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#### **FOREWORD**

Marine biotechnology is key to realising the potential of marine bio-resources – a potential that until now remains largely untapped. These resources could produce new products and processes, and help address the global challenges of food, energy, and health. Other critical outcomes of marine biotechnology work include the development of innovative tools and solutions for more sustainable marine environmental management. As a first step in developing policy and strategic roadmaps to tap that potential, however, countries must first decide on what marine biotechnology actually refers to, and arrive at an understanding of how the effects of policy actions can be evaluated.

The OECD Working Party on Biotechnology (WPB), which has now been subsumed by the Working Party on Biotechnology, Nanotechnology, and Converging Technologies (BNCT), had been examining the topic of marine biotechnology since 2011. Taking that necessary first step, following workshop discussion, the WPB proposed a definition of the term that is based on, and can be used alongside, the existing OECD general definition employed in statistical data collection. Talks held at two workshops that followed focused on lessons to be learned from using the OECD Framework for Biotechnology Statistics, and on how the impact of marine biotechnology can be analysed over time.

A first OECD report from this work, published in 2013, was titled "Marine biotechnology: Enabling solutions for ocean productivity and sustainability". This report highlights the many possibilities for marine biotechnology to address global challenges and to be a driver of economic growth – as well as the challenges inherent in realising that potential.

Some of those challenges were explored further in the programme of work that followed, 2013-14. They included economic monitoring of the impacts of strategic actions or programmes for marine biotechnology; the statistics, and the indicators that such monitoring would entail; the sharing of large research infrastructures for dedicated goals; and governance issues concerning these infrastructures.

The WPB went on to organise a thematic session in Paris in June 2014 to underline the opportunities that marine biotechnology can offer the Next Production Revolution, and to address global challenges for health and well-being or for sufficient food supply for a growing and ageing population.

This report, summarising previous work, is the final report on marine biotechnology for the biennium of the Programme of Work and Budget (PWB) 2013-14. The OECD is grateful to the steering group of the marine biotechnology work. The OECD Working Party on Biotechnology, Nanotechnology, and Converging Technologies approved this report in August 2016. It was subsequently approved and declassified by the Committee for Science and Technology Policy (CSTP) on 24 May 2017.

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#### **EXECUTIVE SUMMARY**

International interest in marine biotechnology has been growing over the years as a result of scientific advances. Our increased knowledge of marine biodiversity, and the subsequent development of tools and technologies to access and study marine organisms and ecosystems, present promising opportunities and great potential for sustainable growth. Marine bio-resources hold untapped potential as a source of new products and processes, and may help to address the global challenges of food, energy and health, as well as contribute to green growth and sustainable industries. Marine biotechnology is key to realising this potential.

Several countries have been setting up strategic roadmaps to support green growth through that technology. Implementation of a roadmap needs to be accompanied by funding and investment plans, and an evaluation to measure the effect of the roadmap and its supporting investments. In that type of policy development process, it is first essential to arrive at a clear definition of marine biotechnology, and to formulate appropriate indicators so as to understand how the effects of policy actions can be evaluated.

It will not be possible to fully develop bio-economy and green growth *without* the contribution of the oceans' potential for biomass and food production. The production from algae of bio-based chemicals, plastics and biofuel has been shown to be promising. In the future, production and bio-refinery costs are expected to decrease; developing integrated marine bio-refineries for the production of high-value bio-based products will be crucial, to capitalise on the opportunities available.

In the field of food production for a growing world population as well, marine biotechnology will be essential. "-omics" technologies for better aquaculture and feed production for aquaculture are giving rise to new innovative applications. Marine biotechnology will also become more important for lifelong health and well-being. Potent new drugs of marine origin are being discovered and tested. Very often these new molecules have very complex structures, so that rational design to develop these activities is hard to imagine. Insights into biosynthetic pathways allow further development through synthetic biology. Although marine biotechnology for drug development indeed appear promising, probably the largest opportunities for innovation will come from building on the new trend of consumers in search of natural products for health and well-being. Nutraceuticals and cosmeceuticals from marine resources are being developed, and their considerable benefits continue to be recognised.

## **Key findings**

A useful single definition for marine biotechnology is the following: "The application of science and technology to living organisms from marine resources, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services." A list of biotechnology techniques can also serve as a definition, and this are provided in the report below. The list is indicative rather than exhaustive and is expected to change over time as data collection and biotechnology activities evolve.

Marine biotechnology is not a standalone field, but is expected to contribute in the future to the development of a mature bio-economy, one that relies on biomass of marine origin for biofuel, and on higher-end bio-based products from marine resources.

- Marine biotechnology's important potential for many applications and in many different industrial sectors is a relevant point when measuring the bio-economy.
- Marine biotechnology's potential for innovative applications and market share is expected to
  grow as more applications based on marine resources become available. Measuring the impact of
  marine biotechnology as a segment contributing to the bio-economy and the ocean economy will
  make this all the more clear.
- There is a gap in accessible research infrastructure for marine biotechnology. Although the needs for research infrastructure generally may be of a more generic character, it is clear that the envisaged scale of opportunities offered by marine biotechnology, linked to the immensity of the ocean's environment, calls for special requirements.
- The shared and dynamic nature of ocean bio-resources, together with the sheer size of the development opportunities (and challenges), means that co-operation, both national and international, is a basic requirement to develop infrastructure to support marine biotechnology.
- One of the most urgent needs related to research infrastructures is standardisation of data or sample collection, storage and management, curation of data, storage and calculation capacity, and legal frameworks to use (raw) data. The linking of and communication among databases is a particular challenge.
- The main infrastructures important for marine biotechnology focus on the collection of marine organisms (EMBRC, the European Marine Biological Resource Centre and MIRRI, the Microbial Resource Research Infrastructure) or on the collection biomolecular data (ELIXIR, the European Life-Science Infrastructure for Biological Information). The listed challenges related to research infrastructures are common goals of the European Strategic Forum on Research Infrastructure.
- Few research infrastructures have drawn firm financial commitments for investments and operations from prospective partners, stakeholders and funding agencies, although long-term financial commitments are in fact thought to be a requirement to meet international ambitions. For the running costs as well, a clear long-term framework should be available. Investments still largely depend on national authorities. Therefore, national infrastructures are also still important to address the wealth offered from marine resources. An overview is given of some national marine research infrastructures that often have international impact.
- Public-private partnerships can engage in joint financing of data collection and management
  equipment and functions, while taking into account the different interests of well-established and
  emerging marine industries.

## **PART I**

## MARINE BIOTECHNOLOGY DEFINITIONS, INDICATORS AND INFRASTRUCTURES

Part I tracks the efforts of various bodies to determine the specific elements covered by the term "marine biotechnology", and the resulting evolution toward both single and list-based statistical definitions. The section then explores the considerations necessary in defining indicators to enable the collection of related statistical data. The importance of open access to research infrastructure is stressed, along with the urgent need for standardisation in the way data are handled, from sample collection to management. Considerations regarding new vs. existing infrastructures conclude the section.

## **Defining marine biotechnology**

Understanding the current global use of the term "marine biotechnology" and the specific elements that the term covers is important for arriving at a consensus for an ultimate, harmonised definition. That consensus is essential – for measuring the impact of national or regional strategies, for public or private investments in marine biotechnology, and for enabling the comparison of biotechnology indicators across countries and over time. In the course of a workshop to discuss the definition of marine biotechnology, the European Commission stressed the importance of consensus regarding the term for developing policy options and new initiatives, and specifically for maritime affairs policy. The definition would need to delineate what is covered by marine biotechnology as contributing to one of the five areas (blue energy; aquaculture; maritime, coastal and cruise tourism; marine mineral resources; and marine biotechnology) of the long-term European Union (EU) strategy "Blue Growth: Opportunities for Marine and Maritime Sustainable Growth". That strategy provides for additional effort at EU level to 2020 to stimulate long-term growth and jobs in the blue or ocean economy, in line with the objectives of the Europe 2020 strategy. 

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In the context of the EU, two groups have been instrumental in contributing to the development of a suitable definition. One group was the Collaborative Working Group (CWG),5 which acted as a sub-group within the high-level expert group called KBBE-net6 (Knowledge Based Bio-Economy Network). The second was the European Marine Board.7 The input of both groups has been drawn on, for example, in European Commission policies and programmes.

The definition provided by the Mediterranean Science Commission (CIESM) on behalf of the Mediterranean region is also worth noting as it points out the potential of the marine biotechnology sector for economic and social wealth. Indeed, the areas of application of marine biotechnology products and services create a great deal of indirect activities and may include all maritime industrial stakeholders – from maritime transport to offshore industries and aquaculture. The workshop debate also underlined those specific features of the marine biotechnology sector in which marine genetic resources are the focus of international agreements at UN level, so that international multilateral agreements will be crucial for this part of the sector.

To identify the definitions of marine biotechnology that are commonly used or known in OECD countries, and how these definitions are built, a questionnaire was sent to OECD delegations for completion. The definitions collected through the questionnaire were compared with the OECD statistical definition for biotechnology, which consists of a single definition and a list-based definition used in combination.8 The list-based definition provides a list of biotechnology techniques that functions as an interpretative 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.

As with the general OECD statistical (single) definition of biotechnology, the majority of the definitions collected via the questionnaire include three elements, i.e. they:

- involve knowledge building (the science)
- focus on the utilisation of that knowledge (the products and services)
- make reference to societal aims.

Box 1 contains the OECD definition and two other internationally known definitions of marine biotechnology, with the recurring elements above marked in bold text.

#### Box 1. International definitions of marine biotechnology

**OECD** statistical single definition for biotechnology:<sup>7</sup>

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.

Marine Board definition of marine biotechnology:9

Marine biotechnology encompasses those efforts that involve **marine bio-resources**, as either the **source or the target** of **biotechnology applications**.

**CIESM** definition for marine biotechnology: 10

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.

The questionnaire also looked at those technologies commonly understood as being part of marine biotechnology. Analysis of the technologies showed that these could be grouped under the seven headings used in the OECD biotechnology list-based definition, found in Box 2.

Crafting of the definition of marine biotechnology for which the questionnaire provided the input was further discussed in the workshop mentioned above.

Specifically, the discussions addressed:

• the potential construction of an overarching definition (a "single" definition) for marine biotechnology

• Identification of elements of marine biotechnology to be included under such a "single" definition, to form a "list-based" definition.

One option considered by the workshop was a three-part approach:

- To adapt the single OECD definition for biotechnology
- To use the OECD list-based definition for biotechnology as a basis for a technology-based definition of marine biotechnology
- To adapt the OECD list-based definition for biotechnology to include technologies specific to marine biotechnology.

It was suggested at the workshop that the existing OECD statistical definition for biotechnology (single and list-based parts) could be the most suitable way by which to agree on a common understanding and definition of marine biotechnology. The single OECD definition of biotechnology can include marine biotechnology by adding reference to marine organisms and/or the use of biotechnologies in the marine environment. The list-based part of the OECD statistical definition can be adapted to include marine biotechnology by adding the technologies relevant for marine biotechnology. The technologies tested with the questionnaire can be covered under the seven headings of the existing OECD list-based definition for biotechnology. The definition for marine biotechnology could therefore approximate the one in Box 2.

#### Box 2. Statistical definition for marine biotechnology

## Single definition for marine biotechnology

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

## List-based definition for biotechnology

The following list of biotechnology techniques functions as an interpretative guideline to the single definition. The list is indicative rather than exhaustive and is expected to change over time as data collection and biotechnology activities evolve.

#### 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, bio pulping, bio bleaching, bio desulphurisation, bioremediation, bio sensing, bio filtration 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.

#### Nano biotechnology

Applies the tools and processes of nano/microfabrication to build devices for studying biosystems and applications in drug delivery, diagnostics, etc.

It was also considered by most workshop participants that freshwater aquaculture need not be mentioned specifically, as this is already covered under the general OECD statistical definition of biotechnology. Marine biotechnology takes a special place because of the dimension of the environment, the difficulties accessing this environment, the specialised physicochemical biotopes it includes, and the wide biodiversity linked to it.

## **Indicators for marine biotechnology**

Defining marine biotechnology is the first requirement when addressing the significance of an enabling technology on a segment of the economy, and when measuring the impact of dedicated programmes to stimulate this segment or to build on the opportunities offered by marine biotechnology.

Equally important in measuring these impacts is to define a set of indicators to enable the collection of related statistical data.

The OECD Framework for Biotechnology Statistics currently used described eight application areas for biotechnology, but adapted to what most countries, based on the industrial classification, actually use to collect data – i.e. Health, Agriculture, Food and beverages, Natural resources, Environment, Industrial processing, Bioinformatics and Other. Marine biotechnology may contribute to each of these applications, and it is not given a separate category. The fact that marine biotechnology has potential importance for many applications and in many different industrial sectors should be kept in mind when collecting and using statistics and indicators. In addition, marine biotechnology may have indirect economic effects as well as direct ones, and care should be taken when studies are planned to clearly define the sectors and applications under examination. Experiences of the OECD work indicate that it is important to pilot test definitions and indicators in a small setting, to ensure that the stakeholders addressed recognise themselves and their activities.

Experience from NIFU, the Nordic Institute for Studies in Innovation, Research and Education in Norway, was shared in the thematic session on marine biotechnology that was held in Paris 12 June 2014 in the context of the 34<sup>th</sup> meeting of the WPB. NIFU began collecting data on marine biotechnology when addressing the priority areas "Marine Research and Aquaculture Research" (in 1999) and "Biotechnology R&D" (in 2003). Regular R&D statistics only provide a global picture of biotechnology and marine biotechnology, and although marine biotechnology as such is not a priority area mapped by NIFU, it is covered by those two priority areas. The general approach of NIFU is to combine data from regular R&D statistics with separate questionnaires that address these specific areas. Often these NIFU studies are accompanied by a bibliometric study. Analysis of the governments' priority areas indicated that biotechnology R&D and marine R&D are the two largest priority areas in Norway with respect to R&D expenditure.

The NIFU surveys collect data on R&D expenditure by funding source and in various fields of science and categories as defined in collaboration with the Norwegian Research Council. Other data that are collected concern the number of people working in R&D; their age, gender, skills and education level; and co-operation in R&D.

Although care must be taken when extracting numbers on marine biotechnology R&D from the two surveys – as they had a different focus and were to some extent complementary – a number of overlapping categories are addressed. Analyses from both surveys over time reveal how marine biotechnology R&D expenditure has evolved, indicating that it has more than doubled. Interestingly, both surveys indicate that the growth of marine biotechnology R&D is faster than total R&D growth. This accords with the fact that marine R&D is a top political priority area for Norway, and has been for several years. Considering the importance of the country's fish farming and fish exporting, the NIFU analysis is of great interest to the Ministry of Trade, Industry and Fisheries.

The Norwegian results show that collecting statistics allows the evolution of a sector to be followed over time, providing information on the results of government actions and incentives.

Other indicators for consideration have been suggested by CIESM, such as the revenues of universities and research centres from licences executed; start-ups created in the field of marine biotechnology; patent ownership; and the nationality of public and private actors engaged in R&D ventures. Scientific articles cited on the cover page of patents issued are another indicator of the contribution of research to the development of practical innovation.

One of the practical hurdles that should be recognised when setting up a statistical survey is that developing and testing a new survey is a slow process that creates an extra burden for the national statistics offices; recently, a trend has become evident that national statistics offices are cutting down on activities and surveys. Ideally, the proposed indicators for marine biotechnology should be integrated into existing surveys of statistical agencies or offices.

## Infrastructures for marine biotechnology

To help create consensus on a definition and indicators to be monitored, so as to then be able to measure marine biotechnology, recommendations were published in the OECD report "Marine biotechnology – Enabling solutions for ocean productivity and sustainability" at the end of 2013. Another recommendation in this report was to improve the R&D infrastructures and platforms, and increase national and international co-operation to address the infrastructure needs, such developing new infrastructures, integrate and co-ordinate existing infrastructures and facilitate access to research infrastructures. Access to specific research infrastructures, including research vessels or databases for storage and data sharing, is considered crucial to advance this field of biotechnology. Governance of large distributed research infrastructures is of particular interest in dealing not only with access but also for financing regulation.

Distributed research infrastructures composed of several local infrastructures arise from integrating different complementary national or regional infrastructures to reach added value. A number of issues arise with distributed infrastructures, and it should be noted that these issues are not specific to marine biotechnology but in fact relate generically to all research infrastructures.

One such issue is how to achieve long-term sustainable financing as multiple financing partners have to agree on and align the funding. In line with this, access should be regulated. Open access is important, although open is not synonymous with free – which is to say, at no cost. Access for free may create the impression that the infrastructure is not valuable. Access issues may also have important implications for intellectual property, as there needs to be agreement on the ownership of the data, its use, and the possible applications that are developed from it. In the GSF work, it was noted that tested accession models for non-profit use and non-profit organisations should be made available.

Next to the need for large databases, the need for access to vessels for marine research (including biotechnology research) was noted as being important. Given the specific expertise required and the high maintenance and operational costs involved, access regulation of access to research vessels is particularly complicated.

One of the most urgent needs related to research infrastructures is standardisation – of data or sample collection, storage and management, curation of data, storage and calculation capacity, and legal frameworks to use (raw) data. This need is, again, not specific to marine biotechnology but rather a generic requirement to accelerate building a knowledge base and developing innovative applications. Linking of and communication among databases is a particular challenge.

The need for access to data is equally generic throughout research and development. For marine biotechnology, data are important in enabling access to the wealth of the ocean's biodiversity, and in enabling fuller exploration of the marine environment. In order to achieve this, dedicated databanks may be necessary. Access to raw data is considered a major element, to enable further unbiased research that is independent of previous work for which data had been collected. In this regard, and with respect to other elements of the R&D system and the use of infrastructure, there is an urgent need for data management standards.

Databases, but other distributed infrastructures as well, need not necessarily be new; pre-existing infrastructures can also be used. The question of whether it is better to set up new, state-of-the-art infrastructures or to build on pre-existing ones is a matter of ongoing debate when setting up new co-operating initiatives. Both options have advantages, but operational infrastructures that have been successful should not be wasted. The choice will involve consideration of the headquarters' location and central facilities including administration. Different partners in a distributed infrastructure may wish to host the headquarters of the initiative because of the visibility and possible extra economic activity it creates. It was noted that this is a sensitive issue and that these discussions may slow down or even prevent setting up the infrastructure.

The importance of research infrastructures cannot be overestimated, even though not all infrastructure initiatives have the ambition to become highly integrated. In addition, other global international collaborations are likely to open many more opportunities. Part II of this report provides an overview of large research infrastructure initiatives that are important for marine biotechnology. Although this overview is not exhaustive, it indicates that global initiatives to access the marine environment and capitalise on the opportunities that marine biotechnology is holding are limited. Global initiatives should be considered in the future so as to take marine biotechnology further.

### PART II

## INFRASTRUCTURES FOR MARINE BIOTECHNOLOGY AROUND THE GLOBE

Part II provides an overview of a number of large research infrastructure initiatives worldwide, some not dedicated solely to marine biotechnology. International collaboration is seen to be the one real way forward to enable the sharing of infrastructure. Specific requirements for qualification as IDRIS (International Distributed Research Infrastructures) are listed, as well as possible additional features. Open access, data sharing and funding issues are illuminated through an in-depth examination of the European Strategy Forum on Research Infrastructures (ESFRI), an initiative notable for its long-term strategic planning. The examples of the Academic Research Fleet, the Reef Base Global Database, BOLD, MBIK, ELIXIR and Marbank are presented to show possible new ways to create access to, and enable sharing of, new knowledge from marine resources so as to support innovation while contributing to the protection of biodiversity.

## Introduction

The recent OECD report "Marine Biotechnology – Enabling Solutions for Ocean Productivity and Sustainability" formulates a number of policy needs and identifies measures to address them. One of these needs is for better R&D infrastructures and platforms to improve our understanding of marine bio-resources, and mechanisms to improve access to and development of those resources. The shared and dynamic nature of ocean bio-resources, together with the sheer size of the development opportunities (and challenges), means that co-operation, both national and international, is a basic requirement to develop infrastructure to support marine biotechnology.

In addition to a need for standard infrastructure for general and routine biotechnology applications, the report identified as well that specialised infrastructure dedicated to marine research is necessary. Infrastructure such as specialised vessels to access extreme environments, means for culturing and preserving marine resources, access to big data related to marine organisms, etc. are seen as crucial to further develop this field. Rather than relating specifically to marine biotechnology, such infrastructure is often dedicated to general marine sciences, including ecology and biodiversity or biophysics; nevertheless, it is also likely to advance marine biotechnology. Understanding ecology and biodiversity at molecular level will lead to new applications; to the development of cultivation procedures for the (so far) "unculturables"; and to the development of new biosensors or to methods to protect and restore vulnerable ecosystems, among other things. In addition, access to biodiversity in combination with molecular biotechnological analysis is crucial for bio-prospecting to find new bio-active compounds.

A workshop was organised by the OECD Working Party on Biotechnology at the OECD headquarters in Paris, France, on 7 November 2013 to explore challenges related to the establishment of marine biotechnology infrastructure. One major challenge is the collection and storage of vast quantities of data – the so-called big data issue – in a standardised way, and providing appropriate access to those data. Big data issues are not specific to marine biotechnology, but specific infrastructures may be required for this field to fully seize opportunities from marine resources. The amount of data is so huge, and the results of calculations presented in publications so complex, that it is impossible for peer reviewers to verify the results and the conclusions. Access to raw data that is open but not necessarily free of charge was

considered important by the workshop participants, to allow for unbiased and independent testing and research.

The need for access to Maritime Research Infrastructures (MRI) was also identified in the European Commission's 2008 European Strategy for Marine and Maritime Research. <sup>11</sup> The Commission established an expert group in March 2010 to identify important gaps and needs in European-scale MRIs. The ultimate goals of these efforts were to propose mechanisms to link MRI needs with funding opportunities; and to advise on governance of European-scale MRIs that are directly or indirectly supporting the collection and use of marine data, i.e. marine observation infrastructures. The Group took a strategic approach, looking at the wider dimensions of governance so as to identify major gaps. The final report of the expert group, "Towards European integrated ocean observation" was published in January 2013. <sup>12</sup>

The MRIs considered by the expert group included a wide range of different infrastructures, dealing with data collection, data management and data assembly. In order to acquire marine data and use them in an effective and efficient way, all stages of the data processing chain need to be managed well, and data flows – from data collection to the delivery of services to end-users – need to be optimised.

In their conclusion the expert group recommended exploring public-private partnerships related to data collection and management, as well as opportunities for public-private partnerships to finance European-scale MRIs. Partnership models should be developed as a means of maximising incentives for marine industries. Such partnerships can engage in joint financing of data collection and management equipment and functions, while taking into account the different interests of well-established and emerging marine industries.

In general, the expert group found that biochemical sensors for use in the marine environment were less developed than physical sensors. It was felt that new biochemical sensors and devices are required to measure environmental pressure and the effect of climate change and variations on marine biodiversity. The expert group recommended exploring the potential of new methods and technologies such as genomics and marine acoustics to assess (pressures on) biodiversity.

In addition, it is anticipated that oceanographic vessels will remain an essential component of MRIs. However, the development of sensors and the increasing use of autonomous and unmanned platforms may change how ships are utilised. It is projected that many oceanographic vessels of the European regional fleet will need to be renewed in the coming years. The expert group identified a need for strategic reassessment and co-ordination, at European level, of oceanographic vessels, as part of a broader assessment and co-ordination of European MRIs.

The objectives identified to capitalise on marine biotechnology are so ambitious, and the environment is so specialised, that only international collaboration can offer a robust way forward to enable the sharing of infrastructure; no single entity would be able to cover all needs.

These findings are also in line with the conclusions of the Group of Senior Officials (GSO) of the G8 that was established for the first time in 2008 in response to the recognition that research infrastructures are essential to support research and innovation. The GSO were tasked to develop and promote a "Framework for a coherent and co-ordinated world-wide development and operation of global research infrastructures".

At their meeting of 12 June 2013 the G8<sup>13</sup> science minister endorsed the work of the GSO and recognised the need for Global Research Infrastructures (GRIs). They encouraged the G8 to agree on global challenges and address those through international collaboration. The global nature of the challenges ahead requires facilities that are too complex, and too expensive to be built and operated by individual countries. GRIs were therefore identified as key elements to reach the goals. In the same

reasoning, the importance of open access to scientific research data and open access to the peer-reviewed, published results of scientific research were put forward as crucial elements to address the global challenges.

It was concluded that only internationally orchestrated research infrastructures, including single and distributed research infrastructures will ensure the required critical mass of highly qualified human resources to operate and use the infrastructures for its intended purposes and be able to produce a crosscutting impact for the benefit of society.

To identify areas of potential benefit that could be achieved through the sharing of research infrastructures, information on national research infrastructure priorities will be collected and prioritisation processes will be analysed. A representative list of GRIs, open to global co-operation and of interest to new partners will be created. A report from the Group on the co-ordination of GRIs is expected. A progress report was presented in 2015. Among such infrastructures, ocean and sea floor observatories, including oceanography fleets of research vessels and polar research facilities (both for the Arctic and Antarctic) were specifically mentioned as examples in the broad categories of research infrastructures of global relevance.

#### **IDRIS**

Governance needs relating to establishing large research infrastructures was also addressed in the work of the OECD. Following on from the publication of the "Report on road mapping of large infrastructures" (2008) and the "Report on establishing large international research infrastructures: Issues and options" (2010), the OECD Global Science Forum (GSF) published a "Report on International Distributed Research Infrastructures (IDRIS)" in 2013. This report can serve as a reference document that may be used when new initiatives to share infrastructure are being prepared. It identifies challenges, options and solutions when it comes to setting up new initiatives in which distributed infrastructures have to be integrated for better research. The report gives a broad definition of IDRIS, listing requirements for qualification as IDRIS and possible additional features. Different organisational forms exist with or without legal identity, but a key point is that IDRIS should have clear added value. The OECD reports provide relevant information for IDRIS, summarising issues on road mapping and single-sited large international research infrastructures that may also be applicable to IDRIS.

Specifically, the OECD IDRIS report states that IDRIS should have all of the following:

- An identity and a name.
- A set of international partners who are, typically, research institutes, academic institutions, foundations, or other research-oriented organisations from the public or private sectors. Often, only parts of these entities (as opposed to entire entities) collectively constitute the infrastructure.
- A formal agreement by the partners to contribute resources, expertise, equipment, services or
  personnel to achieving a common scientific purpose. The agreement need not necessarily define a
  new legal entity, or be legally binding.
- A strategic plan, or work programme, that conveys the rationale for establishing the IDRIS and
  the added value over and above the separate activities of the partners. A governance scheme (for
  decision making, at a minimum) and a set of officers (not necessarily salaried staff) with welldefined responsibilities.
- A focus on the provision of services to its members and users.

In addition, IDRIS may have the following:

- an independent legal status (or an equivalent legal identity under the terms of an existing intergovernmental agreement)
- a common fund and rules for the acquisition/spending of funds
- a secretariat
- a host institution
- a central entry point for users
- explicit policies for access by users to research resources and to data, and for managing any intellectual property generated.

## European Strategy Forum on Research Infrastructures (ESFRI)

Highly organised forms of IDRIS are being set up within the European Union. Already in 2001, the European Council of Ministers acknowledged the need for and benefits of shared large research infrastructures. The European Commission, in close collaboration with the EU Member States, was invited to explore what shared research infrastructures were needed and what policies were required for closer collaboration in order to provide access to these infrastructures. It was concluded that a collective approach was needed to guide the complex policy making for the sharing of research infrastructures in the Member States. To achieve this, the European Strategy Forum on Research Infrastructures (ESFRI) was set up in 2002, with the following mandate:

- to support a coherent and strategy-led approach to policy making on research infrastructures in Europe
- to facilitate multilateral initiatives leading to better use and development of research infrastructures.

ESFRI explores initiatives to set up new or to upgrade existing research infrastructures of major significance across Europe. The Forum also helps identify gaps in pan-European research capacity as well as strategic needs associated with research infrastructures. Moreover, the Forum issues periodic recommendations on the management of research infrastructures and related human resources. Finally, ESFRI members are tasked with communicating the significance and importance of research infrastructures to a wider public.

ESFRI defined a European (distributed) research infrastructure as necessarily having:

- a common legal form
- a single management board responsible for the whole research infrastructure
- one single access point for users, although the research facilities may have multiple sites.

The research infrastructure should demonstrate *added value* as they provide *unique* laboratories or facilities accompanied by user services to ensure top-level European research. That research should stimulate integration and convergence of scientific and technical standards in the specific field of science

and technology, while enabling research that cannot be realised without access to these facilities. The research infrastructures should develop and build on a strategy and development plan to ensure scientific and technological cutting-edge knowledge and managerial excellence.

The Forum also advocates that the research infrastructure should *ensure open access* to all interested researchers, provided that access will be awarded through international competition on the basis of scientific excellence that is granted after peer review of the project proposals. Research results should be published in the public domain. Additional access may be offered for industrial research, on a payment basis, and as a marginal, non-economic activity that does not interfere with the peer-reviewed access.

The ESFRI research infrastructures should also provide unique opportunities to train scientists and engineers while facilitating knowledge, technology transfer and innovation. This mode of operation should ensure a substantial added value with respect to national facilities.

A first roadmap for pan-European research infrastructures was published in 2006 and updated twice, in 2008 and 2010. A further update 2016 of the roadmap is being prepared and is ongoing. So far, 48 research infrastructure needs were identified that may lead to the development of new research infrastructure initiatives. Most of the current ESFRIs related to distributed infrastructures, in addition to 15 single-sited research infrastructures.

The different research infrastructure initiatives proposed were evaluated in 2010-11 in terms of their contribution to addressing scientific needs, added value and technological and financial feasibility, as well as their contribution to tackling the grand challenges identified within the European context.

It was quickly realised that to be able to deal with the increasing complexity and the costs of high-end, shared and open access research infrastructures – often beyond the reach of individual countries – a new legal framework containing the procedures and conditions for operating and executing research and technology programmes was needed. Such a framework, or European Research Infrastructure Consortium (ERIC)<sup>17</sup> mechanism, was created to ensure that the infrastructure to which it applies operates as an independent legal entity, and its operation legally complements other legal forms existing under national, international or Community law. Nevertheless, the adoption of an ERIC is not obligatory – other forms of legal identity and operation remain possible in the European ESFRI context.

The stipulations for an ERIC are that:

- An ERIC should run on a non-economic base with a primary task of establishing and operating a
  research infrastructure.
- As an ERIC is to be recognised as an international body; it is subject to tax exemptions, although
  only at the central node or headquarters and only for the issues that concern the international
  functioning of the initiative.
- It takes a minimum of three European Member States to establish an ERIC, which may include associated or other countries as well as specialised intergovernmental organisations.
- The ERIC must have statutes and set up the necessary bodies for effective management.
- The ERIC should be established and run under Community law, while specific operations of the ERIC that take place in another state should be according to laws in that country.

Selected proposals for an ESFRI initiative receive funding from the European Commission to embark on a preparatory phase, during which the governance, technical, legal and financial issues that are to be dealt with prior to implementation are prepared. While ESFRI funds the preparatory phase of new research infrastructures, it does not fund the operation or maintenance of existing research infrastructures. The implementation phase itself is to be funded by the participants or through external funds. Of the 48 infrastructure priorities identified, 10 were under implementation at the end of 2012. The goal was to have 60% of the ESFRI roadmap implemented by 2015.

A first assessment report from a high-level expert group on the ongoing EFSRI projects was published in August 2013.<sup>18</sup> The assessment indicated that although some projects are likely to reach maturity by 2015, all projects analysed need to follow up on governance and financial sustainability.

One of the more popular organisation models used within the context of the ESFRI roadmap is the "hubs and spokes" model of shared distributed infrastructures. "Hubs and spokes" is accepted as a workable model for global (virtual) infrastructures, while the creation of super-large infrastructures, integrating different complementary infrastructures, is very often considered to be counterproductive and unwieldy. The expert group found, however, that most ESFRI projects have no clear activity/implementation plan that specifies the roles of the different partners – and that includes the relative position of the central hub to the distributed nodes.

It was also concluded that details on the value added that justify the European dimension and investment decisions should be specified more clearly. According to the assessment report 40% of the research infrastructures still need to develop credible performance indicators to monitor the research infrastructure's progress and achievements. The expert group reasoned that this is needed to allow assessing the degree of success of the project, and in this way to document the added value of the research infrastructure for prospective stakeholders and funders.

The experts recommended that the central hubs and directors should have sufficient power to interact with the national authorities. They consider this a requirement to allow the research infrastructures to become truly integrated rather than networks of national independent infrastructures. It is felt that this would also ease the way to reaching financial sustainability. In this respect the assessment, as stated in Part I, found that few research infrastructures can show firm financial commitments from prospective partners, stakeholders or funding agencies for investments and operations, even though long-term financial commitments are thought to be a requirement to meet international ambitions. Investments still largely depend on national authorities. For the running costs as well, a clear long-term framework should be available.

The high-level group also found that none of the research infrastructures assessed had done a thorough risk analysis. Risk analysis is judged essential to create the trust – both in the expected outcome of research activities, and in the data's quality and financial sustainability – necessary to ensure investments.

Most of the EFSRI projects in the assessment were found to have no, or at best only a limited, idea of the initial and prospective user communities of the research infrastructure. This should be addressed, and accompanied by the development of a well-defined user policy in which scientific and ethical goals are considered and user-related performance indicators are defined. In addition, user training programmes are believed to have a positive effect in that they can expand the research infrastructure utilisation to other thematic areas.

The report also recommends that special attention be accorded to ICT platforms; all ESFRI projects target production of large amounts of data, which has immediate consequences for data storage, protection

and sharing. From the start of the projects, according to the experts, synergies should be sought with ESFRI projects that operate in the same field to ensure common standards; this allows easy sharing of data and ensures cost efficiency. In this discussion mention was made of (again) appropriate risk analysis concerning data confidentiality and IPR protection, essential for industrial users.

Three ESFRI projects may be of particular interest to marine biotechnology development:

- EMBRC, the European Marine Biological Resource Centre<sup>19</sup>
- ELIXIR, the European Life-Science Infrastructure for Biological Information<sup>20</sup>
- MIRRI, the Microbial Resource Research Infrastructure.<sup>21</sup>

Two other collaborative efforts that started earlier have contributed to the development of marine biotechnology, although they did not meet the level of integration and governance at which the ESFRI initiatives are expected to operate. One is Euro marine, a so-called Network of Excellence, which were designed in the Sixth Framework Programme (FP6) of the European Commission to reduce fragmentation of research by integrating the research capacity of the participating members. <sup>22</sup>. Euro marine, which sought to achieve many of the same goals for marine biology as are described in the ESFRI initiatives – access to research infrastructure, sharing of expertise, developing common research strategies, sharing of databases, etc. – ended in January 2012.

The other collaborative initiative is ASSEMBLE – the Association of European Marine Biological Laboratories, funded under the Seventh European Framework Programme (FP7) and also ended in 2012. It was a research infrastructure initiative comprising a network of marine research stations across European waters as well as the Red Sea and the Pacific Ocean. Each infrastructure site offers access to different installations such as general and climate controlled laboratories, state-of-the-art experimental facilities, technological platforms, research vessels, and a wide variety of marine organisms. ASSEMBLE coordinated access to the different infrastructures. These activities will be continued by the ESFRI initiative EMBRC.

The difference between the previous two projects and the ESFRI initiatives is the higher form of the latter's organisation, its longer time frame of effort, and the commitment it receives from local governments or authorities to finance long-term operability. As outlined above, an ESFRI initiative is expected ultimately to adopt an independent legal identity, in addition to a sustainable management and financing strategy of its activities. Such long-term strategic planning, in co-ordination with multiple organisations and different countries, is a major step forward, one that should contribute to research and innovation in general and in the field of marine biotechnology in particular.

The following paragraphs explore in greater depth the different ESFRI initiatives, describing their aims, governance and functioning.

## EMBRC - European Marine Biological Resource Centre

The EMBRC was setup to co-ordinate distributed state-of-the-art research and training facilities at leading marine research stations across Europe, to provide access to marine biodiversity, the associated metadata, and extractable products to end-users from academia and industry. Besides providing an open platform for data sharing and standardisation of data gathering and storage, EMBRC facilitates more general activities such as promoting mobility, fostering interdisciplinary research and developing innovation capabilities. EMBRC will also provide interdisciplinary training for researchers and ensure dissemination of knowledge and communication to users and the general public. Through EMBRC,

researchers will have easier access to marine resources and ecosystems, aquaria and state-of-the-art biobanks, as well as to culture strategies and research platforms – such as those related to advanced biotechnologies, including -omics technologies – that are dispersed throughout Europe. The Centre will also foster interaction with other facilities with specialised infrastructure, such as for structural biology and imaging. All these measures should allow for better access and understanding of marine ecology and biodiversity, and may open up ways to new applications through marine biotechnology.

The proposal for EMBRC was launched in February 2011 with an initial three-year preparation phase. The budget from the European Commission for the preparative phase was EUR 3.9 million. In this preparatory phase, thirteen European marine stations in eight countries were involved, five of which were already previously collaborating in ASSEMBLE.

Issues concerning national funding were addressed during the preparatory phase, with the aim of influencing national funding priorities to create direct funding opportunities for EMBRC. Communication with other ESFRI infrastructures was meant to avoid duplication and to enhance complementarity and collaboration. It was in this phase that initiatives for data management and database consolidation were adopted to ensure efficient access to data. In particular, initiatives to increase sharing of expertise were taken, in addition to identification of best practices for experimental methods, culturing, data collection and analysis. Furthermore, mapping began of the needs for access to -omics facilities and bioinformatics platforms; a web-based searchable directory of facilities and services was developed; efforts to support the mobility and training of researchers were organised with a single access point in EMBRC, based on the model developed in ASSEMBLE; and the need for training capacity was mapped and efforts to increase industry participation pursued. Finally, the foundation of a legal framework was developed prior to the construction phase.

The construction phase was begun in 2014. According to the planning a Legal structure under the form of an ERIC is planned in 2016, which will then be the start of the implementation phase. EMBRC partners have agreed on a long term planning and the initiative is expected to be operational for at least 25 years, with budgets from the Member States, the EU and users of the infrastructure. One of the priorities in the operational phase is to secure longer-term funding by national and other bodies and to co-ordinate proposals to address this priority. Furthermore, this phase will see analyses of the scientific and technological system to identify where expansion is needed and to allow evolution towards larger-scale integration of new members and facilities. At the onset of the operational phase, EMBRC will co-ordinate activities throughout the research infrastructure. The headquarters and central nodes will be governed by service agreements.

## ELIXIR - European Life-Science Infrastructure for Biological Information

While EMBRC addresses only marine bio-resources, ELIXIR will be a secure, rapidly evolving platform for the collection, storage, annotation, validation, dissemination and utilisation of all kinds of biological data, including from marine species. It comprises a distributed and interlinked collection of core and specialised biological data resources, and aims to unite Europe's leading life science organisations in managing and storing the massive amounts of data. The data infrastructure should be suitable for rapid search and access, while providing a sophisticated but user-friendly portal, to ensure efficient use of data by research institutes in biological, medical sciences and environmental sciences. The goal of ELIXIR is to reduce the fragmentation and heterogeneity of data integration, and guarantee open access to biological data. In addition, the initiative offers training and tools to use the data. ELIXIR builds upon the existing molecular data resources at the European Bioinformatics Institute (EBI), which will be further substantially upgraded and expanded with new resources as appropriate.

The four-year preparatory phase, funded by the EU's FP7 (EUR 4.5 million), was completed by the end of 2012 and was the result of the collaborative work of 32 organisations from 13 countries. It was decided that ELIXIR would consist of a central hub and interlinking nodes distributed throughout Europe in different centres of excellence. The hub, hosted by the European Molecular Biology Laboratories - European Bioinformatics Institute – EMBL-EBI – accommodates the executive management and secretariat, co-ordinates services, and provides core data to users. ELIXIR's distributed nodes form the other components of the research infrastructure. The nodes are configured to be interoperable both with the central hub and with each other. This will require an agreement with the hub and funding by the Member States.

The governance and legal framework of ELIXIR is different from the ERIC framework, and takes advantage of the EMBL legal status to develop an ELIXIR Consortium Agreement (ECA) for the initiative. The ECA entered into force on 12 January 2014. Thirteen Countries and the EMBL signed the ECA at the moment of this writing in early 2016, while two more countries progress towards ratification of the ECA.

Funding of the ELIXIR hub comes from the partnering Member States, while funding of the nodes will be decentralised, coming from national funding organisations and consortia of funding agencies.

## MIRRI - Microbial Resource Research Infrastructure

The focus of MIRRI, as a pan-European distributed research infrastructure, is on micro-organisms – providing access to microbial collections, their derivatives, and associated data for research, development and application. MIRRI co-ordinates a network of biological resource centres of microbial organisms to operate according to common standards and to ensure the validation of sequence data. It connects resource holders with researchers and policy makers to improve access to biological material for research and better uptake into innovation. Microorganisms include bacteria, archaea bacteria, fungi, microalgae, yeast, unicellular organisms, viruses, and phages as well as animal, plant and human cells and their genetic material. Microorganisms provide essential raw material for biotechnology – but to date less than 1% of the estimated number of species are described and available for use. A co-ordinated and targeted approach will be developed within a legal operational framework to comply with the Convention on Biological Diversity and its Nagoya Protocol on Access and Benefit Sharing (ABS) as well as other legislation, governing biosafety, biosecurity and intellectual property. Like ELIXIR, MIRRI is not solely dedicated to marine organisms, but it is likely to be very important and complementary to the other research infrastructure initiatives discussed, for activities involving marine biotechnology.

MIRRI began its preparatory phase in November 2012 with EC financial support of EUR 3.14 million. Key resource centres have been identified and are well established across Europe. The infrastructure project includes over 40 public culture collections and research institutes in 19 European countries. Preparations started in 2015 to establish the legal status of MIRRI as an ERIC.

As made clear in Part I, the importance of research infrastructures cannot be overestimated, even though not all infrastructure initiatives have the ambition to become highly integrated and adopt an independent legal identity like those defined in the EFSRI roadmap. Other global international collaborations are likely to open many more opportunities.

## Global initiatives

The year 2012 saw the first global initiative to link infrastructures internationally, during the Danish presidency of the European Commission. The International Conference on Research Infrastructures, ICRI

2012, called for a Global Network of Policy Makers for research infrastructure, building on the experiences of ESFRI and the work of the Group of Senior Officials (GSO).

Global initiatives on research infrastructures often focus on climate and geophysical data, and sometimes correlate these data to biodiversity. Marine biodiversity-related databases can contain massive amounts of information, and when combined with genomics and other -omics data will facilitate marine biotechnology applications.

Other global initiatives relevant to marine biotechnology have been operating for some time, although most do not have an independent legal identity. Nevertheless, they qualify as IDRIS because they meet all other requirements.

# The Global Biodiversity Information Facility - GBIF<sup>24</sup>

Several initiatives were taken to collect data on wider biodiversity. Combining -omics information with more general descriptive information may accelerate innovation, including for marine biotechnology. In 1999, the Biodiversity Informatics Subgroup of the Mega science Forum, set up by the OECD, concluded in its panel report that "an international mechanism is needed to make biodiversity data and information accessible worldwide". It was felt that such a mechanism would enable sustainable development through access to reliable scientific information and in doing so generate economic and social benefits. The OECD panel specifically recommended the establishment of a Global Biodiversity Information Facility, to "enable users to navigate and put to use vast quantities of biodiversity information, advancing scientific research ... serving the economic and quality-of-life interests of society, and providing a basis from which our knowledge of the natural world can grow rapidly and in a manner that avoids duplication of effort and expenditure".

OECD science ministers endorsed this recommendation and in 2001 GBIF was officially established through a memorandum of understanding among participating governments. The governments fund GBIF, which is an international open data infrastructure

GBIF grew to a mature international distributed research infrastructure and is now financed by national contributions based on the GDP of the participating countries. A governing board and executive committee are in place and meet on a regular basis. Three standing committees have been set up by the governing board to act as advisory bodies on the scientific work programme, budget, and management of the nodes. Task groups have been set up to address issues according to needs defined by the governing boards.

GBIF is not focused solely on marine biodiversity but rather addresses biodiversity in general. GBIF data have been used *inter alia* for marine conservation planning,<sup>25</sup> and collecting information on marine species.<sup>26,27</sup> It is likely that this facility will also play an important role in the development of marine biotechnology, especially if biodiversity data can be linked to -omics data.

# The Census of Marine Life – CoML<sup>28</sup>

A complementary international effort that may be considered an international distributed research infrastructure and that will be important for marine biotechnology is the Census of Marine Life – CoML that started in 2000. It has involved 2 700 scientists, of whom about 44% were from the United States and Canada, 31% from Europe, and 25% from the rest of the world, including Australia, New Zealand, Japan, the People's Republic of China, South Africa, Indonesia and Brazil. The initiative ran over ten years to assess the diversity, distribution and abundance of marine life. The overall goal was to assess what lived in

the oceans since human predation, what lives in the oceans now, and what will live in the oceans in the future.

Most of this effort went into assessing what lives in the oceans today. For this, the oceans were divided into six realms (and subzones where necessary); projects were developed to explore each of these. Genetic barcoding techniques that automate and allow speed identification of species were used in addition to innovative acoustic methods and tagging and tracking methodologies, while sampling protocols were standardised. These tools and strategies may be important not only for cataloguing per se, but also for biotechnological applications.

To allow easy data sharing and to improve understanding of the patterns and processes that govern marine life, a data assimilation framework was established. The Ocean Biogeographic Information System (OBIS) is the world's largest open access, online repository of spatially referenced marine life data, and will continue under the auspices of the UNESCO International Oceanographic Commission's programme, the International Oceanographic Data and Information Exchange.

The CoML received support from the government agencies of over 80 countries, as well as from private foundations and corporations. The scientific results were reported on 4 October 2010 at the Royal Institution in London. The whole effort was co-ordinated by a secretariat and governed by a scientific steering committee. Thirteen national and regional implementation committees were established under the guidance of the International Scientific Steering Committee, to strengthen the global reach of the census. By engaging scientists, funding agencies, policy makers and the broader user community, the national and regional committees identified research and data priorities related to marine biodiversity. Partnerships were built to address these priorities, to explore funding opportunities for local science, and to promote the census to local audiences. A synthesis group was established to organise and integrate the vast amount of information gathered by the census, so as to ensure comprehensive content and products for 2010. Finally, a solid communication strategy was developed.

The CoML also supported the World Register of Marine Species<sup>29</sup> and serves as the marine component of the GBIF.

# International Barcode of Life Project - $iBOL^{30}$ – and the Barcode of Life Data Systems - $BOLD^{31}$

Complementary to the CoML and in collaboration with it, the International Barcode of Life Project (iBOL) is an ambitious international project. Co-ordinated by Genome Canada, it is the largest biodiversity genomics initiative ever undertaken. Over 250 researchers from 25 countries are working together to construct a DNA barcode reference library that will serve as the foundation for a rapid and inexpensive DNA-based identification system for all multi-cellular life. At the heart of the project is the Barcode of Life Data Systems (BOLD), a web platform designed to support the generation and application of DNA barcode data. The platform provides the cyber infrastructure needed to support applications such as food safety and traceability, conservation, ecosystem monitoring, forensics, and detection of agricultural pests and invasive species. BOLD is an informatics workbench for the acquisition, storage, analysis and publication of DNA barcode records; the project in effect bridges a longstanding bioinformatics chasm by assembling molecular, morphological and distributional data.

iBOL invites countries to participate as Nodes of the project. New Nodes officially join iBOL by signing a memorandum of understanding (MOU). Institutions and individuals who affiliate with iBOL Nodes can then participate in its programmes by contributing to the activities of its working groups and core facilities.

These core facilities provide the DNA barcoding community with the sequencing, analysis, bio-informatics, bio-repository, training, and knowledge mobilisation resources appropriate for a project of iBOL's scale. Core facilities do the bulk of DNA sequencing for iBOL, and establish robust protocols and informatics resources.

Over the past six years, efforts have been undertaken to collate and share information on the collection and registration of DNA barcodes from specific families and regions of life. The ultimate goal is to establish a barcode reference library of all life on earth. The different projects that are relevant for marine biotechnology are:

- The *Marine Barcode of Life campaign (MarBOL)*, <sup>32</sup> a joint effort of the Consortium for the Barcode of Life (CBOL) and the Census of Marine Life to barcode life in the world's oceans.
- The *Fish Barcode of Life Initiative (FISH-BOL)*, <sup>33</sup> a global effort to co-ordinate assembly of a standardised reference DNA sequence library for all fish species.
- The Sponge Barcoding Project, <sup>34</sup> the first global barcoding project on such simple organisms and covers the complete taxonomic range of this group of organisms. <sup>35</sup> Sponges are the most primitive multi-cellular organisms with a very limited number of differentiated cell types, while highly diverse and very difficult to characterise. They are ecologically important and of significant commercial importance to the pharmaceutical and biomaterials industry as they were found to synthesise the largest number of bioactive substances among all multi-cellular organisms. These characteristics make sponges of particular interest for marine biotechnology. Sponge barcodes provide tools for the easier identification of sponge species, which will enhance the discovery of drug-producing species.
- The *Polar Barcode of Life campaign* (*PolarBOL*)<sup>36</sup> co-ordinates barcoding bio-inventory projects in Arctic and Antarctic marine, freshwater and terrestrial ecosystems. Similar to the other barcoding projects, PolarBOL aims to provide efficient and accurate tools for mapping and monitoring and focusses on inventorying polar biodiversity.

## The World Data Centre for Microorganisms - WDCM<sup>37</sup>

Another research infrastructure that will contribute to the further development of marine biotechnology is the World Data Centre for Microorganisms – WDCM. This initiative supports a data management system for Culture Collections Information Worldwide (CCINFO). The CCINFO database is the basis for the world directory of culture collections providing data on the organisation, management, services and scientific interests of the collections registered.

The WDCM published an overview of all culture collections in 1972, 1982, 1986, 1993 and 1999. The sixth edition, published in August 2013, records 647 culture collections from about 70 countries, as well as 2 357 224 preserved microbial strains.<sup>38</sup> These collections include marine fungi, (micro-)algae, bacteria, cyanobacteria and protozoa, from all climate zones globally. Use of these collections varies, from mere descriptive taxonomic relevance to (for example) bio-prospecting, biofuel production, and relevancy to address fish diseases. Many of these collections are deposited in the ATCC culture collection (see below).

# Reef Base 39

Certain database initiatives are targeted towards specialised organisms or environments, such as coral reefs. Reef Base is an initiative funded by the United Nations Foundation to develop a database and

information system on coral reefs and to provide analytical tools for use in reef management, conservation and research. In addition, Reef Base wants to address the relationships among coral reef health, fishery production and the quality of life of people dependent on the reefs. The organisation wants to provide key information to support decision making with respect to fisheries and environment. The integrated approach envisioned by Reef Base is likely to contribute to knowledge creation and sustainability.

The information gathered from this initiative will be of interest to marine biotechnologists: the development of new applications from marine resources through biotechnology can only take place in the context of environmental sustainability, while biotechnology may help to conserve, restore and protect these complicated ecosystems. Coral reefs in addition house a wealth of specialised organisms and symbionts, offering new opportunities for bio-prospecting towards new applications and bioactive substances.

#### Other infrastructures

The global initiatives listed above mainly address biodiversity. Combining biodiversity data with insights into ecology and the food chain, as well as with -omics data, is likely to open many new opportunities for marine biotechnology. Understanding complete ecosystems and food pyramids in combination with the underlying biology at the molecular level will open ways to develop sustainable applications, while guaranteeing the protection and maintenance of marine biodiversity. In addition, at this moment many marine species cannot be cultured *in situ*; understanding the requirements for, e.g., co-cultivation may help advance the field and lead to new biotechnological applications. The sharing of existing databases - to provide access to and ensure communication among them - is expected to enhance the discovery of innovative applications. Bioinformatics is an essential and powerful tool for data mining from these databases and for further developing applications from marine biotechnology.

Many initiatives may not qualify as IDRIS because they are not supranational, even if they are of general importance and serve a global network. In addition, most are not directly dedicated to marine biotechnology but are likely to support this field more generally – by providing access to the marine environment, supporting general marine knowledge, or providing biotechnology tools and databases. A good overview of existing relevant databases for, *inter alia*, marine biotechnology may be found on the link: <a href="http://artedi.ebc.uu.se/course/overview/database\_industry.html">http://artedi.ebc.uu.se/course/overview/database\_industry.html</a>.

Other important infrastructure initiatives found in individual countries can have an impact that is much more global than simply national.

#### **United States**

In the United States there are initiatives similar to those in Europe for developing and operating a national integrated ocean and marine data management infrastructure. Different projects aim at improving the flow of data from oceanographic cruises and observatories to the national data management infrastructure, as well as refining standards for marine data management. Most of these initiatives focus on environmental, climate and geophysical data rather than on marine biotechnology. Nevertheless, the wealth of information and integration of expertise, knowledge and technological advances, including for marine biotechnology, is necessary to build on the opportunities offered by the seas and oceans.

The National Science Foundation (NSF) is an important source of funding to enable advanced equipment, facilities and shared cyber infrastructure to be made broadly available to the entire research community. Equipment and research facilities provided by NSF research infrastructure investments include distributed instrumentation networks, arrays, accelerators, telescopes, research vessels, aircraft, and earthquake simulators for research and education.

One of the most important infrastructure projects funded by NSF with relevance to marine biotechnology is the Academic Research Fleet.

## The Academic Research Fleet<sup>40</sup>

The Academic Research Fleet consists of 23 vessels in the University-National Oceanographic Laboratory System (UNOLS). UNOLS is an organisation of 62 academic institutions and national laboratories involved in oceanographic research, joined for the purpose of co-ordinating oceanographic ships' schedules and research facilities. The original UNOLS Charter was written in 1972 and most recently revised in 2013. Since 1 May 2009 the office for UNOLS is located at the University of Rhode Island Graduate School of Oceanography in Narragansett, Rhode Island.

One of the primary functions of UNOLS is to ensure the efficient scheduling of scientific cruises aboard the fleet's research vessels located at 16 operating institutions in the UNOLS organisation. <sup>41</sup> An institution can request the designation of their vessel as a UNOLS vessel; the requirements are that the institution is a UNOLS member, and that the vessel is used for oceanographic research and education purposes. UNOLS membership does not supply funding. It is up to the operating institute to find sufficient support for the operation of its vessel in adherence to UNOLS safety standards, and the vessel must be regularly available for federally funded users.

The Academic Research Fleet vessels vary in size, endurance, and capabilities to conduct marine research in coastal and open waters. Funding for the fleet includes investments in ship operations; shipboard scientific support equipment; oceanographic instrumentation and technical services; and submersible support. NSF owns seven of the fleet's ships and has proposed another vessel for construction.<sup>42</sup>

# NOAA - National Oceanic and Atmospheric Administration 43

Another major actor is the National Oceanic and Atmospheric Administration, but again not exclusively for the development of marine biotechnology. NOAA is a scientific agency within the United States Department of Commerce that is focused on oceanography and meteorology.

The first US scientific agency, the Survey of the Coast, was established in 1807 and transformed into NOAA under President Richard Nixon in October 1970's as a new organisation "for better protection of life and property from natural hazards ... for a better understanding of the total environment ... [and] for exploration and development leading to the intelligent use of our marine resources ...". NOAA is represented in every state, and is highly appreciated internationally for its scientific and environmental contributions.

The NOAA research network consists of internal research laboratories, programmes for undersea research and ocean exploration, and long-term collaborative partnerships, including 16 Cooperative Institutes consisting of 42 universities and research institutions across 23 states and the District of Columbia. 33 Sea Grant Programs are co-ordinated under the National Sea Grant College Program, and the NOAA Climate Program Office that manages the Regional Integrated Science and Assessments (RISA) programme, which includes 10 active projects.

NOAA's activities have an impact on more than one-third of the US gross domestic product and have several specific roles in society. NOAA is the main supplier of environmental information on the state of the oceans and the atmosphere, such as weather warnings and forecasts through the National Weather Service. The administration furnishes in addition, accurate scientific information on ecosystems, climate, weather and water, and commerce and transportation which are considered of national and global

importance. Furthermore, services are provided in co-ordination with federal, state, local, and international authorities, to manage the use of US coastal and marine environments, and regulate fisheries and marine sanctuaries as well as for protecting endangered marine species. NOAA combines human resources, technology, infrastructure, exploration missions, and data delivery to create more profound understanding of deep ocean areas and environmental issues to address both current and emerging threads and needs in these areas.

The NOAA Office of Ocean Exploration and Research (OER) is the only federal organization currently dedicated to exploring our unknown ocean. OER explores the ocean for national benefit by reducing unknowns in deep-ocean areas and providing high-value environmental intelligence needed by NOAA and the nation to address both current and emerging science and management needs. OER provides partnership coordination, funding, staff, tools, and expertise needed to develop exploration missions that deliver rigorous, systematic observations and documentation of biological, chemical, physical, geological, and archaeological aspects of the ocean. The office promotes technological innovation, provides public access to data and information, and trains the next generation of ocean explorers, scientists, and engineers. Since 2008, in collaboration with the NOAA Office of Marine and Aviation Operations, OER has been systematically exploring unknown ocean areas and phenomena on NOAA Ship Okeanos Explorer, a specialised platform that uses broadband telepresence communications technology to allow anyone with an internet connection to participate in offshore expeditions in real-time. The ship is equipped with cutting edge sonar systems and a dual body remotely operated vehicle (ROV) system that establish baselines where none existed before.

A substantial funding programme underpins the goals of NOAA. For fiscal year (FY) 2017, NOAA requested a total of USD 519 789 000 to support the OAR. This total budget includes operations, research, and facilities and procurement, acquisition and construction accounts, and incorporates a net increase of USD 37 812 000 from the FY 2016 enacted.<sup>44</sup>

USD 493 410 000 of this total budget was requested to support the operations, research and facilities of OAR, which incorporates a net increase of USD 31 512 000 from the FY 2016 enacted.

The total budget assigned to OAR also covers the Marine Aquaculture Programme for which NOAA requested USD 7 000 000 to support research for industry development. NOAA technology transfer will support the development of sustainable aquaculture. In addition, there is also a budget assigned to the Innovative Research and Technology sub-programme, for which NOAA requested a total of USD 22 144 000.

Two other infrastructure initiatives funded by NOAA that contribute significantly to the development of marine biotechnology should be mentioned here: the Ocean Biotechnology Centre and Repository, and the Cooperative Institute for Ocean Exploration, Research and Technology.

# The Cooperative Institute for Ocean Exploration, Research and Technology (CIOERT)<sup>45</sup>

The Cooperative Institute for Ocean Exploration, Research and Technology (CIOERT) is a consortium led by and headquartered at the Harbor Branch Oceanographic Institute at Florida Atlantic University in Fort Pierce, Fla. The other partners are the University of North Carolina Wilmington, SRI International in St. Petersburg, Fla., and the University of Miami. CIOERT supports the OER programme for ocean exploration and research by developing, testing and applying new and innovative uses of existing technologies to activities to expand the scope and efficiency of ocean exploration.

The Cooperative Institute focusses on better understanding of ecosystems and habitats of economic, hazardous, scientific or cultural importance within and beyond the eastern US Continental Shelf. There is a

special emphasis on the exploration and research of the vulnerable deep and shallow coral and sponge ecosystems.

Although there are more universities with departments that address the marine environment and ecology and may contribute to marine biotechnology, it is impossible to list all of the many here. In addition, the scope of this document is to identify large shared research infrastructures that contribute to the development of marine biotechnology. In this respect, a selection is made of some of the larger institutions and initiatives in the United States and discussed below.

# Woods Hole Oceanographic Institution (WHOI)<sup>46</sup>

The Woods Hole Oceanographic Institution (WHOI) is the world's largest private, non-profit oceanographic research institution, dedicated to research and education for better understanding of the ocean and its interaction with the earth system. WHOI operates important marine research infrastructure, such as two large research vessels and several smaller boats to support oceanographic research worldwide, in addition to a diverse fleet of underwater vehicles. The institute also provides training for scientists and supports the designing and deploying of relevant new technologies. Many of the instruments and tools that researchers use to sample and study the oceans are designed, built or improved upon by WHOI engineers and technicians. New approaches include the development of robotic systems to analyse deep waters or difficult to reach areas or for long-term analysis. In collaboration with different academic partners, the WHOI co-ordinates the Centre for Marine Robotics and offers a variety of facilities and services for use.

WHOI has a wide expertise across different oceanographic research areas. Scientists and engineers collaborate within and across six research departments to achieve better understanding of the ocean and its global and fundamental importance. Problems that have a direct impact on the ocean are addressed. The interaction of expertise and knowledge about marine life and phenomena, in combination with technological advances to allow access to environments that were unreachable before, will eventually contribute to the development of marine biotechnological applications for the benefit of society. WOI has contributed significantly to development of the Census of Marine Life.

# SCRIPPS Institution of Oceanography<sup>47</sup>

The Scripps Institution of Oceanography is a department of the University of California, San Diego. Founded in 1903, it is one of the oldest, largest and most important centres for ocean, earth and atmospheric science research, education, and public service in the world. Scripps undergraduate and graduate programmes encompass physical, chemical, biological, geological and geophysical studies in addition to degrees in climate science and policy and marine biodiversity and conservation.

With its four oceanographic research vessels and the research platform FLIP (Floating Instrument Platform) the Scripps Fleet is one of the largest academic fleets in the world. In 2016, a new ocean-class research ship will be joining the Scripps fleet on behalf of the Office of Naval Research. In addition, Scripps Institution of Oceanography works on the development of novel sensors and platforms, including autonomous underwater vehicles, floats, and sea-floor, terrestrial and atmospheric instrumentation to provide information about the changing environment.

Scripps Institution of Oceanography is also home to the Centre for Marine Biotechnology and Biomedicine, and to the Centre of Marine Biodiversity and Conservation:

1. The Centre for Marine Biotechnology and Biomedicine<sup>48</sup> (CMBB) offers a "Training Program in Marine Biotechnology", which is funded by the National Institute of General Medical Science one of the National Institutes of Health, NIH). The training is a collaborative initiative with the

UCSD School of Medicine, School of Engineering and its basic science departments and gives a multidisciplinary educational opportunity including research activities and practical experience – within the university, at sea, and through partnerships with the biotech industry. The broad education in marine science, medicine and biotechnology is expected to deliver future leaders in this promising field.

2. The Centre for Marine Biodiversity and Conservation<sup>49</sup> is training scientist in marine biodiversity and conservation and invests in communication strategies to bring scientific knowledge to policy makers and the public at large. The centre aims to integrate biological, physical and social sciences. The research is focussing on assessing the state of marine ecosystems to develop predictive models.

# The Harbor Branch Oceanographic Institute – HBOI<sup>50</sup>

The Harbor Branch Oceanographic Institute (HBOI) started in 1971 as a private institution, and in 2007 joined Florida Atlantic University. It is now home to the Centre of Excellence in Marine Biomedical and Biotechnology Research (MBBR), which was created to explore the scientific potential of the oceans for drug discovery and to develop biotechnology applications. MBBR maintains almost 50 000 samples of marine invertebrates and isolates of marine microbes within the Marine Drug Discovery Program of the Centre for Molecular Biodiversity and Biotechnology Research (CMBBR).

MBBR is supported by the National Institutes of Health, and houses *inter alia* a "Peak Library", of enriched and pure materials for high throughput screening for new active compounds of marine origin. Its collection consists of fractions that are prepared through liquid chromatography. This chemicals/metabolites library of materials is available for screening through collaborative partnerships.<sup>52</sup>

HBOI's Media Labs also maintain the website of marinebiotech.org, which brings together academic and industrial scientists from California, Florida, Massachusetts, Maryland, Mississippi and Oregon. <sup>53</sup>

A foundation, the Harbor Branch Oceanographic Institute Foundation, provides significant support for the institute. It provides direct funding from its endowment and oversees the highly successful Specialty License Plate programme covering aquaculture, protection of Florida whales and wild dolphins, and conservation of marine habitats.<sup>54</sup>

# Natural Products Repository of the NIH National Cancer Institute (NCI) at Frederick National Laboratory for Cancer Research – Developmental Therapeutics Program (DTP)<sup>55</sup>

With its almost 170 000 extracts from samples of more than 70 000 plants and 10 000 marine organisms collected from over 25 countries, and more than 30 000 extracts of diverse bacteria and fungi, the Natural Products Repository of the Developmental Therapeutics Program at NCI is the largest biorepository of natural products in the world. The marine acquired outright or licensed from over 25 tropical and subtropical countries worldwide, but mainly from the Indo-Pacific region, through contracts with the Harbor Branch Oceanographic Institute, the Australian Institute of Marine Science, the University of Canterbury, New Zealand, and the Coral Reef Research Foundation, a non-profit organisation in the State of California and the Republic of Palau and were collected since 1986. The marine collection contract with the Coral Reef Foundation was renewed in February 1997. NCI operates according to policies of fair and equitable collaboration and compensation with the participating source countries, while aiming to ensure the conservation of biological diversity. To ensure benefit sharing, agreements with the relevant government organisations in many of the source countries have been signed. The samples of the source countries have been signed.

Shortly after their collection, the natural products of the DTP repository are screened for potential anticancer activity. So far about 4 000 natural source extracts have in vitro activity against human cancer

cells, and may be further analysed by DTP researchers. The extracts are also available to extramural researchers. Access to the repository materials is subject to signing a Material Transfer Agreement protecting the rights of all parties. Extracts are available either in vials or in 96 well plates for distribution.

In the Active Repository Programme, access to materials that were shown to have anticancer activity is granted to qualified US researchers. Organisation based in the countries that have been collaborating in the NCI collection efforts are granted access to extracts collected in in their own countries. A short description has to be provided, to explain how the extracts will be tested and what the relevance to cancer is.

The Open Natural Products Repository Programme provides access to the natural product extracts for testing against any human disease. A research proposal has to be provided and is reviewed by a committee of the NCI staff to assess the scientific merit and appropriate expertise.

# The American Type Culture Collection – ATCC<sup>58</sup>

The American Type Culture Collection is one of the most important repositories for living material. The ATCC is a private, non-profit biological resource centre that supports life science and biotechnology. The organisation focuses on the acquisition, authentication, production, preservation, development and distribution of standard reference microorganisms, cell lines and other materials for research in the life sciences.

# The Bio Bricks Foundation<sup>59</sup>

The Bio Bricks Foundation is a public benefit organisation founded in 2006 by scientists and engineers who recognised the potential of synthetic biology for science and innovation, and who wanted to ensure that this emerging field would serve the public interest. The Bio Bricks Foundation works in four domains: technology, law, education and the global community.

Bio Bricks are standardised DNA sequences of defined function, designed to be incorporated into living cells to construct new biological systems. The trademarked words Bio Brick and Bio Bricks refer to a specific "brand" of open source genetic parts. Reliable, standardised biological parts that constitute a free operating system for biotechnology are produced through professional research collaborations such as with BioFab, International Open Facility Advancing Biotechnology, while an open-source wiki facilitates teaching, learning, and sharing. The Bio Brick Public Agreement, drawn up in 2011, is a free-to-use legal tool that allows individuals, companies, and institutions to make their standardised biological parts free for others to exchange and use.

Although the Bio Bricks Foundation has no particular focus on marine bio-resources, employing its approach to sharing data and material may be most optimal for building on the enormous potential of marine biotechnology.

#### **CANADA**

The ocean and fisheries are traditionally very important for Canada's economy. Fisheries and Oceans Canada (DFO) has the government's lead responsibility for marine research. DFO Ecosystems and Oceans Science implements the At-Sea Science programme with the aid of 16 Canadian Coast Guard (CCG) vessels, the majority of which are dedicated science vessels that carry out a variety of research activities, involving *inter alia* fisheries, oceanographic science and hydrography. Missions include multi-species surveys; ecosystem, geological and acoustic surveys; environmental research; ocean monitoring; and arctic science.

DFO has developed a Five-Year Research Agenda (2007-12)<sup>62</sup> focused on ten research priorities and associated areas considered essential to address federal and departmental priorities and public good needs. The ten priorities are strongly influenced by the New Ecosystem Science Framework in Support of Integrated Management, <sup>63</sup> which was published in 2007 by DFO to support DFO and Government priorities. The research priorities highlight basic and applied research needed for developing new knowledge while improving the use of existing knowledge.

Biotechnology and genomics are part of the research agenda. To address areas in which it is more effective to partner with academia, other departments and governments, DFO supports Centres of Excellence.<sup>64</sup> Two of these centres that are relevant for marine biotechnology are described below.

# The Centre for Aquatic Biotechnology Regulatory Research - CABRR<sup>65</sup>

The CABRR was created in 2008 to conduct research in support of the risk assessment and regulation of fish with novel traits, including genetically engineered fish. To achieve its goals the institute participates to national and international forums to exchange scientific information and research results to inform risk assessment methodology. It also provides peer-reviewed and other published data on scientific findings, risk assessment theory and methodology and has national and international research collaborations to improve the co-ordination and sharing of regulatory research results to develop regulatory frameworks addressing aquatic organisms with novel traits.

# The Centre of Expertise in Cold-Water Corals and Sponge Reefs - CECCSR<sup>66</sup>

The CECCSR, also established in 2008 develops dedicated tools and approaches, provides strategic advice to senior management, and supports regional, national and international efforts for the conservation of cold-water coral and sponge

# **KOREA**

#### The Marine Biotechnology Research Programme and Research Infrastructure

Korea has set up a major support initiative for research infrastructures. Research infrastructure for marine biotechnology is embedded in the Marine Biotechnology Research Programme that began in 2004; this initiative both is managed by and receives grants from KIMST (Korea Institute of Marine Science and Technology Promotion), the funding organisation under the Korea Ministry of Oceans and Fisheries. The programme aims to use state-of-the-art biotechnology to develop new drugs, bio-energy and biomaterials using valuable marine bio-resources and addressing the marine biosphere with multidisciplinary approaches. The programme also supports research infrastructure development, such as that of biobanks for marine organisms and databanks of genomics and pharmaceutical chemicals of marine origin.

# Korea Institute of Ocean Science and Technology - KIOST<sup>67</sup>

The programme for marine biotechnology is part of a comprehensive strategy that was developed to capitalise on the opportunities offered by the ocean. The Korea Institute of Ocean Science and Technology (KIOST) is a government-sponsored research institute that has driven the marine science and technology development of Korea since its establishment over 40 years ago. KIOST combines multidisciplinary principles of oceanography, physics, chemistry, engineering, biology, and other fields to understand the marine biosphere and to harness the great biodiversity and energy potential of the ocean. KIOST carries out the following activities:

• basic and applied research to promote the efficient use of coastal and ocean resources

- comprehensive surveys and studies of Korea's seas and open oceans
- scientific research in polar and tropical regions, especially in Antarctica and the South Pacific
- the development of technologies related to the coastal and harbour engineering, ships and ocean engineering, and maritime safety
- co-operation with other government agencies, universities and private industries
- development of marine resources and protection of the ocean environment
- participation in international co-operation concerning oceanographic research projects.

KIOST is headquartered at Ansan, and several domestic research branches and international research centres are found throughout the country. The South Sea Research Institute at Geoje is home to research vessels that support bio-prospecting in the ocean.

The Marine Biotechnology Research Division of KIOST is sponsored by the Marine Biotechnology Programme of the Ministry of Oceans and Fisheries and by the KIOST in-house programme. Its focal research areas are marine organisms in the biosphere of Antarctica and the deep sea of the Pacific Ocean; the aim is to develop technologies that will contribute to human welfare. In particular, -omics approaches and the advanced convergence of technologies such as nanotechnologies and IT are used to analyse and exploit marine bio-resources. One of the goals is to discover and develop new marine bioactive substances and new biomaterials of marine origin. The research also covers studies on bio-energy and bio-hydrogen production. KIOST also aims to support marine bio-industry development through applied research.

The Marine Biotechnology Research Division also hosts MEBiC, the Marine and Extreme Bio resource Collection, a biobank collection of marine and extremophile organisms that includes marine micro-organisms and marine nematodes. A databank containing genomic, metagenomic and other -omics information on marine organisms is connected to this bio collection. The biobank specimens are accessible to domestic and foreign scientists for research purposes.

Ambitious genome sequencing projects are sponsored by the Ministry of Oceans and Fisheries. Genome sequence information is publicly available at the KIOST genome bank, Marine Biotechnology Research Centre (MBRC). Genome sequences have been determined for marine organisms such as *Gelidinium elegans*, *Brachionus sp.*, and a dinoflagellate. In addition, the sequence for the minke whale has recently been determined and made publicly available at the bank. It is expected that this research will contribute to studies on the evolution of marine mammals and their ageing, cardiovascular diseases, and preservation

The following institutes come under the KIOST umbrella and are relevant for marine biotechnology:

• Korea Polar Research Institute – KOPRI<sup>71</sup>

KOPRI research focuses not only on marine biotechnology but also on geophysical sciences, biodiversity and the environment.<sup>72</sup> In line with the Antarctic Treaty that calls on parties to exchange and make scientific observations and results from Antarctica freely available, the virtual Korea Polar Data Centre (KPDC)<sup>73</sup> provides a gateway to the Korean distributed data holdings. It provides access to data sets that are available for non-commercial scientific or student projects. These databases include genomics data<sup>74</sup> and a microbial collection<sup>75</sup> from polar organisms, including those of marine origin.

KOPRI aims to be a world-class centre in polar research. It co-ordinates three polar stations: King Sejong Station and Jang Bogo Station for Antarctic research at the South Pole, and Dasan Station for Arctic research. In addition, since 2009 KOPRI has been operating the research icebreaker Araon for polar missions. These research infrastructures offer possibilities for international research collaborations.

Korea South Pacific Ocean Research Centre – KSORC

KSORC was established in 2000 to respond to immediate concerns of island nations in the Pacific, such as climate change, coastal pollution and resources development.

## Marine Biodiversity Institute of Korea – MBIK

Another major institute that contributes to the development of marine biotechnology is the Marine Biodiversity Institute of Korea. MBIK aims to protect the marine environment and bio-resources, and to ensure management of and sovereignty over Korean marine bio-resources. The MBIK was set up in 2012 after the Korea National Assembly passed the Marine Bio-resources Management Law at Seo-chon, on the West Coast of Korea. The Marine Bio-resources Research Institute works as a main stock centre that coordinates local centres. Twelve centres are linked at the time of writing, but this number will grow to cover all marine taxons.

The institute is expanding its services towards strategic planning and development of operating programmes, to:

- support the propagation and recovery of endangered marine species
- protect human health from potential risks arising from the import and export of foreign marine species and marine Living Modified Organisms (LMOs), in line with the Cartagena protocol;
- conserve marine ecosystems.

The marine bio-resources will be accessible for researchers from universities, research institutes, and companies with the aim of supporting marine biotechnology research and commercial development.

# National Institute of Fisheries Sciences – NIFS<sup>76</sup>

Complementing the above-mentioned institutes is the National Institute of Fisheries Sciences, former (NIFS), former National Fisheries Research and Development Institute (NFRDI), which falls under the authority of the Ministry of Food, Agriculture, Forestry and Fisheries. The NIFS is the unique national research institute in charge of marine and fisheries science, since its establishment as a Fisheries Experimental Station in 1921. The NIFS is committed to fulfilling various responsibilities, such as developing overseas and coastal fishing grounds monitoring marine ecosystems, building and managing fishery resources, and developing aquaculture technology.

The key research projects of NIFS are:

- conservation of fisheries' life resources and ecosystems
- eco-friendly and low-carbon seafood production technology
- high-functional and high added value seafood production technology

- mitigation technology to counter] climate change impacts on fisheries
- enhancing the competiveness of the fishery industry
- seafood safety management technology
- establishment of a global fishery infrastructure.

The Biotechnology Research Division of NIFS is conducting research on the latest biotechnology for aquaculture and fisheries. Its main research involves:

- the collection, analysis and application of bio-resources
- the study of genomics for marine organisms
- the development of bio-materials from marine organisms
- environment risk assessment and management of aquatic genetically modified organisms.

#### **JAPAN**

# The Leading-edge Research Infrastructure Program<sup>77</sup>

Japan has set up a major support initiative for research infrastructures, similar to the European ESFRI roadmap and US initiatives. The Leading-edge Research Infrastructure Program, begun in 2010, is implemented under the Strategic Fund for Strengthening Leading-edge Research and Development. Emphasising "green innovation" and "life innovation", the programme supports the establishment and operation of state-of-the-art infrastructure needed to advance a wide spectrum of research, from basic to application-oriented R&D. Ultimately, the programme aims to strengthen Japan's capacity to conduct and further advance leading-edge research and development. At least one project may be relevant to marine biotechnology: promotion of life and earth sciences, using the facilities of the Subsea floor-Simulation Laboratory and "Chikyu". This project aims to accelerate the study of subsea floor life and the biosphere related to carbon- and energy-circulating earth systems, through ocean drilling. The project involves developing the Subsea floor-Simulation Laboratory for various onshore experiments in subsea floor conditions (e.g. pressure, temperature) at the Kochi Institute for Core Sample Research, under the Japan Agency for Marine-Earth Science and Technology (JAMSTEC). Among the project objectives, the coring and research functions of the deep-earth research-drilling vessel "Chikyu" will also be strengthened.

## Japan Agency for Marine-Earth Science and Technology – JAMSTEC<sup>78</sup>

JAMSTEC is an independent institute whose main goal is to contribute to the advancement of academic research as well as improvement of marine science and technology. JAMSTEC wants to develop new marine-related scientific knowledge, create advanced technologies, and propose specific solutions for social issues. The organisation focuses on:

- the integrated understanding and prediction of global environmental changes
- advancing understanding of the earth's interior, and applying that understanding to the mitigation of earthquake and tsunami disasters
- a comprehensive study of the evolution of life and the history of the earth

research on bio resources, and use of biotechnology.

JAMSTEC's co-ordination office is located in Tokyo, while headquarters are in Yokosuka, which is also home to the research vessels. There are in total four research and data centres under the JAMSTEC umbrella. The agency is co-ordinating the use of high-end facilities and equipment for research and development, including dedicated research vessels and complementary marine observation systems. A policy is in place for use of the infrastructures by external or internal research staff.

The agency's research, development and promotion programme in the Institute for Bio geosciences, studies the interaction of the biosphere and the geological environment since the origin of life. This institute supports three programmes: the Earth and Life History Research Program; the Marine Biodiversity Research Program; and the Extremobiosphere Research Program.

Biodiversity studies and research on extremobiosphere are expected to lead to identification of new species or active proteins and compounds with special characteristics, because they are functional under extreme conditions of salt, pH, temperature or pressure. Metagenomic approaches may be required, as many of these organisms cannot be grown in monocultures.

Several databases are linked to the JAMSTEC research programmes. These include the Extremo Base (Extremobiosphere Genome Database), which provides data on the genome structure of organisms from extreme environments; an image database of planktonic foraminifera; the Marine Biological Sample Database, which provides metadata, identification, and preservation methods for marine biological samples; the Biological Information System for Marine Life (BISMaL) which provides information on marine organisms around Japan; and the Data Research System for Whole Cruise Information (DARWIN), which provides observational data and sample information obtained by research vessels and submersibles. The handling data and samples have to be in line with a basic policy of JAMSTEC which is published on the agency's website. 80

JAMSTEC in addition has a programme on innovative infrastructural technologies promoting frontline marine science, technology and planning. The aim is to develop tools and data that can be applied in various research fields and used more broadly in society, as well as to promote safe and efficient operation and planning for infrastructures. The programme mainly supports ocean observation technology for vessels and buoy and submersible/vehicle instruments; a deep-sea drilling vessel for ocean floor digging technology; and numerical modelling and simulation technology on its large-scale computing system. To store and classify observation data and sample information, JAMSTEC established the Data Research Centre for Marine-Earth Sciences.

## National Bio Resource Project - NBRP<sup>81</sup> and other Culture Collection

The National Bio Resource Project (NBRP) aims to create systematic and complete collections of all biodiversity in Japan, including from marine resources.<sup>82</sup>

Other infrastructure in Japan that supports marine biotechnology is the National Institute of Technology and Evaluation (NITE) that hosts the NITE Biological Resource Centre (NBRC) which focusses on microbial collections and accompanying information.<sup>83</sup>

#### **NORWAY**

## Marbank<sup>84</sup>

The Norwegian Government's overall objective is to create sustainable growth and development by combining the use of natural resources, environmental management, research and innovation. Along these

lines, Norway established its national strategy for bio-prospecting as a high priority of the government's High North strategy, itself one of the most important priorities for the years ahead. Extensive international co-operation is considered an essential prerequisite to achieve the goals.

According to the national strategy for marine bio-prospecting, the Norwegian Government will regulate marine biological resources and make them more accessible to researchers, industry and international participants. To realise these objectives, a national marine biobank – Marbank – was established in close co-operation with the Norwegian Ministry of Fisheries and Coastal Affairs. Part of the Institute of Marine Research, Norway's largest centre of marine science, Marbank is located in Tromsø, Norway, and is equipped with laboratories and repositories for the preparation and long-term storage of biological samples.

Marbank is appointed a co-ordinating role for establishing a network of marine collections in Norway; initial partners in the network are the University of Tromsø; *Stiftelsen for industriell og teknisk forskning* (SINTEF) or the Foundation for Scientific and Industrial Research; the Norwegian University of Science and Technology (NTNU); and UNI-Research/the University of Bergen. The Research Council of Norway facilitates co-ordination of the network, which will be open to new members.

One objective in establishing the Norwegian network is to build a common database for marine organisms and samples to which access is offered by the network. The database will form the cornerstone of a web catalogue to be launched on the website. An important part of the biobank activity is to apply quality standards for storage and use of collections and ensure samples will be used according to the legal standards applying. Co-ordinating marine samples from different collections maximises the availability of a broad range of samples and associated data.

The material archived and stored includes whole organisms, biochemical extracts and taxonomic and genetic samples from marine micro-organisms, invertebrates and vertebrates. All samples are catalogued in the national database.

While Marbank co-ordinates a network of marine collections in Norway, its mission is also to provide international academia and industry with easy access to marine biodiversity and the associated data. There is a special focus on samples for marine bio-prospecting, to bring new products with interesting characteristics to society. Marbank samples are collected in Arctic, sub-Arctic and boreal habitats, varying from the intertidal zone to the deep seas, and the collection aims to cover a wide assortment of species. So far, the main international focus in marine bio-prospecting has been on organisms that occur in tropical and temperate waters. The cold waters and the Arctic are largely unexplored, and so raise high expectations of finding novel bioactive compounds.

High-quality research in marine biotechnology/marine bio-prospecting requires access to high-quality biological material and associated data. The Norwegian network of marine collections is linked to international collaboration partners, and is a member of ESBB (European, Middle Eastern and African Society for Bio preservation and Bio banking, an international society for the bio banking of human and non-human biological materials.

The list of marine research infrastructures is not exhaustive; many other important national or transnational research infrastructures relevant for marine biotechnology may have been missed. Research infrastructures for marine biotechnology that were not specifically aiming to provide access in a broader network, but were mainly focused on regular research were not included. In addition, the research infrastructures listed here are often not solely dedicated to marine biotechnology. It is likely however that in the future, due to convergence of technologies and expertise, most of these infrastructures will become more important for marine biotechnology and for a broad network of users from the academic environment

as well as from industries. The governance of shared infrastructures to provide open but not necessarily free (of charge) access will continue to be a focal point. Access to and benefit sharing of new knowledge from marine resources needs to be addressed to support innovation, while contributing to the protection of biodiversity. In this respect, efforts such as the Reef Base Global Database, BOLD, MBIK, ELIXIR or Marbank may open new ways.

It should be noted that most research infrastructures listed here address fundamental research rather than translational research. There may be a need for open access to a marine bio-refinery, as the processing of marine biomass is quite different from that of land biomass. There are a number of examples of pilot plants for bio-refining that are used in semi-industrial scale experiments. Similar installations should be accessible for the processing of algae. In the future new developments in this field can be expected.

#### **PART III**

# MARINE BIOTECHNOLOGY'S POTENTIAL FOR HEALTH AND THE NEXT PRODUCTION REVOLUTION

This section looks at the ways in which marine biotechnology can help build the bio-economy of the future. Results of experiments in Korea with a view to the country's conversion to biofuel are presented, as are efforts to produce algae in a cost-efficient manner in the Netherlands. Issues relating to feedstock for fish are raised, and possible solutions described. The discussion then turns to the many benefits and advantages that marine biomaterials have to offer for health and well-being through functional foods, medical devices and cosmeceuticals. Part III concludes by evoking the need for sound data as evidence to support further policy development toward novel foods.

The potential of marine biotechnology for innovative applications that support economic growth is the focus of an OECD project titled "Future of the Ocean Economy". The project, led by the OECD International Futures Programme (IFP), aims to develop a global vision of how marine and maritime policies could contribute to the ocean economy to 2030, focusing on what is needed for that economy to grow in a sustainable way. Marine biotechnology and its applications will certainly play a major role. Tackling issues related to the sharing of marine biotechnology infrastructures and policies for better use of infrastructure will constitute part of the IFP work. With respect to marine biotechnology, the project is exploring inter-linkages among different sectors. For example, deep-sea mining may accelerate bioprospecting of new molecules and enzymes from marine organisms in those specialised marine environments. Aquaculture is already using new approaches derived from biotechnology for breeding marine organisms and for disease monitoring and prevention.

In future projects of the OECD Working Party on Biotechnology, Nanotechnology and Converging Technologies (BNCT), marine biotechnology may be addressed as a horizontal theme. The topic may contribute to work areas on enabling the Next Production Revolution and on enabling and adopting new technologies and new developments in technology to address health challenges.

### **The Next Production Revolution**

The Next Production Revolution is a shortcut term capturing a number of changes in production systems in which, among other technologies, biotechnology and nanotechnology will become more important as the basis for new applications and sustainable developments. The establishment of the bioeconomy is considered an essential part of this Next Production Revolution. The cornerstone of a bioeconomy is biomass to produce bio-based products to replace chemicals, plastics and fuels made from fossil resources. Marine biotechnology offers new opportunities to build this bio-economy, in which algae may become a major source of biomass. The production of algae has a number of major advantages: it has a limited effect on land use; it does not interfere with food production; and systems with minimal input are being developed.

An example from Korea highlights the potential of marine biotechnology as a driver for the Next Production Revolution. Korea set the ambition to replace 3.3% of its fossil fuel needs by biofuel. Today,

Korea needs to import 97% of its energy, which comes from fossil reserves. It is believed that biofuel production will effectively end dependence on imported fuels.

At the National Marine Bioenergy Research Centre in Korea, in collaboration with the Department of Biological Engineering of Inha University at Incheon, an experimental algae production system is being tested. Algae are produced in semi-permeable membranes in the sea. In this system, no energy for the culturing needs to be added as the movement of the sea keeps the culture moving. As seawater contains more nutrients than fresh water, no extra nutrients need to be added, either – they are taken up through the semi-permeable membrane. The eutrophicated water in coastal zones may even be beneficial.

In the experimental set-up, the amount of bioethanol produced from red or brown algae was up to three times higher than that from sugar beet or sugar cane – the best performing land energy crops. For the production of biodiesel from microalgae the yield was even up to ten times higher than from palm oil, which is the best performing biodiesel production crop on land. This production system has in fact passed all government criteria, and the oil produced is of better quality than palm biodiesel.

The idea for the future is to develop in Incheon the concept of a petroleum-free "green island", based on having a large marine energy complex in the coastal waters of an island. Doing so would, in combination with other forms of renewable energy such as wind, enable the entire energy demand of the island to be met.

The feasibility of algae production for sustainable bio-based production is also supported by work and analyses in Wageningen, the Netherlands. The AlgaePARC pilot installation in the Netherlands is used to test different photo reactors. Production systems are also tested under different climate conditions to produce algae in a cost-efficient manner given realistic conditions. Over a period of five years, the production costs were significantly reduced, from EUR 4-5/kg to EUR 2.5/kg on average. It is expected that production costs can be further lowered within the next two to three years, to EUR 0.75/kg – which would guarantee economically viable production.

More recently a bio-refinery installation is being developed in Wageningen to optimise the biorefining processes for different types of products. Testing of algae production and extrapolation studies on the refinery process for different kinds of products indicate that even now, production of higher-value chemicals from algae would be economically sustainable.

Developing better industrial production strains, other than the wild unmodified strains used thus far, will allow further decreases in production costs. Novel innovative reactor concepts will be developed and tested. That includes the use of residual CO<sub>2</sub>, nitrogen, phosphorous and heat to optimise production in the Netherlands and production in other, sunny locations. The bio-refinery process and product development also need further improvement to address whole value chains. Production of high-value products will be optimised, and functionality and quality analysed, to bring the products to the market. In the long term, the technology should allow sustainable production of commodities. Finally, it will be necessary to ensure correct legislation, as well as public acceptance.

The results of this initiative demonstrated that business cases are within reach on the basis of projected costs of biomass production and bio-refining, but a further reduction of the total cost in addition to scaling up is needed to open markets.

Although research results are promising and creating ambitious expectations, in reality investments in biomass/waste-to-energy and marine (including tidal and wave energy) sources for energy production systems dramatically decreased in 2013 when compared to  $2012^{86}$  – especially when compared with investments in solar, wind and geothermal energy. Major government support programmes that have been

set up for the latter energies may account for these trends. Proof of principle projects or demonstration projects, including those having to do with pilot algae bio-refineries, may be needed to capitalise on the opportunities from algae production systems.

Development of the Next Production Revolution to which the bio-economy will contribute depends not only on the production of plant biomass, but also possibly on aquaculture for food production for a growing population and for novel food and feed. Today, with its current annual growth rate of 7%, aquaculture is the fastest growing animal production sector in the world. This rapid growth puts large demands on feed resources. Wild fish stocks that serve as fish meal and oils have traditionally been the most important feed sources for aquaculture. To minimise the environmental impact however, alternatives are needed. Today, plants make up about 70% of salmon feed. Although they are an abundant and cheap resource with a good environmental profile, there are some drawbacks in using plant feed for carnivorous fish. They have high levels of carbohydrates, and the amino acid profile is suboptimal for a carnivorous diet. Often plant feeds also have a wide range of anti-nutrients that can have negative effects on the growth of the fish, or induce gastrointestinal disorders. These disadvantages have been tackled by optimising the feed processing, mixing appropriate feed ingredients, or supplementing amino acids. However, sustainability is also questionable here, as feed resources – including soybean or peas, which are a source of essential amino acids – should not directly compete with human food resources.

Research at the Norwegian University of Life Sciences (NMBU) in Ås to identify novel feedstock for fish will help to tackle these issues. Three resources are used: from bacteria, *Methylococcus capsulatus*; yeast, *Candida utilis*; and microalgae, *Phaeodactylum* and *Chlorella*. The advantages of using microorganisms are that they have a rapid growth rate; there is no need for agricultural land and little need for fresh water; and they can be produced from non-food sources. A bacterial meal was developed from methanotrophic bacteria using *Methylococcus capsulatus*, produced in a bio fermentation processor using natural gas, with the addition of oxygen, ammonia and minerals. The chemical composition of the bacterial meal proved similar to fishmeal: it has 70% protein, 10% lipids and 12% carbohydrate content. The amino acid composition is even better, because of the higher tryptophan content. In addition, it contains 10% nucleic acids and a wide range of bioactive components, which have a positive effect on fish health. Areas with large reserves of natural gas could develop this technology to industrial scale.

An American Company, Calysta, recently bought the rights to develop the technology further. In the next five years, a new factory to produce this bacterial meal is planned near Houston, Texas where there are large reserves of natural gas. Malaysia too has shown interest in investing in a bacterial meal factory. They have the world's largest supply of natural gas and a growing aquaculture and livestock industry, in addition to the political will to be self-sufficient when it comes to the necessary ingredients.

Another approach to producing new fish feeds was to use trees as the major input source. On the NMBU campus, a high-end bio-refinery demonstration plant was built for this purpose. The plant allows using different types of biomass for a wide range of products. Wood chips are used and broken down to lignin, cellulose and hemicellulose by thermo-chemical processing. The lignin is then separated from the wood biomass, while the cellulose and hemicellulose is further broken down to individual sugars by chemical and enzymatic hydrolysis. The next step involves fermentation of the sugars by yeast, followed by harvesting of the yeast biomass, which is dried to a sterile meal that can be used in fish feed. The yeast meal tested contained about 55% protein, 8-10% nucleic acids and 2-8% lipids, and has a favourable amino acid profile with a high lysine and tryptophan level, but a lower methionine level. Promising results are obtained when using three yeast strains in diets for salmon.

Aquaculture is increasingly important to overcome the global protein shortage, as fish production is the most efficient form of animal protein production. Feed-to-protein conversion is more efficient in fish than in poultry. Marine biotechnology is an important enabling technology at different steps in the value chain of aquaculture. Biotechnology can significantly enhance breeding, and can be used for vaccine development and the development of fish feed. Marine biotechnology therefore is important to help solve global challenges, providing solutions to improve the world protein supply.

### Health and well-being for an ageing population

Marine biotechnology is also believed to hold major potential to deliver new products for better health and well-being, as well as healthy ageing. Potent bioactive compounds of marine origin are being discovered and tested.<sup>87</sup> The chemical structures of these compounds are often so complex that rational design to develop similar bio-activity is hard to achieve.

Different molecules of marine origin with anticancer activity or for treating pain are already on the market, and many more are being tested in clinical trials. Although these molecules are very potent, the road to marketing new drugs is very long. In the case of products of marine origin, one of the additional difficulties is that these organisms are sometimes hard to cultivate in the laboratories on an industrial scale. In addition, the fact that these molecules are so complex makes them difficult to synthesise chemically. Only when the biosynthetic pathways are elucidated can synthetic biology (for example) open the way to large-scale production of these compounds. The well-known example that illustrates all this comes from the development of Yondelis, a product that took 38 years to reach the market and is now approved in 57 countries for the treatment of soft tissues sarcoma. As it takes about one ton of the tunicate from which trabectedin – commercially known as Yondelis – is isolated to produce one gram of the molecule, progress could only be made in 1996, when a semisynthetic production method was developed.

A market analysis of health products in Ireland illustrated where marine-derived products could create huge opportunities. The analysis identified opportunities in terms of functional foods, cosmeceuticals, and biomaterials made from marine resources. For functional foods, three main sources of potential products had been identified. In the first, macro- and micro-algae were identified as a source of pigments, lipids and fatty acids, proteins, polysaccharides and phenolics, with potential implications for gut health and cardiovascular health, and have use as anti-inflammatory, anti-obesity and anti-cancer agents. Secondly, crustaceans and molluscs were identified as sources of chitin, chitosan and protein-derived peptides, with anti-hypertensive, anti-oxidant, anti-microbial, anti-coagulant, anti-diabetic, anti-cancer, immunostimulatory, calcium-binding and anti-cholesterol properties. Finally, finfish are a source of minerals, lipids and fatty acids, carbohydrates and protein, with potential implications for cardiovascular health and use as anti-obesity and anti-cancer agents.

The market analysis indicated that the potential for cosmeceuticals, i.e. cosmetics with extra characteristics for well-being, is indeed huge, given the global trend of increased consumer demand for products based on natural and organic ingredients and a merging of health and beauty products. In addition to the benefits listed above, algal components can be used as anti-oxidants, colours, gels, sunscreens, moisturisers, and skincare and hair care products. Finfish extracted components are used in skin and hair products.

Another important potential application is the use of marine biomaterials in bone and tissue repair. Sponges and the skeletons of calcareous algae can be used as a bone or tissue scaffold or for tissue repair and bone grafting. Chitin or chitosan and special proteins from crustaceans and molluscs or collagen from finfish can also be used for tissue or bone repair. The byssus threads of mussels, for example, can be used as a bone adhesive, or for wound closure in a wet environment.

It is expected that it will be possible to capitalise on the trend of introducing new products into the diet or cosmetics for healthier lives and well-being. Biomaterials are often also biocompatible and biodegradable, and have fewer side effects than traditional materials – characteristics that are highly

appreciated by consumers. The actual size of the marine biotechnology market is not really certain. It is estimated that in the EU, sales of marine products are around EUR 300 million to EUR 750 million. In the United States, sales are expected to be close to USD 5 billion by 2018. The current share of marine materials in the biotechnology market for health is rather low. The primary and easiest target may be the focus on functional foods or cosmeceuticals as the path to drug development and marketing is much more risky and lengthy, due among other things to regulatory and safety issues. Discovery of new sources of materials is a continuing process.

One of the focus areas proposed for the Working Party on BNCT concerns health. The WP will be endeavouring to provide evidence and to support policy development for health claims related to diet and novel foods, and to develop science-based personalised nutrition for health and well-being, both in general and for elderly populations. Such efforts are necessary because research data to support the positive health effects of functional foods, nutraceuticals and personalised nutrition are often inconclusive. And evidence-based decision making requires scientifically sound data.

Equally, better understanding of the individual genetic set-up and susceptibilities of people has the potential to bring clarity to nutritional epidemiologic research, enable diagnosis, provide a personalised nutrition and – ultimately – help to prevent and manage diet-related chronic diseases. Many so-called novel foods in fact have marine origins.

## MARINE BIOTECH ABBREVIATIONS

AlgaePARC	Algae Production And Research Centre, Wageningen University & Research Centre, Netherlands
ASSEMBLE	Association of European Marine Biological Laboratories
ATCC	American Type Culture Collection
AUVs	Autonomous underwater vehicles
BioFab	US International Open Facility Advancing Biotechnology
BISMaL	Biological Information System for Marine Life, Japan
BNCT	(Working Party on) Biotechnology, Nanotechnology and Converging Technologies
BOLD	Barcode of Life Data Systems
BRC	Biological resource centres
CABRR	Centre for Aquatic Biotechnology Regulatory Research, Canada
CBOL	Consortium for the Barcode of Life
CCG	Canadian Coast Guard
CCINFO	Culture Collections Information Worldwide
CECCSR	Centre of Expertise in Cold-water Coral and Sponge Reefs, Canada
CIESM	Mediterranean Science Commission
CIOERT	US Cooperative Institute for Ocean Exploration, Research and Technology
СМВВ	Centre for Marine Biotechnology and Biomedicine (Scripps Institution of Oceanography)
CMBBR	US Centre for Molecular Biodiversity and Biotechnology Research
CoML	Census of Marine Life
CWG	(European Union) Collaborative Working Group
DARWIN	Data Research System for Whole Cruise Information, Japan
DFO	Department of Fisheries and Oceans Canada
DTP	Developmental Therapeutics Program

EBI	European Bioinformatics Institute
ECA	ELIXIR Consortium Agreement
ELIXIR	European Life-Science Infrastructure for Biological Information
EMBL-EBI	European Molecular Biology Laboratories European Bioinformatics Institute
EMBRC	European Marine Biological Resource Centre
ERIC	European Research Infrastructure Consortium
ESBB	European, Middle Eastern and African Society for Bio preservation and Bio banking
ESFRI	European Strategy Forum on Research Infrastructures
EU	European Union
FISH-BOL	Fish Barcode of Life Initiative
FLIP	Floating Instrument Platform, Scripps Institution of Oceanography
FP7	Seventh European Framework Programme
FY	Fiscal year
GBIF	Global Biodiversity Information Facility
GRIs	Global Research Infrastructures
GSO	(G8) Group of Senior Officials
GSF	OECD Global Science Forum
НВОІ	Harbor Branch Oceanographic Institute (Scripps Institution of Oceanography)
iBOL	International Barcode of Life Project
ICRI	International Conference on Research Infrastructures
IFP	OECD International Futures Programme
IDRIS	International Distributed Research Infrastructures
ISBER	International Society for Biological and Environmental Repositories
JAMSTEC	Japan Agency for Marine-Earth Science and Technology
KBBE-net	Knowledge Based Bio-Economy Network
KIMST	Korea Institute of Marine Science and Technology Promotion

KOPRI	Korea Polar Research Institute
KPDC	Korea Polar Data Centre
KSORC	Korea South Pacific Ocean Research Centre
LMOs	Living Modified Organisms
MarBOL	Marine Barcode of Life campaign
MBBR	Marine Biomedical and Biotechnology Research
MBIK	Marine Biodiversity Institute of Korea
MBRC	Marine Biotechnology Research Centre, Korea
MEBIC	Marine and Extreme Bio resource Collection, Korea
MIRRI	Microbial Resource Research Infrastructure
MOU	Memorandum of Understanding
MRI	Maritime Research Infrastructures
NBDC	Biotechnology Development Centre, Japan
NBRP	National Bio Resource Project, Japan
NBRC	National Biological Resource Centre, Japan
NCI	NIH National Cancer Institute
NCNPR	National Centre for Natural Products Research, University of Mississippi
NFRDI	National Fisheries and Development Institute
NIFU	Nordic Institute for Studies in Innovation, Research and Education
NIH	National Institutes of Health
NIUST	US National Institute of Undersea Science and Technology
NOAA	US National Oceanic and Atmospheric Administration
NPMD	Patented Microorganisms Depository, Japan
NSF	US National Science Foundation
NTNU	Norwegian University of Science and Technology
NURC	NATO Undersea Research Centre
NURP	US National Undersea Research Program

05	Outreach Five
OAR	US Oceanic and Atmospheric Research
OBCR	Ocean Biotechnology Centre and Repository
OBIS	Ocean Biogeographic Information System
OER	US Office of Ocean Exploration and Research
OWW	OpenWetWare.org
PolarBOL	Polar Barcode of Life campaign
RISA	Regional Integrated Science and Assessments
ROVs	Remotely operated vehicles
SINTEF	Stiftelsen for Industriell og Teknisk Forskning or the Foundation for Scientific and Industrial Research
SMEs	Small and medium-sized enterprises
UNOLS	University-National Oceanographic Laboratory System
WDCM	World Data Centre for Microorganisms
WHOI	Woods Hole Oceanographic Institution
WPB	OECD Working Party on Biotechnology

## **ENDNOTES**

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## MARINE BIOTECHNOLOGY: DEFINITIONS, INFRASTRUCTURES AND DIRECTIONS FOR INNOVATION

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