation of preliminary bioactivity in further tests.
3. Product development: This step may involve the development of sustainable production strategies, chemical synthesis, gene isolation and the transfer to an industrially-useful organism with effective expression. Other potential activities include a demonstration of scale-up, stabilisation of the production process, preliminary demonstration of cost-efficiency and Life Cycle Analyses. Sufficient material is required during product development to confirm and extend the activity profile and to justify scale-up.
4. Up-scaling and commercialisation: Target organisms or molecules are produced economically and at an industrial-scale during this part of the blue biotechnology value chain. Other aspects include validated and stabilised extraction, purification and derivation processes for target molecules and materials. Positive production economics will also be considered.
5. Marketing and selling: This final step is based on the end-products of the value chain process. End-products may include pharmaceuticals, enzymes, hydrocolloids, nutraceuticals, cosmetic ingredients, biomimetic materials etc.

The value chain appears to become sub-sector specific at the stage of product development. Prior to that (i.e. discovery/bioprospecting, R&D and some aspects of product development) the value chain is normally common to all blue biotechnology applications and is a pre-requisite to the application of blue biotechnology in any given industry. The product development phase is often extensive and specific to the biotechnology or industrial sub-sector for which an application is intended. However, once a product has reached the stage of up-scaling and commercialisation, the ‘blue’ component diminishes and stakeholders are no longer limited to marine biotechnology, but are part of other biotechnology or industry sectors (ECORYS, 2014).

A number of risks are involved in bioprospecting. Firstly, too many novel organisms and molecules will be found, creating a bottleneck in screening, selecting and identifying desirable bioactivity. Another possible issue is the fact that organisms containing novel molecules may not be culturable in the lab. Even if organisms are culturable, the production of valuable molecules may vary between each batch that is grown. Other risks include the potential that molecules may be too complex for chemical synthesis, some genes may be isolatable but unable to express or transfer to a common industrial system, and successful production of target materials may not be replicable when culture is scaled-up. The associated risks are cumulative and may limit industry end-users' ability to see the opportunities present in blue biotechnology. Small and medium sized enterprises (SMEs), whether acting as facilitators or validators, need to be able to address this issue in order to attract end-user investment (ECORYS, 2014).

2.2 Market

2.2.1 Market Trends

The market associated with application of marine resource biotechnology has grown consistently over recent decades. For a number of commercialised products, the market exceeded several billion USD per annum by the year 2010, with a compound annual growth rate of 4–5% (or 10–12% under less conservative assumptions) (Leary et al., 2009). However, due to the absence of a universally accepted definition for the sector, it is difficult to evaluate its scope, structure and socio-economic performance (ECORYS, 2014). Global Industry Analysts, a market research agency, publishes reports on the approximate value of the blue biotechnology sector and estimate that the sector will reach USD 4.8 billion (EUR 3.5 billion) by the year 2020 (Global Industry Analysts, 2015). A study conducted by ECORYS (2014[1]) calculated that blue biotechnology currently contributes approximately 2%–5% of the total biotechnology industry. This suggests that in 2012 the European blue biotechnology sector may have been between EUR 302 million and 754 million (in terms of revenue). Healthcare biotechnology is considered the

[1]ECORYS calculation based on triangulation of ratio of Marine biotechnology compared to the whole biotechnology industry in terms of revenue using table Ernst & Young: Biotechnology Industry report 2013.

biggest and most rapidly growing end-use sector for marine biotechnology (Global Industry Analysts, 2011).

Potential applications of biotechnology in marine environments may include the following:

PUFAs

The discovery of polyunsaturated fatty acids (PUFAs, such as Omega-3 and Omega-6) and their importance for human health has long been established. The extraction of PUFAs mainly from fish has enabled its mainstream use in everyday life. Fish accumulate PUFAs through consumption of algae, and now that extraction of PUFAs directly from algae is possible, efficiency of extraction has increased (Medina et al., 1998). Application of PUFA-related knowledge to the aquaculture industry has for instance shown that PUFA-rich algae also benefits the growth and survival of shellfish (Reis Batista et al., 2013). Applying this knowledge to feedstock may in turn enhance future production of aquaculture and also result in aquaculture products with elevated PUFA concentrations.

Microbiomes

Possible applications in marine pest control include techniques to assess the composition and dynamics of microbiomes. The term microbiome originates from gene sequencing technology in microbiology and refers to an entire microbial population within a specific environmental niche. Microbiomes in different environments have been shown to change in population diversity and density as a function of changes in environmental conditions (for example: change in gut-microbiome in function of dietary shifts). Characterising microbiomes and their dynamics in and around ships (i.e. tanks, outer surfaces, bilges, etc.) can lead to new monitoring systems to check the emergence of environment-damaging organisms on board, and may also lead to advances in bioremediation to degrade organic pollutants in ballast water (Briand, 2011). The same technique can be used to assess fish health and response in rearing in aquaculture.

Coatings

Coatings with anti-fouling or anticorrosive properties are currently being developed and tested (Eduok et al., 2015). Analysis of an anti-fouling biocoating containing encapsulated bacteria from a Saudi hot-spring has been found to inhibit corrosion. This biocoating may have potential applications for ship hull protection and protection of off-shore installations.

2.3 Sector Industry Structure and Lifecycle – Sub-sectors and Segments

2.3.1 Present and Future Centres of Activity

International Level

To date, blue biotechnology has mostly been confined to the European Union (EU), North America and Far East Asia. Countries that have been highly active in the field of marine biotechnology include: USA, Brazil, Canada, China, Japan, Republic of Korea and Australia (Lloyd-Evans, 2013). Thailand, India, Chile, Argentina, Mexico and South Africa have also displayed increasing interest in marine biotechnology research. The United States has established itself as the leader in marine algal fuels and Asia has taken a leading role in the field of bioinformatics.

India has been heavily pursuing the development of a biotechnology sector, and to this end has been providing financial incentives, venture capital and associated infrastructure. DNA sequencing costs in India and other regions in Asia are generally low and may entice European companies to outsource their operations to these Asian countries. This could potentially weaken Europe's ability to advance their own bioinformatics sector (ECORYS, 2014).

European Sea Basins

Blue biotechnology is analysed as follows:

2.3.2 Atlantic Sea Basin

2.3.2.1 Assessment

The Coordination and Support Action (CSA) study "Marine Biotechnology RTDI in Europe – Inventory of strategic documents and activities" (2012) underlined that in the Atlantic, marine biotechnology already contributes to almost all other industry sectors (e.g. healthcare, environmental bioremediation, cosmetics and food). Many parts of the marine environment are still poorly understood. Therefore, marine resources have so far been largely unexploited and there appears to be significant potential for the discovery of new enzymes, biomaterials, biopolymers, and other associated products such as bio-pharmaceuticals and nutraceuticals. These products could potentially meet the needs for innovation required by industry to remain competitive in global markets.

The Atlantic area plays host to many Centres of Excellence in science, technology and innovation, has a solid reputation in the field of engineering, a stable political and governance system and a number of knowledge-based SMEs. This represents an exclusive opportunity for collaboration to improve the existing resource base and create new knowledge-based and internationally-traded goods and services that will improve the quality of life for local populations (Calewaert et al., 2012).

The following research issues have been identified by Calewaert et al. (2012) as of high importance for the Atlantic Sea Basin:

1. Molecular biology investigation in life science. Genomic and meta-genomic analysis of systematically sampled marine organisms, including microorganisms (i.e. bacteria, viruses, archaea, pico- and microplankton), algae and invertebrates;
2. Cultivation of marine organisms and cell lines. Development of technologies to isolate and culture previously uncultivated microorganisms. Developing culture methods for vertebrate and invertebrate cell lines for the production of active compounds;
3. Bio-mass production. Development and application of new and effective systems, including bio-engineering, bioreactors and cultivation systems, for the production, use and transformation of biomass from marine organisms. The production systems and organisms are optimized to target specific applications (e.g. biorefinery and aquaculture);
4. Marine model organisms. Identify and prioritise new organisms of marine origin to increase life science knowledge and provide new opportunities for biotechnological exploitation;
5. Production of biofuel from marine algae.

2.3.2.2 Main initiatives

Many infrastructures and initiatives related to marine biotechnology R&D are already present in countries of the Atlantic Sea basin area. However, there are as yet no major capacities organised at the regional level. An Atlantic macro-regional strategy is currently under development which may help to create a wider framework for regional collaboration. This strategy could also assist with addressing common goals associated with science and technology as well as targets linked to marine biotechnology.

Regional funding is mostly provided by the European Regional Development Fund (ERDF)[2], as well as through various other interregional co-operation programmes that aim to encourage collaboration between different regions within the EU (Calewaert et al., 2012).

[2]Based on the Seas-ERA (www.seas-era.eu) Atlantic Sea Basin Strategic Research Agenda (SRA).

2.3.2.3 Way forward

The European Atlantic is in a good position to take full advantage of marine biotechnology potential. With an established maritime heritage, extensive marine territories covering a wide variety of marine habitats (including the deep ocean) and renowned capability in the field of marine sciences, the European Atlantic Sea Basin area has plentiful opportunity to develop and exploit marine biological resources (Calewaert et al., 2012).

An EU Strategy for the Atlantic Region (EUSA) was launched in 2011 and represents one of the main science-policy developments currently implemented in the area. The aim of the EUSA is to provide a strategic framework and action plan to enable improved cooperation at the Union level. This will be achieved by improving the coordination of actions across a number of policy areas (Calewaert et al., 2012). Science, R&D and the management of research infrastructures are aspects of policy which stand to gain from improved regional coherence with the added bonus of potentially promoting technology transfer and innovation. This strategy is likely to significantly influence and benefit regional marine biotechnology activities (Calewaert et al., 2012).

2.3.3 Baltic Sea Basin

2.3.3.1 Assessment

The "Study on Blue Growth, Maritime Policy and the EU Strategy for the Baltic Sea Region" conducted by the EC (2013), identified the potential for Blue Growth in each of the EU Member States (MS) of the Baltic Sea Region (BSR) and at sea basin level. The study revealed that the blue biotechnology industry in the BSR is still nascent and very much focused on R&D. Blue biotechnology still has limited economic performance (it doesn't rank among the largest or fastest growing maritime economic activities (MEAs) in any MS in terms of gross value added (GVA) and employment size) and plays only a small role in the development plans of the region. Data related to GVA and employment MEA is not available for the period 2008–2010 (this is mostly because the data is non-existent but also because data is too limited to be quantified or not captured by statistics). Only Germany could be said to have highly developed biotechnology in the region. While competence centres and private companies working on blue biotechnology topics can be found in all countries around the Baltic Sea, Germany and in particular the State of Schleswig-Holstein is considered as the leader in this field and was selected as the benchmark case for blue biotechnology within the Baltic Sea Blue

Growth study. Denmark has also made strides to foster this sector, setting a strategic direction for the nation's blue biotechnology industry. In addition to Germany, Poland also ranks this sector among the maritime economic activities with most future potential in the years to come.

2.3.3.2 Main initiatives

Initiation of the SUBMARINER (Sustainable Uses of Baltic Marine Resources) Project represents the start of strengthening institutional set-ups for transnational blue biotechnology cooperation within the Baltic Sea area.

Another important initiative is ScanBalt® fmba (or ScanBalt). ScanBalt is an organisation for the Baltic Sea or Nordic-Baltic Region's Health and Bio Economy community. ScanBalt is a non-profit member association and functions as a service provider for members and also promotes the development of the ScanBalt BioRegion as a globally competitive macro-region and innovation market (Calewaert et al., 2012).

2.3.3.3 Way forward

The Baltic Sea Region has a long-standing custom of pursuing transnational cooperative programmes, which is an essential requirement for converting blue biotechnology research into commercially successful products and applications. However, at present, blue biotechnology plays only a minor role in Member State development strategies. This sector could be supported at sea-basin level by establishing joint research initiatives and by bridging the gap between basic and applied blue biotechnology research. The development of suitable funding structures, research networks and clusters would also be helpful (EC, 2014). By creating a targeted research strategy for marine biotechnology in the BSR, regional differences could be turned into advantages. For example, joint ventures between laboratories in the Eastern Baltic and sophisticated pharmaceutical industries in the West would provide mutual benefits (Calewaert et al., 2012).

2.3.4 Mediterranean Sea Basin

2.3.4.1 Assessment

The capacity and potential for marine biotechnology in Mediterranean counties is currently being mapped and some profiles can already be viewed on the Mediterranean Science Commission (CIESM) website. Mapping results are expected to raise awareness of this field of R&D as well as encourage the development of new enterprises both within and beyond the Mediterranean Sea Basin region (Calewaert and McDonough, 2013).

2.3.4.2 Main initiatives

No comprehensive regional strategy focusing specifically on marine biotechnology R&D yet exists within the Mediterranean Sea Basin. However, as stated by Calewaert et al. (2012), general marine science topics in this area may be studied by organisations such as CIESM or through projects like the SEAS-ERA scheme. Since the Mediterranean is regarded as one of the world's most important locations in terms of marine biodiversity (contributing between 4% and 18% of the World's marine species) the SEAS-ERA Project has set the following research priorities in the field of blue biotechnology: Bioprospecting for Marine Drugs and Fine Chemicals; Technologies to Increase Sustainability of Aquaculture Production; Biofuels from Micro- and Macroalgae. The CIESM has a Committee for Marine Microbiology and Biotechnology and their specific research areas include ecology and biodiversity of marine prokaryotes (Archaea and Bacteria), viruses and hetero- and autotrophic protists (i.e. phytoplankton), microbial food web interactions and microbial pathogens. An additional research initiative coordinated by the CIESM, operating within their Marine Economics Research Program, involves marine genetic resources and has resulted in a study focused on the economic models of bioprospecting (ECORYS, 2014).

2.3.5 Caribbean Sea Basin

No comprehensive information is available for the Caribbean Sea basin with regards to marine biotechnology activity. However, the CSA report "Global landscape of Marine Biotechnology RTDI" (Lloyd-Evans, 2013) provides a comprehensive list of research centres in Mexico involved in marine biotechnology, and indicates that bioprospecting is a particular field of interest. It is likely that the Caribbean Sea basin will prove promising as an area for bioprospecting and sampling for European R&D.

2.3.6 Business Lifecycle Stage

2.3.6.1 Overview of sub-sectors

Blue biotechnology can contribute towards several other biotechnology sectors (Figure 2.4). Sectors chosen for review in the ECORYS (2014) study include health, cosmetics, food, energy, aquaculture, environmental services (such as environmental protection and depollution) and other industrial applications (see Table 2.2 for details of sectors). The proportion of marine biotechnology stakeholders associated with any of the other biotechnology

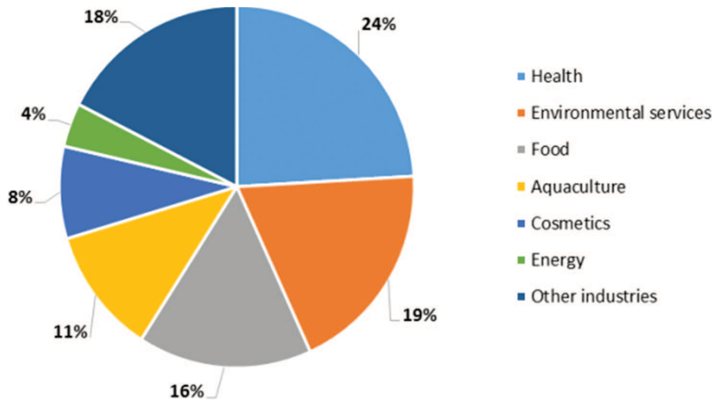

Figure 2.4 Distribution of stakeholders by sub-sector.

Source: ECORYS, 2014.

Table 2.2 Potential marine biotechnology products and services

Sub-sector	Potential Product Areas	Specific Product Areas
Health	Phrmaceuticals	Anti-cancer drugs, anti-viral drugs, novel antibiotics; wound healing; anti-inflammatory; immunomodulatory agents
	Biomaterials	Bioadhesives, wound dressings, dental biomaterials; alternative disinfectants (being more environmentally friendly and avoiding resistance development); medical polymers; dental biomaterials; coating for artificial bones that enhance biocompatibility; medical devices.
	Other	Tissues regeneration, 3D tissue culture
Cosmetics	Functional ingredients	UV-filter, after sun; viscosity control agents; surfactants; preservatives; liposomes, carrier systems for active ingredients; regulation of sebum;
	Raw materials	Micro and Macro-algae extracts; colourants, pigments; fragrances; hair-styling raw materials
Food	Functional foods	Prebiotics; omega 3 supplements;
	Nutraceuticals	Useful as antioxidants, anti-inflammatory; fat loss; reducing cholesterol; anti-HIV properties, antibiotic and mitogenic properties anti-tumour; iodine deficiency, goitre and myxoedema; anti-influenza; treatment of gastric ulcers;
	Food products and ingredients of marine origin	A stabiliser, suspending agents, bodying agents, makes a good jelly, prevents separation and cracking, suspending agent, foaming agent.

(*Continued*)

Table 2.2 Continued

Sub-sector	Potential Product Areas	Specific Product Areas
	Food packaging and conservation	Films and coatings with antimicrobial effects
Energy	Renewable energy processes (micro and macroalgae)	Microalgae; produce polysaccharides (sugars) and triacylglycerides (fats) that can be used for producing bioethanol and biodiesel. Macroalgae; large scale cultivation of macroalgae (seaweed) for the production of biofuel
	Microbial Enhanced Oil Recovery (MEOR)	Enhanced oil recovery and productive life oil reservoirs.
	Industrial additives	Anti-blur additives for textile printing, binding agent in welding rods, drilling fluid
Aquaculture	Seed	Surrogate broodstock technologies; transgenic approaches; developing culture species; selective breeding of existing cultured species for novel and disease resistant hybrids.
	Feed	Fish oils produced from algae; pigments in fish feed
	Disease Treatment	Diagnosis; treatment of disease; disease-resistant strains.
	Aquaculture systems	Treatment of re-circulated water.
Marine environmental health	Bioremediation	Biosurfactants (BS), bioemulsifiers (BE) induce emulsification, foaming, detergency, wetting dispersion, solubilisation of hydrophobic compounds and enhancing microbial growth enhancement; marine exopolysaccharides (EPs) induce emulsification.
	De-pollution	Removal of toxic elements including metals (lead, cadmium, zinc and metal ions); removal of dyes.
	Bio-sensing	Biomarkers and biosensors for soil sediment and water testing; to identify specific chemical compounds or particular physio-chemical conditions, presence of algal blooms, human health hazards.
	Antifouling	Reduce drag and fuel use for boat-going vessels without any negative environmental impacts.
	Bio-adhesives	Underwater industrial adhesives.
Other	Bio-refineries (separation of functional biomass components)	Biodiesel; feedstock for the chemistry industry; essential fatty acids, proteins and carbohydrates for food, feed for animals (replacement of feed with fishmeal) and production of proteins and chemical building blocks;

Source: ECORYS, 2014.

sectors can indicate the relative significance of marine biotechnology to these different fields. Stakeholders are commonly involved in more than one sector, indicating a variety of product portfolios. This also highlights the fact that academic groups routinely conduct a range of research activities associated with biological diversity rather than focusing on just one specific application field (i.e. one particular sector). Figure 2.4 indicates the distribution of stakeholders by sector. The key sectors in which marine biotechnology stakeholders participate are health (24%), environmental services (19%), food (16%) and other industrial applications (18%).

2.3.6.2 Sub-sector lifecycle stage

The lack of clear economic differentiation in blue biotechnology makes it difficult to find evidence for the stage of lifecycle that each associated sub-sector is in. Patents can be used as an indicator of sector development and, together with scientific publications, are a measure of output performance. Patents and publications can also be used to determine the potential strengths of a region, country or organisation with regards to this particular type of intellectual property protection (ECORYS, 2014). It should be recognised, however, that assessment of the patent situation does not always prove the economic potential of a specified sector. This is because other strategies for valorisation also exist. Patenting is regularly avoided due to the high associated costs and efforts, particularly when SMEs are involved. Therefore, this does not necessarily indicate a lack of commercialisation, but suggests a different approach. The majority of patents deal with compounds or genes rather than with particular production processes, leading to at least two possible consequences. Firstly, patents often concern more than one application field and thus, many patents belong to more than one sub-sector. For example, patents on “natural products” belong on average to three sub-sectors. By patenting the resources themselves, use of these compounds and genes in any process is more difficult for competing parties. Secondly, it indicates only the initial stages of product development. Nonetheless, since the costs of patenting are high, a patent can generally be interpreted to indicate high potential for commercialisation.

2.3.7 Trend Analysis of Patents

Trends in patenting-rate over time can indicate commercial profitability of patents in a subsector. According to ECORYS (2014), the number of patent publications has increased exponentially over the last 50 years, with a notable surge between years 2000 and 2010. Rates of increase were comparable across almost all sub-sectors. Analysis of trends up to the year 2020 suggests that the number of patents in most biotechnology sectors will stabilise whilst the cosmetics and energy sectors are likely to rise by a further 10–20% (ECORYS, 2014). In years 2006 and 2010 there was a decrease in the number of patent publications for nearly all fields linked to marine biotechnology. In 2011 and 2012 patenting increased again, but did not reach the levels observed in 2008 and 2009. These dates correspond with fluctuations in the global economy, suggesting that this sector is sensitive to larger economic factors. The majority of patents currently belong to the health sub-sector, indicating that this is likely to be the most financially interesting industry in the near future (see Figure 2.5) (ECORYS, 2014). At present, there is a lack of blue biotechnology products and services on the market, which corresponds with the fact that blue biotechnology is considered a 'young' field of biotechnology. Through observation of the patent categories, the health, cosmetics and food sectors appear to be the largest 'users' of blue biotechnology but their products have extensive trials and testing processes, extending the time taken to reach the market. Other associated subsectors are energy, aquaculture and marine environmental services. Collectively these subsectors are diverse and dynamic in nature, at different stages of development and have so far encountered different stages of growth.

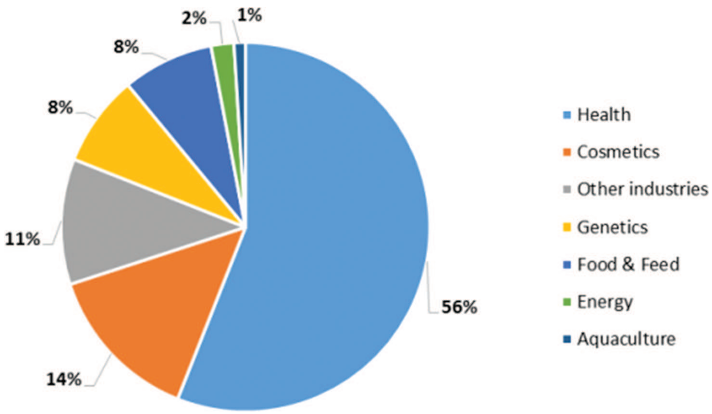

Figure 2.5 Distribution of patents across sub-sectors.

Source: ECORYS, 2014.

2.4 Working Environment

2.4.1 Employment and Skills Availability

Due to the broad nature of blue biotechnology, it is difficult to determine the economic value and employment that this sector creates. Furthermore, it is not possible to evaluate the working environment according to each Sea basin. Based on the stakeholder database developed by ECORYS (2014), total employment is currently thought to be between 11,500–40,000 people. These are usually high-end jobs and are the result of substantial public investment in education and training.

2.4.2 Revenues

Annual revenue for the European biotechnology industry is estimated to be approximately EUR 15 billion. Extrapolation from the entire EU bio-economic sector (using conservative estimates that blue biotechnology accounts for only 2–5% of the whole sector) suggests an annual turnover between EUR 302–754 million. Yearly growth rate of the EU blue biotechnology sector is in the region of 4–5%, slightly below that of biotechnology as a whole (6–8%) (ECORYS, 2014). In terms of end-use, healthcare biotechnology constitutes the largest and fastest growing end-use segment for blue biotechnology (Global Industry Analysts, 2015).

2.4.3 Stakeholders

An assessment conducted by ECORYS (2014) of a representative group of blue biotechnology stakeholders found that there are nine forms of stakeholder organisation. Academic institutions (universities or research institutes), SMEs and blue biotechnology network clusters are the main stakeholder categories. Large companies and infrastructure institutions were also found to be important stakeholders. The remainder were funding agencies, policy makers, medium companies (250–500 employees) and outreach professionals. Many stakeholders are involved in more than one industry sector, with the “other industries” sector as a common second field. This is particularly the case for SMEs that work in a number of product fields, e.g. developing processes for multiple purposes. Higher proportions of stakeholders are present in the health, environmental services and food sectors than in any of the other industry sectors.

ECORYS (2014) found that larger companies (more than 500 employees) do not typically specialise in or limit themselves to blue biotechnology.

Large corporations are typically broader in scope, work mostly within one particular biotechnology/industry sector and have links to blue biotechnology through specialised research centres. They play an important role in product up-scaling and commercialisation as well as in marketing.

2.4.4 Role of SMEs in Blue Biotechnology

SMEs are important actors in the blue biotechnology value chain as they bridge the gap between public sector R&D and commercialisation of products. Blue biotechnology SMEs are generally responsible for the initial product development stage of the value chain: identification, validation and de-risking of industrial opportunities related to marine bioresources (ECORYS, 2014). SMEs tend to be single-focus marine bioactives companies, operating at the high risk 'cash-burn' stage where screened products are converted into potential products for up-scaling and commercialisation. Due to the inherent risks associated with this phase, financing (often from venture capital) is unpredictable. SMEs can therefore be very vulnerable. A 17% fall in venture capital investment in SMEs was observed between 2008 and 2014, illustrating the unstable conditions that SMEs may have to deal with (ECORYS, 2014). This period corresponds to the global financial crisis, so is not unique to this sector. In addition, two SMEs focused on blue biotechnology experienced bankruptcies in 2013: AquaPharm[3] and BioAlvo[4].

The interface between SMEs and the downstream (large) corporations is emerging as one of the weakest links in the value chain (ECORYS, 2014). As noted by the Marine Board (Marine Board, 2010), most industrial contributions to marine biotechnology in Europe are generated through specialised SMEs, assuming most of the risks inherent in R&D and characterised by a rapid turn-over. Given the economic crisis in Europe and the consequent reductions in venture capital and public funding, there is a danger that the capacity of marine biotechnology SMEs to develop new technologies,

[3]Aquapharm Bio-discovery Ltd (founded 2000) was one of the first UK marine biotechnology companies dedicated to the discovery and commercialisation of novel compounds from the marine microbial biosphere, a relatively untapped renewable source of marine bio-diversity.

[4]Bioalvo, the Biotech for Natural Products, is a Portuguese start-up company that focused on fully integrated biotech solutions to maximise natural products market applications in areas as diverse as cosmetics, household products, nutraceuticals, pharmaceuticals or even industrial. It was ranked at the TOP 6 best companies in Europe's Most Innovative Biotech SME Award 2011.

processes and products may decline unless bigger companies are involved as investors.

The weak partnerships between researchers and industry has previously been underlined by the OECD (2013) in their report on blue biotechnology. According to this report, one big challenge is the timing of engagement between researchers and industry: '*Engagement with industry is often regarded as incidental to basic R&D or as post-research, downstream activity. This can leave R&D results stranded, either without a ready market or unable to reach the anticipated market for technical or feasibility reasons.*' Therefore, the OECD recommends an earlier collaboration with industry (within funded R&D projects) which would help to make sure that products of blue biotechnology research are appropriate for up-scaling and commercial production. However, this may also create concern in terms of divulging knowledge of downstream research, and therefore impede the development of research itself, due to confidentiality issues that the industry might want to push forward. EU rules on the management of Intellectual Property Rights (IPRs) in EU funded projects help in solving this issue by prescribing safeguards for confidentiality within the dissemination obligation.

2.4.5 Infrastructure and Clusters

As stated by ECORYS (2014), infrastructure institutions refer primarily to 'Marine Research Infrastructures (MRIs)[5] which support blue biotechnology activities and underpin the discovery and bioprospecting, R&D and to some extent product development stages in the value chain'. MRIs can be broken down into six clusters: research vessels and underwater vehicles; in situ data acquisition systems; satellites; experimental facilities for biology and ecosystem studies; marine data facilities; marine land-based facilities for engineering (for a comprehensive analysis refer to Annex 7 of ECORYS, 2014). Vessels and platforms required for prospecting and capturing marine resources can be extremely expensive to operate and these inherent costs must be properly understood when considering a blue biotechnology venture. Costs may be even higher if exploration takes place in deep water, particularly when extreme environments such as hydrothermal vents need to be sampled. Extreme marine environments are considered to have high potential for the

[5]Research infrastructures are facilities, resources and services used by the scientific community to conduct research and include libraries, databases, biological archives and collections (e.g. biobanks), large and small-scale research facilities (e.g. laboratories), research vessels, communication networks, and computing facilities.

discovery of innovative biological material, with specialised micro-faunal communities that have evolved to function under unusual temperatures, pressures and/or salinities. Therefore, the high costs of working in these areas must be anticipated (ECORYS, 2014).

Clusters and networks typically involve scientists, organisation of research activities and associated infrastructures. These groups can therefore be linked to the initial stages in the blue biotechnology value chain. For example:

- PôleMer France, consisting of the Pôle Mer Méditerranée and the Pôle Mer Bretagne, which has actively involved itself and its SME members in marine biotechnology projects;
- ScanBalt in northern Europe, which is working within the EU Strategy for the Baltic Sea and has established a flagship project SUBMARINER, sustainable uses of Baltic marine resources, with EU region support;
- The German industrial biotechnology cluster CLIB 2021 includes several marine-orientated SMEs amongst its members, including Bitop AG, C-LEcta GmbH, DIREVO Industrial Biotechnology GmbH, Evocatal GmbH and Swissaustral Biotech SA.

There are a number of initiatives and networks in Europe which specifically exist to coordinate marine research infrastructures and to facilitate access to them. For example, the Marine Biotechnology ERA-NET[6] is a consortium of national funding bodies to pool resources and undertake joint funding of transnational projects in the area of marine biotechnology.

2.4.6 Public Policy Regulatory Framework

2.4.6.1 International and regional legal frameworks

All activities undertaken in the marine environment are subject to international law of the sea, codified by the United Nations Convention on the Law of the Sea (UNCLOS) of 1982. However, this Convention does not refer to blue biotechnology, nor to marine genetic resources, as it pre-dates most of the

[6] The **vision of the Marine Biotechnology ERA-NET (ERA-MarineBiotech or ERA-MBT) project** is to support Europe's marine biotechnology community to participate in a lasting enterprise-driven network that adds value to marine biological resources in ways that nurture and sustain the lives of European citizens. The ERA-MarineBiotech is therefore designed to deliver **better coordination** of relevant national and regional Research, Technology, Development and Innovation (RTDI) programmes in Europe, **reducing fragmentation and duplication**, and paving the way for common programmes and cooperation in the provision and use of research infrastructures.

scientific discoveries that resulted in development of these sectors. Accessing marine genetic resources is also subject to the Convention on Biological Diversity (CBD) of 1992 and its Nagoya Protocol signed in 2010 and which entered into force in 2014.

United Nations Convention on the Law of the Sea

According to the law of the sea (1982), several obligations have to be fulfilled before and while undertaking marine scientific research, such as:

- Request to the coastal state for a permit to undertake marine scientific research in its Exclusive Economic Zone (EEZ) or continental shelf (Article 248 UNCLOS);
- Report and share with the coastal states the data, samples and research results (Article 249 UNCLOS);
- To cooperate on a global and regional level (Articles 242–244 UNCLOS);
- If marine scientific research of biological material or sampling of marine genetic resources is undertaken in Areas Beyond National Jurisdiction (ABNJ), access is free (so far) and needs to be conducted exclusively for peaceful purposes;
- Use of appropriate scientific methods;
- Shall not unjustifiably interfere with other legitimate uses of the sea;
- Shall be in compliance with all relevant regulations including adoption of necessary measures for protection of the marine environment (Part XII and XIII UNCLOS).

In 2015, a decision was made by member states of the United Nations to begin negotiations for an Implementing Agreement to UNCLOS with the aim of regulating biodiversity in ABNJ (UNGA resolution 69/292, 2015). This agreement will likely have implications for accessing and utilizing genetic resources derived from ABNJ, in terms of benefit-sharing (UNGA resolution 66/231, 2011).

Convention on Biological Diversity and Nagoya Protocol

Accessing marine genetic resources in maritime areas within national jurisdiction is subject to the prior informed consent (PIC) of the provider country (in case the provider's legislation requires so); to the negotiation of mutually agreed terms (MAT) on utilisation of the accessed genetic resources and to the share of the benefits arising from such utilisation. Therefore, before sampling the seas in areas within national jurisdiction, it is crucial to verify whether the national legislation of that country prescribes any constraints in terms of access and benefit-sharing (ABS). This has an influence on and potentially raises the burden of every scientific expedition in the sea, which is usually undertaken with basic research purpose and which is at the basis of the pipeline of blue biotechnology (ECORYS, 2014).

The Nagoya Protocol has been implemented in the EU (Regulation (EU) No 511/2014, 2014). It does not regulate access (every EU Member State is free to regulate access to its own genetic resources), but it regulates users' compliance. Therefore, the Nagoya Protocol has a more significant impact on parts of the research pipeline following sampling and bioprospecting. Users are obliged to exercise due diligence in order to establish that genetic resources and associated knowledge have been accessed in accordance with applicable ABS legislation. In addition, benefits must be fairly and equitably shared upon mutually agreed terms, also in accordance with applicable legislation. Therefore, users shall transfer information on where the utilized genetic resources have been collected, when and under which legal circumstances (PIC-MAT and benefit-sharing). This regulation has only recently been implemented, so it is still too early to evaluate the impact it will have on blue biotechnology (ECORYS, 2014).

Beyond these international regulations, the research and product development steps of blue biotechnology have to comply with international, regional and national obligations on biosafety and any other relevant rules concerning biotechnology activities. However, these rules and obligations go beyond the scope of the present chapter as they are not unique to blue biotechnology, but instead apply to the whole biotechnology sector.

2.4.6.2 European policy framework

In common with all sectors of the Blue Economy, the primary strategic legal and policy framework is the Marine Strategy Framework Directive (MSFD). In addition, the Sea basins strategy elaborated by the EC has an influence on research activities in the field of blue biotechnology. A number of strategic documents have been published as a result of science, policy and research initiatives over the last decade. The EC has acknowledged the potential of blue biotechnology in Europe through its Communication on Blue Growth (COM/2012/494) and European Bioeconomy Strategy (COM/2012/60), both of which identify blue biotechnology as a sector that has the possibility to contribute to bioeconomy and to economic growth in general. Furthermore, EU research policy has been responsive to the growing awareness of the importance of blue biotechnology: the EU has funded key research on blue biotechnology in its Framework Programmes for Research FP6, FP7 and Horizon 2020. The EU's Horizon 2020 Strategy and support programme specifically addresses blue biotechnology and marine biomass as contributors to the economy of the future (COM/2012/494). However, no comprehensive and specific blue biotechnology policy yet exists in Europe, although Ireland, Denmark and Norway do have relevant national policies in place. Most countries support blue biotechnology R&D under a wider strategic umbrella, either within an overarching science and technology strategy, as part of a more general marine or biotechnology research plan or as a combination of both (Table 2.3) (ECORYS, 2014). Portugal, for example, does

Table 2.3 Overview of European countries with the level of focus and available mechanisms to support marine biotechnology activities, as identified by the CSA Marine Biotechnology project's preliminary landscape profiling exercise (Calewaert et al., 2012). (Adapted from: ECORYS, 2014).

Countries with a dedicated plan, programme or strong policy focus on marine biotech	Countries where marine biotech is supported via more wide-scope programmes and/or instruments (general science and technology plans, marine science plans and/or biotechnology plans/strategies)		
	Countries with considerable interest and/or activities in marine biotechnology research and development*	Countries with some interest and activities in marine biotechnology research and development*	Countries where there is only limited marine biotech focus and activities*
• Ireland • Denmark • Norway	• Belgium*** • France • Germany*** • The Netherlands • Poland • Portugal • Italy** • Spain • Sweden • UK	• Croatia • Greece • Finland** • Iceland • Romania • Slovenia • Turkey	• Austria** • Bulgaria • Estonia** • Latvia** • Lithuania** • Malta** • Switzerland** • Ukraine**

**Based on the information that could be collected within the scope of the CSA Marine Biotechnology;*

***Countries for which no or only limited information could be collected within the scope of the CSA Marine Biotechnology;*

****Countries with a federal structure with considerable activities in one or more specific coastal regions* not have a dedicated blue biotechnology strategy or plan, but a more generic marine strategy (National Strategy for the Sea) containing ample reference to the strategic importance of blue biotechnology research while currently, in practice, the R&D activities in this field still remain very fragmented. In a growing number of countries there is also significant focus on support for activities that stimulate what is called the “biobased economy”, echoing largely the EC’s strategy and action plan “Innovating for Sustainable Growth: a Bioeconomy for Europe” which was adopted in early 2012 (Calewaert et al., 2012). The report also underlined difficulties in gathering up-to-date information in the different countries.

The CSA Marine Biotechnology analysis (Calewaert et al., 2012) revealed that the national priorities identified include the following:

- Marine bioprospecting/biodiscovery (in particular for human health and new industrial compounds);
- Development of robust, biotechnology-based state of the art R&D tools and infrastructures tailored for blue biotechnology;
- Molecular aquaculture;
- Biomass production for bioenergy and fine chemicals;
- Marine environmental biotechnology applications and bio-sensors in the context of the European Marine Strategy Framework Directive (MSFD).

2.5 Innovation

2.5.1 State of Technology and Trends

Europe is active within the R&D stage of the blue biotechnology value chain and generates almost a third of the scientific publications in this field. However, a striking difference emerges when comparing scientific activity to trends in patent publication. Europe represents only 13% of patents filed in connection with new marine molecules, suggesting limited success in developing products from promising resources. In contrast, Japan and China appear far more active in patent publication than in scientific publication (ECORYS, 2014). Therefore, it seems that whilst Europe is strong in coordinating research activities in the early stages of the value chain, there may be a lack of coordination further along the chain between those conducting research or initial product development (mainly research institutes and SMEs) and investors (larger companies with the resources to up-scale and commercialise a product) and the industry within which the blue biotechnology application will be used.

2.6 Investment

Blue biotechnology is a new area of biotechnology that is considered rather 'invisible' by current key players. The sector is complex and from the outside there is little understanding of what exactly it is. As such, blue biotechnology is seen as fairly unattractive to investors and investment has so far been hard to come by (ECORYS, 2014).

In the context of blue biotechnology, research institutes and universities are fundamental to the discovery, bioprospecting and R&D phases, and are also central to research associated with the identification of new species and molecules from different marine environments. SMEs are similarly focused on the earlier stages of the value chain, concentrating efforts on identification, validation and de-risking of industrial opportunities linked to marine biological resources. This is because for SMEs these stages often represent a cost chain (in other words, the cash-burn stage prior to income-generation). Nevertheless, SMEs are commonly also the most active generators of innovation, with the generic business model based on a very diverse product portfolio, often comprising of non-marine in addition to marine related services. SMEs tend to be absent from industrial production of natural marine products, for reasons mostly linked to high capital expenditure. They will also not be involved in the commercial-scale or demonstration-scale levels of energy production from algae, again due to the associated high capital expenditure.

ECORYS (2014) found that financing is a major issue for SMEs involved in blue biotechnology. Typically, an investment company will have only one marine-orientated/ -involved company in its portfolio. Therefore, in the absence of easy access to investment, publicly funded research collaborations are usually part of a funding model and SMEs may work in collaboration with researchers at universities or institutes and also with larger industrial companies. Universities and research organisations are frequently involved in the stages from bioprospecting to identification and characterization, but may also be involved in industrial adaptation, often as part of contract funding by industry or publicly funded, industry-facing consortia. As a result of the cash-limitations associated with SMEs, plus the limited power they have to bring blue biotechnology products to market, they require downstream linkages to end-users to whom they can sell or license their innovations, products and processes or who may become their exits through trade sale, and to investors who can help them survive longer while they validate and de-risk their developments. The difficulty for SMEs in maintaining momentum through the value chain when blue biotechnology is being applied to biomedical and industrial applications has been recognised by CIESM. As an innovative policy initiative, the CIESM advocates linking SMEs with biotechnology associations, venture capitals, financing bodies and other stakeholders who can help them tackle financial challenges and constraints (Briand, 2011).

According to ECORYS (2014), there is at present no comprehensive European inventory of micro-, small- and medium-sized enterprises working in the field of blue biotechnology. A brief scan for this type of information returns more than 140 SMEs working on various aspects of the marine bioresource value chain.

A literature review and stakeholder discussions (conducted as part of the public consultation launched by the EC in November 2013 and also in various stakeholder workshops organised on blue biotechnology) indicated that the lack of coordination and collaboration between academia and industry at the EU level was the biggest barrier to the development of blue biotechnology, even though it was noted that some examples of productive partnership do exist, such as the open innovation approaches adopted both by Unilever and P&G. ECORYS (2014) also suggest that there may be a lack of collaboration between investors, SMEs and industry in relation to product development, up-scaling and commercialisation. Stakeholders identified the need for an interface between industry, research and policy because the approach to blue biotechnology research in Europe is still fragmented. The Marine Biotechnology ERA-NET does in fact aim to close this loophole and improve coordination between funding agencies. Important efforts have recently begun at the national, regional and European level to create clusters, initiatives and networks with the aim of providing a coherent framework for blue biotechnology activities. However, at present there are still too few platforms through which investors and SMEs can be brought together and in general the number of clusters remains small compared to the number of areas that could potentially use blue biotechnology to assist with regional development (ECORYS, 2014).

2.7 Uncertainties and Concluding Remarks

2.7.1 Bottlenecks and Way Forward

The EU blue biotechnology sector is not yet fulfilling its true potential. This is likely due to a number of barriers specific to the EU blue biotechnology sector (ECORYS, 2014):

- Difficulty in sampling the huge diversity of resources;
- Potential high cost of sampling some of these;
- The consequent preponderance of public funding for Research and Development;
- The complexity of property rights under marine governance mediated by UNCLOS;
- The lack of clarity on the mechanism for benefit sharing, particularly in marine systems with regards to the Nagoya Protocol;
- The uncertainty of the status of genetic resources in Areas Beyond National Jurisdiction;
- The dependence upon vulnerable SMEs and high risk investments to translate R&D results into a marketable product for commercialisation;
- Problems of economic data availability within a poorly defined sector, and
- Weak coordination between public research, SMEs and investors, due to a low number of clusters compared to other sectors.

Blue biotechnology still needs to deliver a huge amount of basic research, given that marine biotechnology is a relatively new area and considering the current low level of knowledge on marine biodiversity. It might be the case that incentives are needed for all key players to ensure that the whole innovation and development pipeline is established (OECD, 2013). ECORYS (2014) found that EU competitiveness in the field of blue biotechnology lies in support of R&D activities. The EU appears to be particularly strong in developing important infrastructure, financial support for companies involved in research and innovative new ways to access marine biological resources. The ability for researchers and companies to access new marine resources is crucial and may currently be limiting the European blue biotechnology sector. As competition between countries increases, it is thought that access to material (particularly from extreme environments) will become more difficult. Access will also be influenced by the development of legislation in coastal states concerning protection of genetic resources within their EEZs.

Several cross-cutting and interwoven barriers currently exist with regards to the development of the blue biotechnology sector. One of the most significant barriers is related to the fact that blue biotechnology has so far been sponsored and promoted mainly by policy bodies and rather ignored by "the sector" (i.e. large companies) which has all the means to make it a success. Other issues are associated with benefit sharing from the discovery of new marine biological resources, both on the high seas and between states.

The lack of clarity can cause legal uncertainty and risks to investment in terms of the source and traceability of material used in blue biotechnology products. These uncertainties also have implications for policy required to overcome barriers and to help the EU reach its full blue biotechnology potential.

References

Arrieta, J., Arnaud-Haond, S., Duarte, C. M., (2010). What lies underneath: Conserving the Ocean's Genetic Resources. Proceedings of the National Academy of Sciences 107(43): 18318–18324.

Blunt, J. W., Copp, B. R., Keyzers, R. A., Munro, M. H., Prinsep, M. R., (2013). Marine natural products. Natural Product Reports 30: 237–323.

Børresen, T., Boyen, C., Dobson, A., Höfle, M., Ianora, A., Jaspars, M., Kijjoa, A., Olafsen, J., Querellou, J., Rigos, G. and Wijffels, R. H., (2010). Marine Biotechnology: A New Vision and Strategy for Europe. Marine Board-ESF Position Paper, 15. www.marineboard.eu/file/45/

Briand F (Ed.) (2011). New Partnerships for Blue Biotechnology Development: innovative solutions from the sea. Proceedings of the CIESM International Workshop, Monaco, 11–12 Nov 2010. http://www.ciesm.org/WK_BIOTECH_REPORT_2010.pdf

Calewaert, J-B., Piniella, Á. M. and McDonough, N., (2012). Marine Biotechnology RTDI in Europe – Inventory of strategic documents and activities. Deliverable No. 3.5. Inventory report of marine biotechnology RTDI in Europe. Part of Task 3.1. Inventory of Marine Biotechnology RTDI Strategies, Programmes and Initiatives Report. Marine Board-ESF http://www.marinebiotech.eu/sites/marinebiotech.eu/files/public/library/CSA%20project%20reports/Marine%20Biotechnology%20RTDI%20in%20Europe%20Inventory%20of%20strategic%20documents%20and%20activities.pdf

Calewaert, J-B. and McDonough, N., (2013). Marine Biotechnology RTDI in Europe – Strategic Analysis. Deliverable No. 3.6 Report on strategic analysis of marine biotechnology RTDI in Europe. Part of Task 3.3. Preliminary Analysis of the European Marine Biotechnology RTDI Landscape. Marine Board-ESF http://www.marinebiotech.eu/sites/marinebiotech.eu/files/public/library/CSA%20project%20reports/Marine%20Biotechnology%20RTDI%20in%20Europe.pdf

Convention on Biological Diversity (CBD), Nairobi, (1992). In force 29 December 1993, 31 International Legal Materials 822.

Collaborative Working Group on Marine Biotechnology, (2009). Background and recommendations on future actions for integrated marine biotechnology R&D in Europe http://www.marinebiotech.eu/sites/marinebiotech.eu/files/public/library/MBT%20publications/2009%20kbbenet%20report%20distributed.pdf

European Commission, (2012). Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. Blue Growth: Opportunities for Marine and Maritime Sustainable Growth. http://ec.europa.eu/transparency/regdoc/rep/1/2012/EN/1-2012-494-EN-F1-1.Pdf

European Commission, (2012). Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. Innovating for Sustainable Growth: A Bioeconomy for Europe http://ec.europa.eu/research/bioeconomy/pdf/201202_innovating_sustainable_growth_en.pdf

European Commission, (2013). Study on Blue Growth, Maritime Policy and the EU Strategy for the Baltic Sea Region. https://webgate.ec.europa.eu/maritimeforum/en/node/3550

European Commission, (2014). A Sustainable Blue Growth Agenda for the Baltic Sea Region. http://ec.europa.eu/maritimeaffairs/policy/sea_basins/baltic_sea/index_en.htm

ECORYS, (2014). Study in support of Impact Assessment work on Blue Biotechnology, FWC MARE/2012706 – SC C1/2013/03 – 13 June 2014

Eduok, U., Suleiman, R., Gittens, J., Khaled, M., Smith, T. J., Akid, R., El Ali, B., Khalil, A., (2015) Anticorrosion/antifouling properties of bacterial spore-loaded sol–gel type coating for mild steel in saline marine condition: a case of thermophilic strain of Bacillus licheniformis. RSC Advances 5: 93818–93830. DOI: 10.1039/c5ra16494j

Global Industry Analysts Inc. (2011) "Marine Biotechnology: A Global Strategic Business Report"

Global Industry Analysts Inc. (2015) "Marine Biotechnology: A Global Strategic Business Report" http://www.strategyr.com/pressMCP-1612.asp

Hayes, M., Carney, B., Slater, J., Brück, W., (2008). Mining marine shellfish wastes for bioactive molecules: Chitin and chitosan – Part B: Applications. Biotechnology Journal 3: 878–889. DOI 10.1002/biot.200800027.

Heip, C. and McDonough, N., (2012). Marine biodiversity: a science roadmap for Europe. European Marine Board. http://www.marineboard.eu/images/publications/Marine%20Biodiversity-122.pdf

Kafarski, P., (2012). Rainbow code of biotechnology. CHEMIK nauka-technika-rynek, 1(66), pp. 811–816.

Leal M. C., Puga J., (2012). Trends in the Discovery of New Marine Natural Products from Invertebrates over the Last Two Decades – Where and What Are We Bioprospecting? PLoS ONE 7(1): e30580.

Leary, D., Vierros, M., Hamon, G., Arico, S., Monagle, C., (2009). Marine genetic resources: A review of scientific and commercial interest. Marine Policy 33(2): 183–194.

Lloyd-Evans, M., (2013). A Global Perspective: High-level analysis of key trends and developments in global marine biotechnology RTDI. BioBridge Ltd. Marine Biotechnology CSA – Task 3.2

Medina, A. R., Grima, E. M., Giménez, A. G. and González, M. I., (1998). Downstream processing of algal polyunsaturated fatty acids. *Biotechnology Advances*, *16*(3), pp. 517–580.

Molinski, T. F., Dalisay, D. S., Lievens, S. L., Saludes, J. P., (2009). Drug development from marine natural products. Nature Reviews Drug Discovery 8: 69–85.

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 (the 'Nagoya Protocol'), Nagoya (2010). In force 12 October 2014. Convention on Biological Diversity.

OECD, (2005). A framework for biotechnology statistics. Paris.

OECD, (2012). OECD Global Forum on Biotechnology: Marine Biotechnology Enabling Solutions for Ocean Productivity and Sustainability. Workshop (Vancouver, Canada, 30–31 May 2012).

OECD, (2013). Marine Biotechnology: Enabling Solutions for Ocean Productivity and Sustainability, OECD Publishing. http://dx.doi.org/10.1787/9789264194243-en This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 652629.

OECD, (2016). Marine Biotechnology: Definitions, Infrastructures and Directions for Innovation. Working Party on Biotechnology, Nanotechnology and Converging Technologies. http://www.marinebiotech.eu/sites/marinebiotech.eu/files/public/DSTI_STP_BNCT_2016_10.pdf

Regulation (EU) No 511/2014 of the European Parliament and of the Council of 16 April 2014 on compliance measures for users from the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization in the Union Text with EEA relevance (OJ L 150, 20/05/2014, p. 59)

Reis Batista, I., Kamermans, P., Verdegem, M. C. J., Smaal, A. C., (2013) Growth and fatty acid composition of juvenile Cerastoderma edule (L.) fed live microalgae diets with different fatty acid profiles. Aquaculture Nutrition 20(2): 132–142. DOI: 10.1111/anu.12059 http://www.marinebiotech.eu/sites/marinebiotech.eu/files/public/library/CSA%20project%20reports/Marine%20Biotechnology%20RTDI%20in%20Europe.pdf

United Nations Convention on the Law of the Sea (UNCLOS), Montego Bay, (1982). In force: 16 November 1994, 1833 United Nations Treaty Series 396

United Nations General Assembly (UNGA) resolution 69/292, (06 July 2015). Development of an international legally-binding instrument under the United Nations Convention on the Law of the Sea on the conservation and sustainable use of marine biological diversity of areas beyond national jurisdiction. UN doc A/RES/69/292

United Nations General Assembly (UNGA) resolution 66/231, (24 December 2011). 'Oceans and the law of the sea.' UN docA/RES/66/231, paragraph 167.

Van der Graaf, A. J., Ainslie, M. A., André, M., Brensing, K., Dalen, J., Dekeling, R. P. A., Robinson, S., Tasker, M. L., Thomsen, F. and Werner, S., (2012). European Marine Strategy Framework Directive-Good Environmental Status (MSFD GES): Report of the Technical Subgroup on Underwater noise and other forms of energy. *Brussels*.