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Marine biotechnology as a generating tool for shared value creation in the Mediterranean

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1. Introduction

Panoramed is a governance platform framed within axis 4 of the Interreg-Med program[1], which aims to support processes of strengthening and creation of multilateral cooperation frameworks in the Mediterranean in order to respond to common challenges and opportunities. The Panoramed approach adopts a variety of perspectives, one of which is biotechnology, in order to have a holistic vision and thus provide valuable proposals that help solve these challenges. The European Commission (EC) defines bioeconomics as the parts of the economy that use renewable biological resources from land and sea, such as crops, forests, fish, animals, and micro-organisms, to produce food, materials, and energy. In alignment with this definition, the EC defines the sector of marine biotechnology (MBT) as a provider of high value-added and specialised commercial products coming from such renewable biological resources. MBT is considered one of the five specific European activities or focus areas of the blue growth strategy (European Commission, 2012), and is the one with the greatest potential for job creation and for innovations that can be transferred to society.

The main objective of this report is to provide governance recommendations to European public administrations in order to promote MBT as an agent that generates systemic and transformational changes in the Mediterranean. These changes must pursue shared value creation (SVC) in society while stimulating the generation of blue economic oceans by the business sectors of the blue economy.

In section 2, a contextualisation of MBT in the Mediterranean is provided along with an introduction to the concepts of SVC and blue oceans. Sections 3 and 4 (and sub-sections therein) show the potential industrial applications of the main Mediterranean marine resources from a technological point of view. A couple invasive species are put as examples at Section 5. Section 6 describes the potential impact of MBT in terms of SVC, with a detailed analysis of good practices. The thorough analysis of all of this information, supported by bibliographic documentation of other European initiatives and projects (Bluemed, platforms such as Biomarine, MBT ERA-NET projects, studies and projects of Interreg-MED, etc.), is used to compile the final list of recommendations to public administrations regarding stimulation of MBT in the Mediterranean.

[1] More information at a: *https://governance.interreg-med.eu/*

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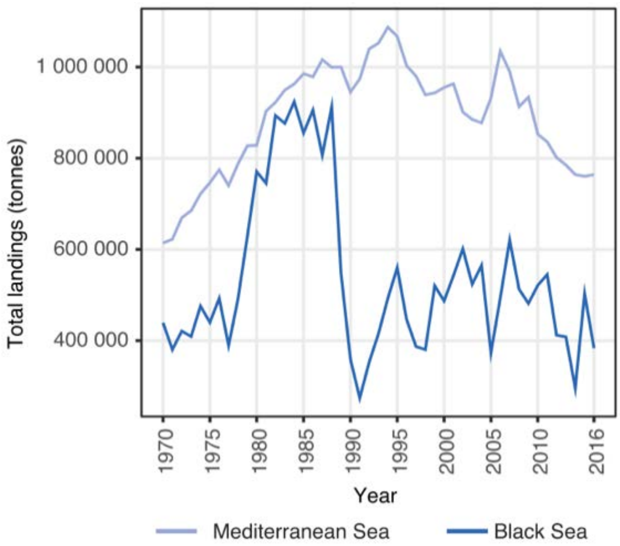
2. MBT in the Mediterranean

Due to excessive diversification of blue biotechnology, it is difficult to obtain statistics of its real impacts. However, the global MBT market, from both the products and processes perspectives, is estimated to reach $4.8 billion (USD) by 2020, reaching $6.4 billion by 2025. In Europe, the blue growth strategy proposed by the EC in 2012[2] frames MBT as a fundamental facilitator for blue bioeconomics, hoping that its turnover will reach $1 billion by 2020 in Europe if the market continues growing at the current rate of 6-8%, and consequentially creating 10,000 new jobs annually (ECORYS, 2014).

Aquatic organisms inhabiting seas and oceans live very different lifestyles adapted to some of the extreme physical and chemical conditions on the planet concerning pressure, temperature, light, concentration of gases, etc. Organisms that develop in water have evolved in very specific physiological ways, which have stimulated the expression of genes and the generation of bioactive molecules allowing them to survive under such conditions. This diversity provides a great range of opportunities for the generation of value-added products and services with biotech tools. In order to detect and collect these bioresources in such complex environments with limited accessibility, MBT depends on collaborative research with disciplines other than biological sciences. For example, the development of devices such as remotely operated vehicles (ROVs) has allowed the efficient and safe collection of samples (Hurst, Børresen, Almesjö, De Raedemaecker, & Bergseth, 2016).

Prospection activities and sample collection shall always prevent any negative impact on the marine ecosystems. Moreover, the final goal of every biotechnological discovery (product or service) should include a feasibility study together with a commercialization plan ensuring the preservation of the wild populations.

Figure 1. Fishing sector catches in the Mediterranean (in tonnes)

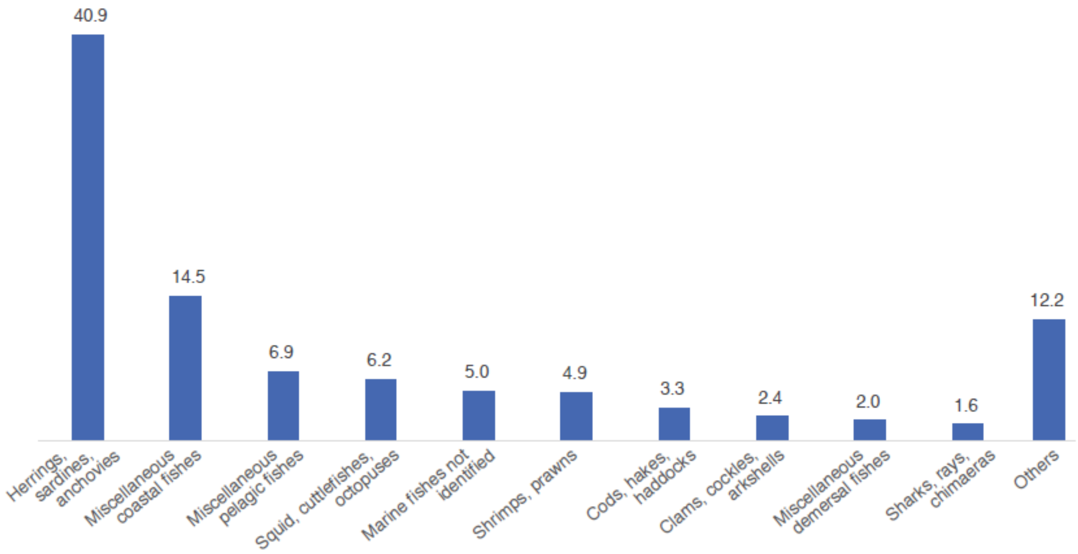


Source: FAO, 2018a

[2] Available at: *https://ec.europa.eu/maritimeaffairs/sites/maritimeaffairs/files/docs/body/com_2012_494_en.pdf*

Primary sectors such as fishing and aquaculture are great alternatives for detecting and collecting organisms and biocompounds with potential biotechnological applications. These sectors are excellent sources of resources due to their volume and the diversity of organisms in the Mediterranean. Catches from the fishing sector in the Mediterranean, although unstable, amounted to 850,000 tonnes in 2016 (Figure 1) and consisted mainly of fish, molluscs, and crustaceans (Figure 2). On the other hand, it is estimated that fishing in the Mediterranean produces an annual average of 230,000 tonnes of rejection, which represents approximately 18% of the total catch volume (FAO, 2018a). As for aquaculture in the Mediterranean, around 450,000 tonnes were produced in 2015 according to FISHSTAT data[3], of which 90% consisted of sea bream, sea bass, rainbow trout, common carp, tilapia, mussels, oysters, and Japanese clam (Nunes, Svensson, Markandya, & Massa, 2017). The desired fishery and aquaculture products co-generate some rejection products which, in the case of fish, reach more than 50% of the total catch weight (including fins, heads, skin, and viscera), generating economic and environmental problems in their management (Caruso, 2016). These products can be valuated using biotechnological techniques to provide answers to these problems.

Figure 2. Average landings in the Mediterranean in the period 2014-2016, by groups of species



Source: FAO, 2018.

In addition to the valuation of living marine resources, MBT is also a useful tool for solving environmental problems, such as plastic pollution, which currently comprises 95% of all pollution in the Mediterranean (WWF, 2018). Each year, between 150,000 and 500,000 tonnes of macroplastics and between 70,000 and 130,000 tonnes of microplastics are thrown into European seas, mainly the Mediterranean Sea (European Commission, 2018). In this case, MBT can provide a battery of tools to attack this important problem which affects marine fauna in the Mediterranean sea.

[3] FISHTAT is the statistical database on global fisheries prepared by the United Nations Food and Agriculture Organization (FAO).

From an economic point of view, the MBT sector, like the rest of the blue sectors, must guarantee its long-term sustainability in order to be able to carry out transformative actions in its environment. For this reason, the examples, good practices, and recommendations appearing in this report are in line with two economic theories; the Blue Oceans theory of professors Mauborgne and Chan Kim, and the Shared Value Creation (SVC) theory of professors Porter and Kramer.

According to the Blue Oceans theory, developed in the book 'Blue Ocean Shift: Beyond Competing. Proven Steps to Inspire Confidence and Seize New Growth' (Chan Kim & Mauborgne, 2017), the ideal business model for a company or sector must be based on innovation as a differentiating engine for competition. This theory also presents a 'red ocean' situation, which is produced when there is a high competition for a product or service and low or no entry barriers for potential competitors. This situation causes companies to compete for price and not by value, maximising their own resources to achieve market share without the possibility of investing in technological developments. In this theory, the red of the ocean represents, in a metaphorical sense, the blood of the members of the ecosystem resulting from this struggle. On the other hand, the Blue Ocean concept consists of the creation of new market niches with strong entry barriers, which causes a decrease in competition. These can be technological barriers, barriers related to industrial protection (patents, industrial secrets, utility models, etc.), or legal barriers. Innovation is the main driver for the creation of the economic blue oceans and the evolution of the leading industries.

On the other hand, the SVC theory (Porter & Kramer, 2011) proposes a business strategy in which companies aim beyond the achievement of economic benefits, acting as transformational agents in their environments and thereby generating environmental, social, and economic value (shared value). This theory is developed more extensively in section 5 of this report. Initiatives identified as good practices for generating shared value in the MBT sector are also described in section 6.

3. Biological marine resources with biotechnological potential in the Mediterranean

This section describes the potentialities of MBT from a scientific point of view, listing the main marine products and by-products present in the Mediterranean, its bioactive components, and the potential applications in different industrial sectors. The most representative biological groups are described in terms of biomass according to section 2, and are fish, bivalve molluscs, and crustaceans. In the following sections, we provide examples from applications of marine resources species from outside the Mediterranean. These examples, even in cases of species not present in the region, can work as inspiration to explore similar properties in local species.

3.1. Fish

The fish group is extraordinarily broad and diverse in terms of form, composition, and physiological characteristics, being adapted to all natural ecosystems in the world. This diversity makes them a biological group with high potential in terms of biotechnological applications.

Table 1. Average composition of fish

Component	Average weight (%)
Head	21
Gut	7
Liver	5
Fish eggs	4
Spine	14
Fins and lungs	10
Skin	3
Fillet	36

Source: Waterman, 2001

The main suppliers of fish are fisheries and aquaculture sectors, sales from both of which are intended for human consumption. Approximately 70% of fish sold pass through some sort of processing procedure, which involves classification, slime elimination, washing, peeling, slicing, fin cutting, and separation of bones from meat and fillets. During this processing, a residue of 20% to 80% by weight is generated, depending on the extent of processing and the type of fish.

Fish wastes can be used in silage production, in meat and fish sauces, or in/as other value-added products such as proteins, oils, amino acids, minerals, enzymes, bioactive peptides, collagen, and gelatine (Ghaly, Ramakrishnan, Brooks, Budge, & Dave, 2013).

The following sections describe different biocomponents of fish and their applications in different industrial sectors.

3.1.1. Human health, food, and cosmetics sector applications

3.1.1.1. Skin

Fish skin represents only 3% of the total weight of the fish on average (Waterman, 2001), but has a wide range of industrial applications. For example, tilapia skin is used in medicine to reconstruct organs and human skin, and in surgical interventions for second- and third-degree burns (Costa et al. 2019). Currently, in Brazil, several university research groups, public health centres, and private companies have collaborated to advance in the search for other such techniques. The Burn Treatment Centre of the Dr. José Frota Institute (Brazil), the Federal University of Ceará (Brazil), the Mayo Clinic (Florida USA), and the Nuclear Energy Research Institute (Brazil) have evaluated the effectiveness of the use of Nil tilapia skin (*Oreochromis niloticus*) in burn treatment (Costa et al. 2019). The use of tilapia skin in burn treatment presents several improvements over the traditional treatment in that it reduces pain and the number of treatments required. Tilapia skin provides a significant amount of type 1 collagen, offering a resistance very similar to that of human skin and a degree of humidity that promotes scarring. It also exhibits very good adhesion to the muscle tissue, avoiding protein and plasma loss and minimising external contamination and dehydration of the patient.

The use of tilapia skin requires a prior scale-cleaning process and the elimination of muscle tissue, pathogens, and odours. It is then pressed and cut into strips of 10 cm by 20 cm, which can be stored at 2–4 °C for a maximum period of 2 years.

Tilapia skin has also been used in surgical interventions for reconstruction of human organs and tissues, such as vaginal reconstructions (Bezerra et al., 2018). This is a less-invasive technique than the traditional method and poses a lower risk for the patient since it is not necessary to use parts of other tissues such as the patient's own bowels. These interventions are still in the initial stages of development, but the advantages that they present over traditional techniques make them alternatives worthy of consideration.

3.1.1.2. Collagen and gelatin

Collagen is a fibrous protein present in the intercellular layer and connective fibrous animal tissue, and constitutes 30-60% of total protein content in mammals. It promotes blood clotting and confers firmness and elasticity to the organs and tissues. Collagen is obtained from fishing and aquaculture by-products, especially skin and bones, using an acid solubilisation process or by enzymatic treatment. Collagen is used as a nutritional supplement aimed at preventing and treating osteoarticular problems.

Controlled hydrolysis of collagen produces gelatin, which is used for encapsulation of compounds in the pharmaceutical industry, as a support material in cell cultures in laboratories, and as dressing in wound care. In the food sector, gelatin is used as a stabilising and emulsifying ingredient, and in the manufacture of products such as jams, desserts, soups, and ice cream. In the cosmetic sector, collagen is a common ingredient used for the treatment of rough skin and its prevention due to aging.

3.1.1.3. Chondroitin sulfate

Chondroitin sulfate is part of the connective tissues of vertebrate and invertebrate animals, such as cartilage, skin, blood vessels, ligaments, and tendons, conferring certain mechanical and elastic properties. It is extracted primarily from marine species such as sharks, but also stingray and sturgeon. It is highly water soluble in its pure form but insoluble in the protein-bound form, proteoglycan.

In the health sector, chondroitin sulfate is classified as a symptomatic slow-acting drug for treatment of osteoarthritis in several European countries and as a nutritional supplement in the United States. The World Health Organization (WHO) classifies it as an anti-inflammatory and non-steroidal antirheumatic compound. Other uses, such as in the treatment of articular pathologies in animals, have also been documented (ANFACO CECOPESCA, 2012).

3.1.1.4. Hyaluronic acid

Hyaluronic acid is a polysaccharide very similar to chondroitin sulfate, with water retention capabilities. It intervenes in the process of collagen synthesis and acts as an anti-inflammatory and lubricant of the articulations. The main marine sources are fins and the vitreous humour of species such as shark and tuna.

In medicine, hyaluronic acid is used as an implant filling material in cosmetic surgery or in rheumatoid arthritis treatments.

Products obtained from fish also have applications in cosmetics, an industry characterised by high value addition. The applications of hyaluronic acid are mostly focused in treatments of the epidermis.

3.1.1.5. Squalene

Squalene is a natural hydrocarbon, which acts as an intermediary in the biosynthesis of cholesterol. One of its functions is strengthening of the immune system, preventing cardiac damage and exerting antioxidant properties. The main source of this molecule is shark liver.

Squalene is mainly used in the medical sector as an adjuvant in flu and malaria vaccines, but it also has applications in the fields of cosmetics and human nutrition. In cosmetics, it is used as an ingredient with moisturising and emollient properties in creams, lotions, and enamels.

3.1.1.6. Protein hydrolysates

Protein hydrolysates are a set of peptides of different sizes originating from chemical or enzymatic protein hydrolysis. The enzymatic hydrolysis process has greater technification, control, and selectivity than the chemical process, giving a final product of higher quality. In the enzymatic hydrolysis process, the control of parameters such as pH, reaction time, substrate concentration, enzyme to substrate ratio, temperature, and type of enzyme used is essential.

Protein hydrolysates can be obtained from wastes of the fishing sector and used in human food and gastronomy. Depending on the degree of hydrolysis degree, the hydrolysates have different characteristics. If the degree of hydrolysis is less than 10%, the hydrolysate supports improvement of the functional properties of the food. On the other hand, if the degree of hydrolysis exceeds 10%, extensive hydrolysates are obtained, which are used as food supplements for use in special diets. High-protein diets often adopted by athletes are an example of this application. Another use of such hydrolysates is in the treatment of patients with liver problems. Meanwhile, low molecular weight hydrolysates are used as a foaming ingredient in the production of cakes and as an emulsifier for the manufacture of mayonnaise and ice cream (ANFACO CECOPESCA, 2012). Despite the degree of maturity of the current techniques for protein hydrolysis, it is still necessary to improve the enzymatic effectiveness and reaction time required in the enzymatic hydrolysis, in order to make it more feasible as an alternative to the chemical hydrolysis technique.

3.1.1.7. Essential fatty acids

Another type of compound found in fish are omega-3 fatty acids. These are essential fatty acids, which means that they are needed for some vital reactions but that the human body cannot synthesise them, so they needs to be consumed from an external source. Essential fatty acids come mainly from blue fish, such as sardines, tuna, mackerel, and Atlantic krill, and are obtained by a process of oil extraction from fish tissues. The extract obtained is pressed and centrifuged in order to isolate these oils, and is then refined and purified to obtain the acid(s) or fatty acid(s) of interest. Once purified, the fatty acids are concentrated in order to stabilise and pack them for use/consumption.

The most common commercial form of essential fatty acids is as soft gelatin capsules, which are used as a food supplement in the food industry. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the most commonly used fatty acids, and are commonly added to bread products, dairy products, cereals, and beverages. Both EPA and DHA come from fish, and some world health and nutrition authorities, such as the WHO[4], PAHO[5], and FAO[6], have described their beneficial properties in terms of preventing cardiac conditions and other diseases (Ghaly et al., 2013).

3.1.2. Animal feed sector applications

Currently, the production of flours and fish oils as the main ingredients of animal feed is one of the most common industrial applications of products proceeding from the fishing industry. Small pelagic species and other fish residues are the main sources of components for this sector (mainly amino acids and lipids such as omega-3 fatty acids) in the Mediterranean (see figure 2), and allow the production of animal feed products with high protein content (60%-75%). Chile, Peru, Denmark, Iceland, and Norway are the main producing countries, and China and countries in the EU are the main buyers (FAO, 2018b).

The extraction of fish oils and proteins requires different crushing, baking, and pressing stages in order to obtain solid and liquid phases, the bases of fishmeal and fish oil, respectively. After these procedures, the solid phase is subjected to crumbling, drying, cooling, grinding, and

[4] World Health Organization. More information: *https://www.who.int*
[5] Pan American Health Organization. More information: *https://www.paho.org*
[6] Food and Agriculture Organization. More information: *http://www.fao.org*

silage processes, while the liquid phase passes through decanting, centrifugation, and purification processes (ANFACO CECOPESCA, 2012). All of these processes have high technological maturity corresponding to level TRL9[7] in the Mediterranean, although there is still room for certain improvements.

Figure 3. Handbag made with fish leather.

Source: FAO, Luis Tato.

3.1.3. Fashion sector applications

Fish skin exhibits a very useful surface composition, which can be of interest for the fashion industry. However, the skin of some species is not suitable for extraction and treatment for later manipulation due to its consistency or the amount of skin that can be obtained per individual. The treatment that is applied to fish skin is very similar to that applied to mammalian skin, which involves tanning, staining, and seeding processes. Atlantic salmon, sturgeon, eel, wolf fish, stingray, tilapia, shark, and cod are some of the most interesting species because the consistency and physicochemical characteristics of their skins make them suitable for treatment[8]. Some fashion companies such as Dior, Gucci, and Prada have designed entire collections (belts, wallets, shoes, etc.) made from fish skin.

3.1.4. Other industrial applications

Fish gelatin is also used in the manufacturing of photographic films, graphic films, and X-ray films.

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[7] Technology readiness levels according to Horizon2020 program. Available at: *https://ec.europa.eu/research/participants/data/ref/h2020/wp/2014_2015/annexes/h2020-wp1415-annex-g-trl_en.pdf*
[8] More information at: *http://www.leather-dictionary.com*

3.2. Bivalve molluscs

Aquaculture of bivalve molluscs in the Mediterranean in 2013 consisted of 73% Mediterranean mussels, *Mytilus galloprovincialis*, 19% Japanese clam, *Ruditapes philippinarum*, and 3% flat oyster, *Ostrea edulis*, and pacific oyster, *Crassostrea gigas* (Nunes et al., 2017). Although this data corresponds to the year 2013, the proportion of each species can be extrapolated to production in 2019.

Figure 4. Mussel culture

Source: IPACuiltura

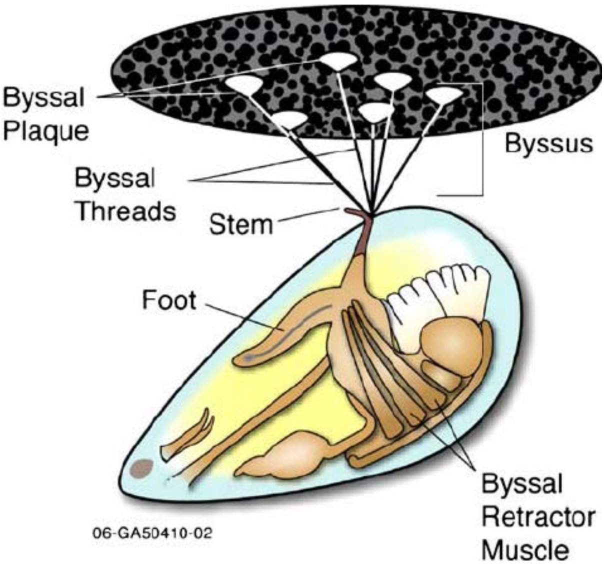
The group of bivalve molluscs is comprised by more than 9,000 species. Some of them are traditionally reared in aquaculture around the world, thus representing the most important group of species in aquaculture production worldwide. Spain generates more than 90,000 tonnes/year of waste of *Mytilus galloprovincialis*, a raw material that should be valorised (Smaal, Ferreira, Grant, Petersen, & Strand, 2018). Bivalve mollusc wastes can cause both environmental and economic problems. High quantities of the mussels, clams, and oysters produced fall in areas close to the capture and production areas, causing problems both on the ground and in the water column due to their degradation. In addition, the collection and destruction of this waste implies high costs for the production companies.

Bivalve molluscs are interesting from a biotechnological point of view because they are filtering organisms and therefore their bodily composition can be a good indicator of the state of the water and sediments in terms of pollution levels. Thus, molluscs are excellent living environmental monitoring tools. Furthermore, they are a very good source of several useful biocomponents used in various industries. Its shell, which accounts for between 30-60% of the total weight, the muscle, which represents 40-70% of the total weight, and the byssus, the anchoring button of the valves and the bodies attached to the valves which represent 1-3% of the total weight (Iñarra et al., 2018), are the main parts used for such purposes. Some of these industrial applications are described in the following sections.

3.2.1. Human health sector applications

Mussels, clams, and oysters have some relevant applications in biomedical research. They can be used as animal models in oncology research and in research into the influenza virus, for example, because bivalves can fight off some common human pathogens but without the need to produce antibodies to defend themselves. This characteristic makes them an appropriate model of study to evaluate alternative human defenses against pathogens. Further, species in this group are capable of generating substances with effects analogous to those of antimicrobials, so they can also be used in the search for alternatives to existing antibiotics and other drugs to which resistance has been demonstrated. Bivalves also present antiviral, antibacterial, and antiparasitic activity, and can produce other substances such as MytiLec-1 (produced by the Mediterranean mussel, *Mytilus galloprovincialis*), which is able to inhibit bacterial growth in gram-negative and gram-positive cultures. At the same time, this compound can be related in the treatment of Burkitt's lymphoma and the induction of apoptosis in breast cancer cells.

Figure 5. Mussel (*Mytilus edulis*) anatomy and structures of the byssus



Source: Francisco F. Roberto. Research Gate.

Hydrolysates, the result of enzymatic digestion of bivalves and other marine invertebrates, contain dozens of peptides with antioxidant and other healthful properties and can be used as novel food ingredients. In the case of mussels, although some antimicrobial peptides from these species have already been commercially exploited, some pilot studies have demonstrated their biotechnological potential in fighting certain diseases such as shrimp white spot syndrome (Smaal et al., 2018).

Another research line on the potential applications of bivalves concerns their use as a biomaterial in the medical field due to their properties related to tissue regeneration and repair and bone growth. Byssus protein filaments and mussel adhesive plates contain Mfp proteins (mussel foot proteins) which are highly resistant in the marine environment and effective defenses against predators and the mechanical forces of waves and ocean currents.

Currently, these proteins are being studied in the development of adhesives and resistant biomaterials that can be used as self-curable polymers, water-resistant materials, artificial joints, contact lenses, dental sealers, and hair- and skin-repair products. Each bivalve has its own Mfp composition, providing a myriad of different structural and functional characteristics.

Another biomedical application, currently in the initial research stage, is the use of the adhesive properties of the byssus to design new drug delivery systems, encapsulating bioactive compounds that will be released once the capsule comes in contact with mucous membranes. In fact, the ancient Egyptians used byssus filaments to make mummies' dresses due to their high resistance. Byssus filaments of Nara (*Pinna nobilis*) were also used as a textile element by Arabs.

According information from 2014 (Smaal et al. 2018), there are more than a thousand healthcare products derived from substances extracted from molluscs, such as Liprinol and Biolante Seatone, both of which are extracted from the *Perna canaliculus* mussel, or an analgesic approved by the FDA for human use that is derived from the *Conus sp.* snail. Table 2 shows different patents inspired by or derived from the byssus gland of bivalves.

Table 2. Patents inspired by the byssus gland of bivalve molluscs

Patent number	Owner of the patent	Patent
US7622550B2	Posco Co., Ltd., Pohang University of Science and Technology Foundation	Mussel bioadhesive
US7943703B2	Northwestern University	Modified acrylic block copolymers for hydrogels and pressure-sensitive wet adhesives
US8911831B2	Northwestern University	Surface-independent, surface-modifying, multifunctional coatings and applications
US9801972B2	Postech Foundation and Postech Academy Industry Foundation	Mussel-inspired bioactive surface coating composition generating silica nanoparticles
EP2013290B1	AMSilk GmbH	Multilayer silk protein films
US9617433B2	Biopolymer Tech of Sweden AB	Corrosion-inhibiting coating based on cerium oxide and a catecholic polymer
US8575276B2	DSM IP Assets BV	Biomimetic compounds and synthetic methods therefor

Source: Google Patents (date and search criteria: September 2019; byssus-inspired)

3.2.2. Cosmetic and personal hygiene sector applications

Some proteins extracted from mussels are also used in industries of high added-value, such as the cosmetic and hygiene sectors. Such proteins have been tested successfully in skin care products, due to their content of compounds such as collagen. They have also been satisfactorily tested in anti-aging products, skin repair products, and toothpastes due to their bleaching properties.

3.2.3. Animal feed sector applications

The calcium carbonate ($CaCO_3$) from the mollusc shell can be used as an ingredient in animal feed. Chickens are the main consumers of such feed and the carbonate has benefits in terms of the production of more consistent eggs.

3.2.4. Agriculture sector applications

In the agriculture sector, some of the functions of calcium carbonate from the shells of molluscs are the correction of soil acidification and as a component of fertilisers.

3.2.5. Construction sector applications

The inorganic fraction of bivalves, especially the shell, is used as a filling material in thermoplastic polymers such as propylene, used in the construction of water supply pipes, and even as a component of asphalt mixtures, as is confers absorbent capability and can capture some heavy metals from the surrounding environment. Bivalve shells are also used in the production of cement and other materials. Within the framework of the Biovalvo project, co-funded with the FEDER Interconecta program, a module has been built on the University of A Coruña campus which employs this material[9].

New coatings and lubricating materials are other mollusc-derived products used in the construction sector. These materials can also be used by the nautical and marine engineering sectors due to their anti-fouling properties.

3.3. Crustaceans

Crustaceans constitute a very important product of fisheries in the Mediterranean area, primarily due to their high market value. The main species in this group are prawns, lobsters, Norway lobsters, scallops, and spider crabs (FAO, 2018a). The exoskeleton or shell is the body part serving defense functions, and it is the main waste product generated from crustaceans that can be evaluated from a biotechnological point of view. More than 50% of the total weight of crustaceans becomes by-products or waste, which explains why their treatment is relevant.

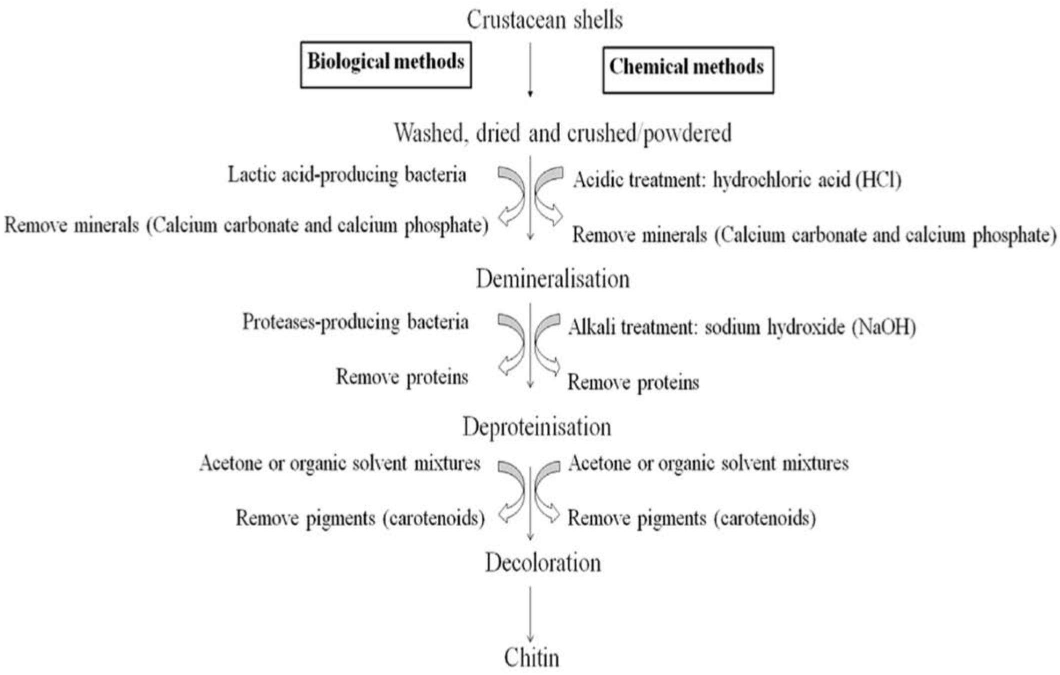
Chitin and products derived therefrom, such as chitosan, are some of the main substances constituting this waste. The chitin content in crustaceans is highly variable, ranging from 24% by weight in krill to 75% by weight in lobster. In general, crustaceans have a total protein content of 30-40% by weight, a mineral content of 30-50% by weight (mainly $CaCO_3$), and chitin, lipids, and other pigments such as astaxanthin comprise 20-40% of the total weight (Özogul, Hamed, Özogul, & Regenstein, 2018).

Chitin is also present in the beak of some molluscs such as cuttlefish or octopus, but it is analysed and described in the present section due to its higher relative importance in crustaceans. Chitin is the second most widely available polysaccharide in nature after cellulose. A remarkable property of chitin is that it exhibits polymorphism. Its alpha form is the most stable form, and comprises part of the fungi cell wall, the shells of crabs, lobsters, and prawns,

[9] Informació disponible a: *https://proyectobiovalvo.wordpress.com*

and is also present in the structure of marine sponges. Its beta form is found in the extracellular part of fibres of diatoms, in squid endoskeleton, and in the quills of some annelids. The gamma form, which is the least common, is a combination of the alpha and beta forms and is present in the exoskeleton of some beetles.

Figure 6. Chitin extraction using chemical and biological procedures



Source: Hamed et al., 2016

Chitin is extracted from crustacean exoskeletons following some mechanical procedures like shell washing, drying, and reduction by contusion. After these processes, additional biological or chemical processes should be carried out (Figure 6). Chemical chitin extraction consists of its demineralisation with HCl, followed by deproteinisation with NaOH, and finally discolouration with acetone or other organic solvents. On the other hand, biological extraction avoids the use of these acid and alkali compounds, thereby avoiding their negative environmental impacts. Instead of these compounds, some bacteria are used in the demineralisation stage to produce dairy acid instead of HCl, and bacterial proteases are used instead of NaOH in the deproteinisation stage. *Pseudomonas aeruginosa* K-197*, Serratia marceslens* FS-3, *Bacillus subtilis*, *Bacillus cereus*, and *Exiguobacterium acetylicum* are the most common bacteria used.

The chemical extraction procedure is the most widely used method due to its rapidity, despite being more expensive and less environmentally friendly, and the negative effects exerted on the chitin produced (Hamed, Özogul, & Regenstein, 2016). The biological chitin extraction procedure is increasing in popularity due to the benefits it entails, but has not yet been widely adopted in the scientific community yet. Comparative studies between the two methodologies have been conducted, and have concluded that the biological method is more efficient than the chemical procedure (Hamed, Özogul, & Regenstein, 2016).

Chitin and its derivatives have some interesting industrial applications, since they are renewable, biocompatible, biodegradable, non-toxic, and present anticancer, antioxidant, anticoagulant, and antimicrobial properties. These properties make them suitable for incorporation in different biomaterials.

Chitin is hydrophobic and, therefore, insoluble in water, which prompts the search for water-soluble derivatives to facilitate several chemical reactions. Chitosan is the most important water-soluble derivative, and is obtained from the deacetylation of chitin. In fact, most chitin-related applications use chitosan as the raw material instead of chitin.

3.3.1. Human health sector applications

Chitosan and its derivatives are used in the human health industry due to their biocompatibility, biodegradability, and low toxicity. Table 3 summarises their main applications in the human health sector.

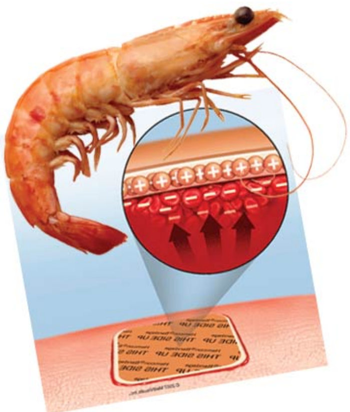
Table 3. Applications of chitosan and its derivatives in the human health sector

Description of the application
Medications and genetic material transporters
Encapsulation and protection of bioactive compounds and genetic material
Gradual and controlled drug release
Manufacture of scaffolds for surgical use for tissue regeneration
Manufacture of surgical wires with antimicrobial properties

Source: Bou, unpublished data.

Chitosan and its derivatives are used as the main material for nano- and micro-encapsulation of bioactive compounds, isolating them from the external environment and thereby avoiding their degradation and decrease in viability. The encapsulation structures can be nano-spheres, arrays, microspheres, hydrogels, capsules, or micelles.

Figure 7. Positive charge of chitosan attracts negatively charged blood cells



Source: Askix

Chitosan and its derivatives present other interesting properties for the human health industry. They are used as ingredients in bactericidal creams used in treatment of burns. Another example is their use in the production of gases and bandages due to their haemophilic properties. The positive charge of chitosan attracts blood cells, which have negatively charged surfaces (Figure 7), increasing adhesion and thus improving their functions.

The anticancer, antioxidant, anticoagulant, and antimicrobial properties of chitin and its derivatives make it applicable in the artificial regeneration of skin, bones, and cartilage.

3.3.2. Cosmetic sector applications

The cosmetic industry uses crustacean chitosan in the manufacturing of substance-transporting capsules, to eliminate fat, as a moisturising agent for the skin, as a bactericidal additive in soaps, and as a component in toothpaste.

3.3.3. Human food sector applications

The antioxidant and antimicrobial properties of chitin and its derivatives are interesting for the food industry because they increase food quality, food safety, and the shelf life of products. Nowadays, it is estimated that this industry uses 80,000 tonnes of chitin per year from wastes of marine origin (Hamed et al., 2016). Their antioxidant properties makes them suitable as functional ingredients in specialised diets for treatment of pathologies such as cancer, cardiovascular disease, rheumatoid arthritis, and in the prevention of premature aging.

Chitosan is also used as a food additive and as a component of edible food coatings, commonly used in ‘novel foods’. These coatings exhibit several advantages compared to traditional plastic wrap, as they present antimicrobial properties, acting as a barrier against microorganisms. Thus, such biofilms have greater durability, preventing/delaying microbial degradation of the food. Chitosan-based coatings can also transport bioactive substances that improve the quality of packaged food, and in combination with other substances with antimicrobial properties (for example organic acids of plant origin, proteins, antibiotics, and chelating agents), reduce their deterioration.

Ultimately, these coatings are biodegradable and can be consumed along with the food product, providing a mechanical and antimicrobial barrier against external agents.

Another nutritional application of chitosan is its use as a functional fibre-enriching ingredient, as it is not digested by enzymes of the human digestive tract and thus stimulates the proliferation of beneficial bacteria in the intestinal tract.

3.3.4. Other industrial applications

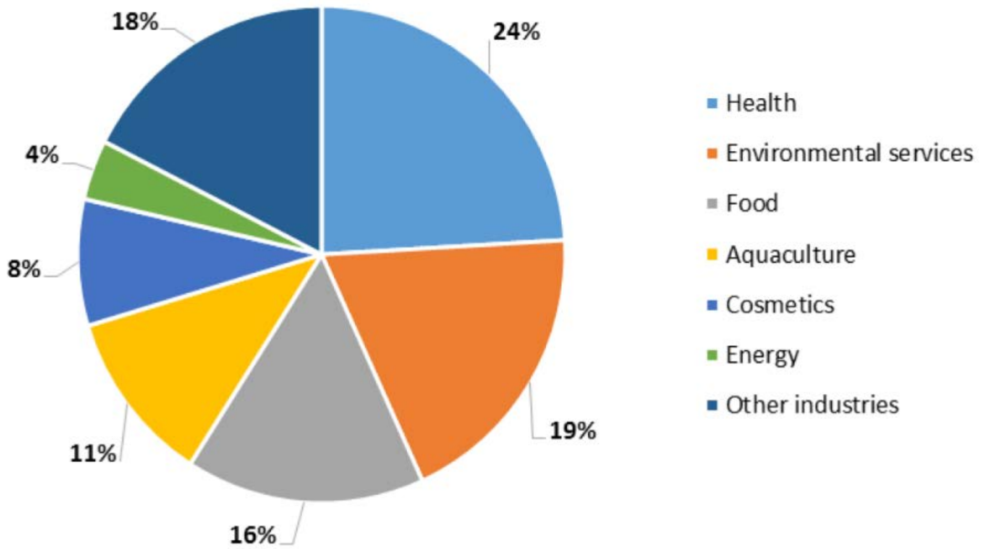
In the agricultural sector, chitosan is used as a seed coating improving their conservation, and as a bactericidal and fungicidal agent in the treatment of some crop diseases.

On the other hand, chitosan is also useful as a primary coagulant for sewage, and as a flocculant in heavy metal capture treatments of aqueous solutions.

4. Opportunities for MBT by industrial sector

This section describes other groups of species, which are important in terms of their potential biotechnological and industrial applications. The MBT subsectors mentioned in this report have been chosen based on the amount of agents in the complete MTB value chain (Figure 8), and include health, environmental services, human nutrition, aquaculture, cosmetics, and energy.

Figure 8. Proportion of agents in MBT value chain by sector.



Source: ECORYS, 2014

4.1. Human health sector applications

The health sector is the main industry of interest given the high amount of agents involved in its value chains, its high economic returns, and its high impacts on society. The healthcare industry is very broad and includes several aspects, some of them closely related to other sectors such as functional nutrition, pharmaceuticals, and surgery. The pharmaceutical industry is one of the most important sectors and is mainly focused on the production of biomolecules with antitumoral, anti-inflammatory, analgesic, immunomodulatory, anti-allergenic, and antiviral properties.

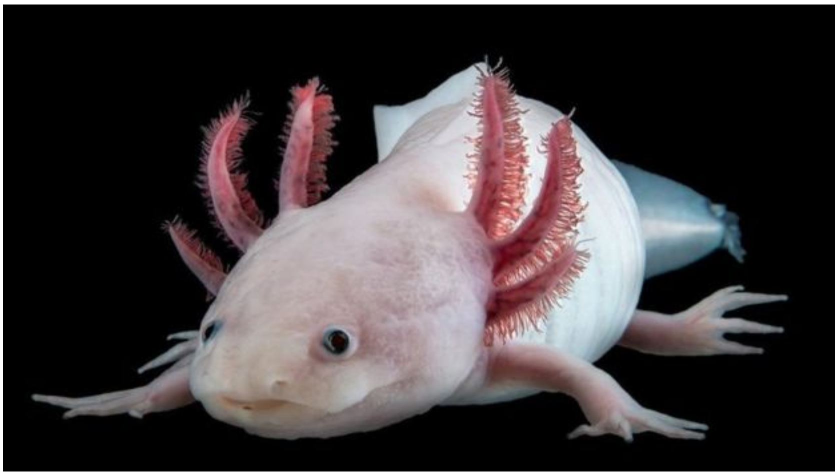
For every 5,000-10,000 molecules tested by the pharmaceutical industry, only one of them arrives to market, with the time-to-market, after preclinical research, ranging from 10 to 15 years (Farmaindustria, 2014). Despite the high entry barriers, the pharmaceutical sector offers great return potential in the case that the product reaches the market. Lately, applications of marine products in human health has become an important scientific research line because seas and oceans offer many biological resources, many of them unknown, opening a new door for MBT innovations related to health.

Figure 9. Medical products

Source: Arek Socha - Pixabay.

An example of this scientific research is the study of the Mexican axolot *Ambystoma mexicanum*, an amphibian which can regenerate amputated limbs and other organs and tissues such as the dorsal cord, bones, tendons, and muscles. This property is interesting for biomedical applications related to the repair of brain lesions and dorsal cord and to the healing of cardiac scarring. The scientific community has been breeding this species for more than 150 years in order to avoid collecting individuals from the wild (Nowoshilow et al., 2018).

Figure 10. Mexican axolot (*Ambystoma mexicanum*)



Source: Research Institute of Molecular Pathology (IMP)

Sea cucumbers, which are part of the echinoderms group, exhibit anticancer properties. Scientific studies say that extracts of *Cucumaria frondosa* cucumber inhibit the proliferation of cancerous pancreatic cells and induce their apoptosis. Author Ethan Evers mentions in his book 'The Eden Prescription' (Evers 2010) that the sea cucumber is effective against lung, skin, colon, prostate, and liver cancer cells. Apart from these properties, sea cucumbers present other benefits to health, such as their regulatory effect on the human hormonal system which derives from its arginine content. They also increase general well-being and are immunostimulatory, delay aging, improve sleep and memory quality, regulate levels of lipids and sugars in the bloodstream, prevent the formation of tumours and the onset of osteoporosis, and promote body growth due to high contents of arginine, lysine, taurine, calcium, phosphorus, iodine, iron, and zinc (Rampelotto & Trincone, 2018).

The health sector demands alternative protein sources other than those of animal origin such as collagen, which is traditionally obtained from pigs, cows, and sheep. However, some recent regulations have recommended that these sources be avoided because they can be possible vectors for viral diseases, which presents an opportunity in the search for alternative sources of marine origin. Several private companies, such as the British company Jellagen Marine Biotechnologies[10] are working on collagen generation via jellyfish rearing. In the 1990s, the protein responsible for the green fluorescence of the *Aequoria Victoria* jellyfish was cloned for the first time, and through genetic mutation techniques, its production was achieved in vitro, enabling it use as a chromoprotein for diagnostic imaging.

It has also been possible to isolate protease inhibitors and ion channels of marine species such as anemones or *Conus magus* conical snails, which have a strong biotechnological and therapeutic potential. The American company Jazz Pharmaceuticals[11] has produced the drug Ziconotide, a synthetic peptide used to treat severe chronic pain which is analogous to the Ω-conotoxin of the conical sea snail.

Red algae have also been studied in the human health sector. Carragelose®, for example, is a nasal spray used to treat the cold and flu produced from extracts of red algae. Other tunicates also have sanitary applications. In fact, the first antitumour medication developed in Spain by Pharmamar [12] comes from such species. The blood of some animals can also be a good source of bioactive components in the search for molecules of pharmacological interest, for example novel chelating agents, among other possibilities. In line with this idea, several companies in the pharmacological sector are conducting research on species such as sturgeon.

4.2. Environmental services applications

MBT has a strong relationship with different environmental services sectors, in activities such as bioremediation (biosurfactants, bio-emulsifiers) and elimination of pollutants such as heavy metals and plastics, in biosensors for monitoring the ecotoxicological status of water bodies, and in anti-fouling or bioadhesive products. Section 4.2 of this report addresses the problems associated with contamination of the marine environment due to the accumulation of plastics (marine plastic litter), since this material represents 95% of the waste discharged into the Mediterranean (WWF, 2018).

The use of maritime spaces by human beings is usually accompanied by pollution and alteration of the marine, aquatic, and terrestrial natural environments. Fisheries, aquaculture, and maritime tourism are some of the most-polluting sectors. In the case of fisheries and aquaculture, some of their wastes come directly from the activity itself (equipment and material such as fishing nets). According to United Nations Organization data, approximately

[10] More information: *https://www.jellagen.co.uk/*
[11] More information: *https://www.jazzpharma.com*
[12] More information: *http://pharmamar.com*

640,000 tonnes of fishing gear and equipment are dumped every year worldwide. Moreover, fishing nets represent 10% of the total pollution of the sea (World Animal Foundation 2018). Among this fishing and aquaculture gear, ‘ghost nets’ (Figure 11), are responsible for serious impacts on the marine environment and also present serious threats to boats. A large number of these ghost nets are deposited in the marine soil, destroying species of benthic organisms such as sea sponges or corals, which are the trophic base of the marine ecosystem. On the other hand, ghost nets can drift around, trapping diverse fauna from fish to marine mammals and even turtles and seabirds.

Figure 11. Ghost nets (left) and species affected by ghost nets in the Mediterranean (right)

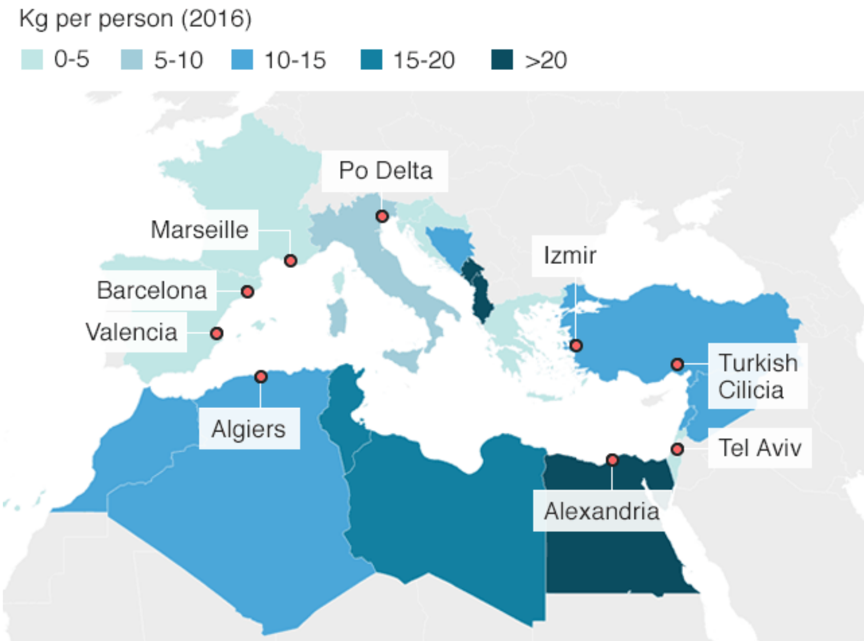
Source: FAO and WWF

Some studies have estimated that these nets directly cause the death of about 10% of all fish worldwide (World Animal Foundation 2018). When nets reach the end of their useful life, some fishermen save them, others burn them on beaches, and others abandon them in the sea. In order to reduce these practices, efficient collection and management protocols are needed.

In addition to plastic litter coming from fishing and aquaculture sectors, plastics from other original uses or industries can also be found in the Mediterranean. According to the World Economic Forum, 311,000,000 tonnes of plastic waste were generated in 2014, an amount which is expected to increase three-fold by 2050. Only 15% of this plastic waste generated is recycled, which presents an enormous technological and social challenge since the remaining 85% is either burned or abandoned in the natural environment, causing serious impacts on ecosystems.

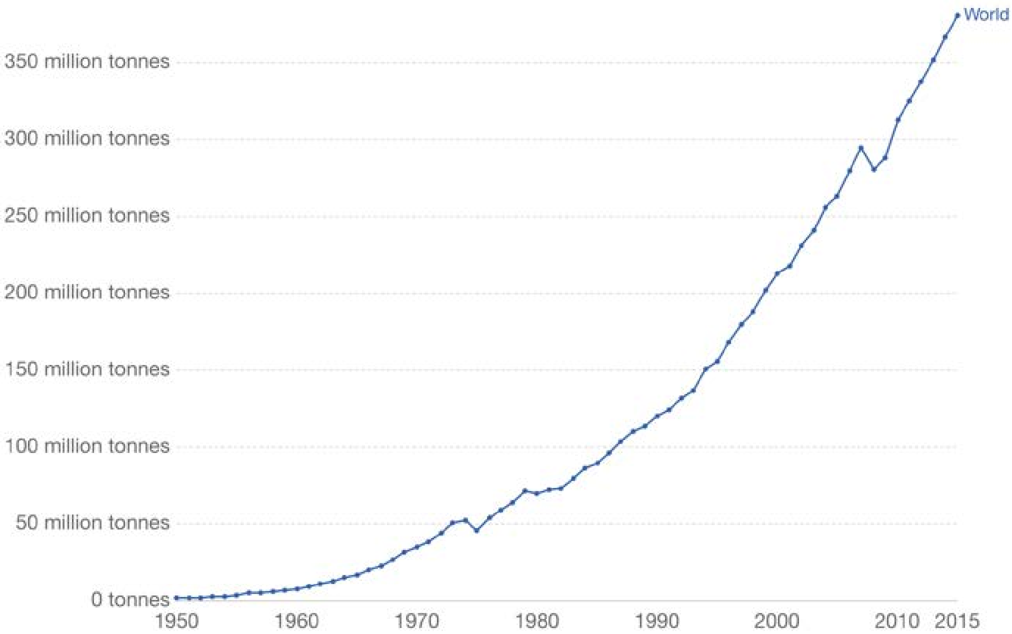
According to WWF data published in the report ‘Out of the plastic trap’, 95% of waste found on Mediterranean beaches is plastic, and European countries dump approximately 500,000 tonnes per year. The same report states that 7% of the plastic used worldwide is found in the Mediterranean. This waste, in addition to its environmental impact, also causes economic losses for the fishing industry (estimated at 61.7 million euros) due to direct catch losses and indirect impacts caused to vessels engaged in fishing activities in the Mediterranean. Some studies have pointed out that 15,000 pieces of plastic are released daily into seas worldwide, and 95% of the samples analysed therein were found to contain microplastics. This type of pollution directly impacts marine fauna, since this material is accumulated all along the trophic chain until eventually reaching humans. Globally, it is estimated that the presence of plastic in the seas represents $13 trillion in economic losses (WWF, 2018).

Figure 12. Amount of plastic generated in the Mediterranean (kg/person) and most-affected cities.



Source: WWF (2016)

Figure 13. Plastic production worldwide



Source: Our world in data.

Plastic production has increased exponentially worldwide in the last decades (Figure 13), and as a result, the generation of plastic waste has increased in similar proportions. The scientific community is searching for biotechnological solutions focused on three main aspects: the elimination of plastics via microorganisms; its reuse by other industries; and the search for alternative materials to reduce the use of plastic. Some of these technological solutions and the industrial sectors involved are presented in the following sections.

4.2.1. Plastic bioremediation applications

Some microorganisms such as bacteria and fungi, as well as plants, have traditionally been used as bioremediators in environments polluted with hydrocarbons, heavy metals, or other pollutants. There is thus a strong background in both land and water bioremediation methods. There are bioengineered microorganisms designed with the ability to disintegrate plastics, using the plastic as a carbon source and producing energy. An example of this use is illustrated by the good practices by the BioCellection company, which is discussed more extensively in section 6.3 of this report.

4.2.2. Textile sector applications

An alternative to the biotechnological bioremediation is the conversion of plastic waste into textiles. Companies like the multinational company G-Star Raw have designed a collection of jeans, t-shirts, sweatshirts, and hats called ‘Raw for the Oceans’, in which all textile pieces come from treated marine plastic fibres. The Running Republic (Figure 15), a Catalan company, also works with recycled plastic to make technical sports clothing. On the other hand, the Ghost Fishing Foundation and Aquafil and Starsock, Italian and Dutch textile companies, respectively, have promoted the *Healthy Seas* initiative in order to transform plastic waste from the sea, especially that generated by the ghost nets, into nylon threads for textile use.

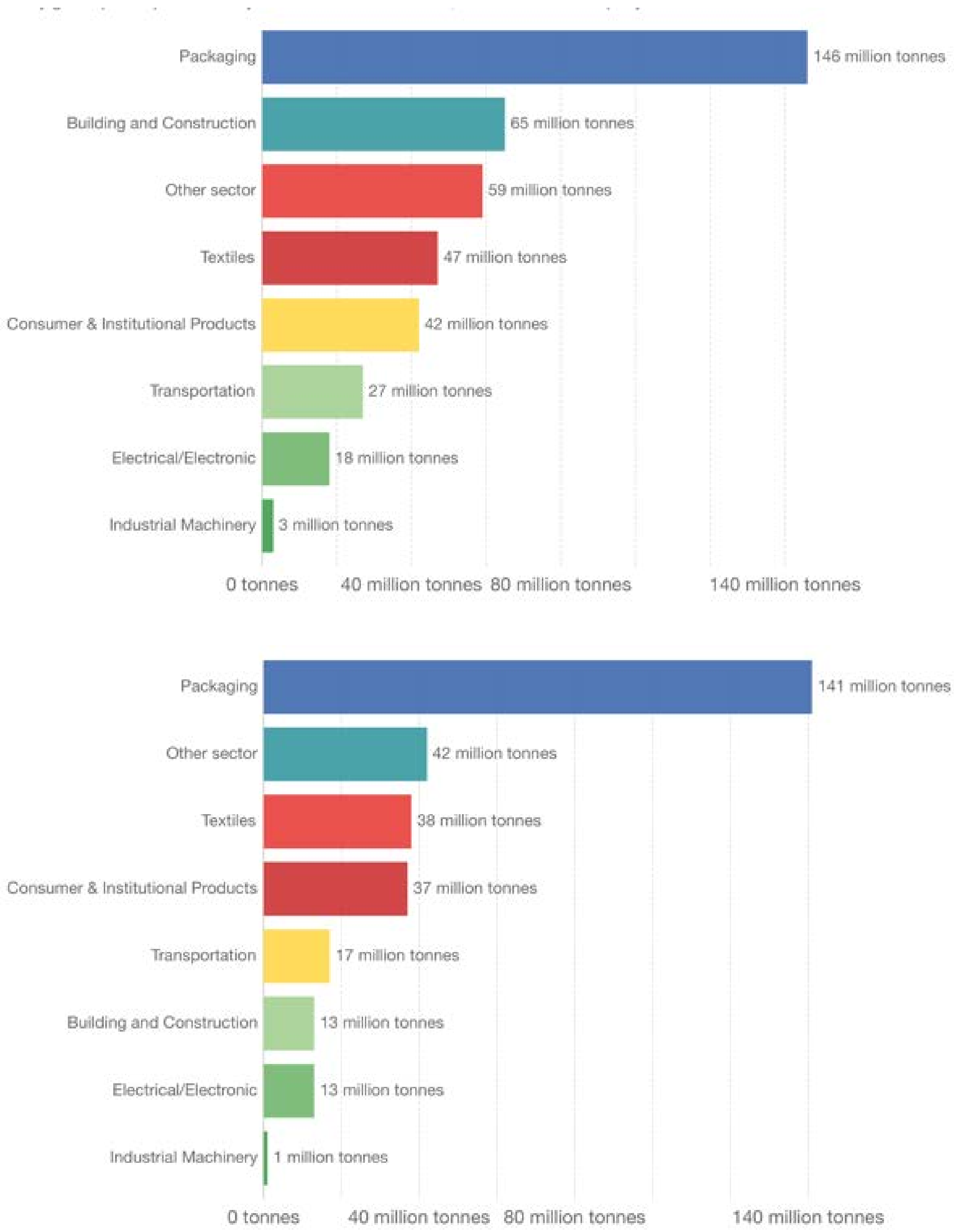
Figure 14. Technical clothing made with plastic fibres. The Running Republic.

Source: The Running Republic

4.2.3. Packaging sector applications

The packaging subsector is the most relevant in terms of environmental impact since it produces 42% of all plastic produced worldwide. Of the 146 million tonnes produced annually, 96.57% becomes waste (Figure 15). This is a problem that still needs to be solved and which must be addressed globally. Currently, there are several companies working on solutions to this problem.

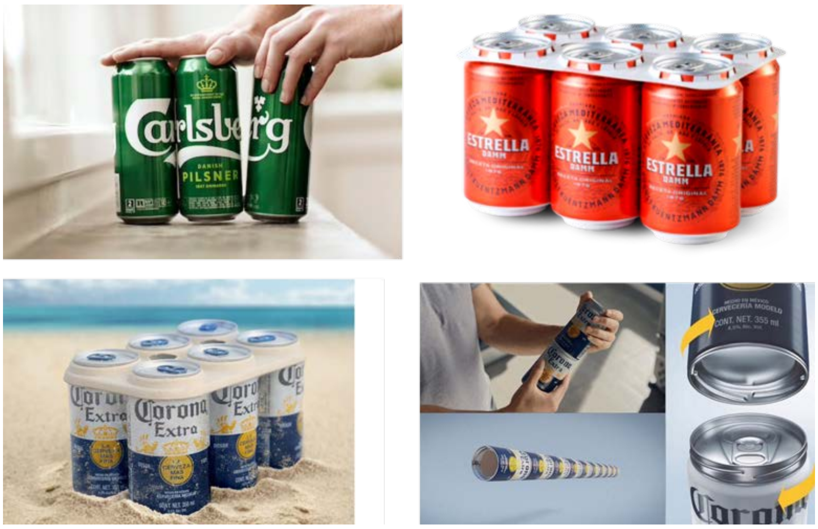
Figure 15. Global plastic production (upper) and plastic waste (lower) by industrial sector in 2015 (millions tonnes/year)



Source: Our world in data

The food industry is one of the most relevant in terms of plastic use in product packaging. Several companies in the sector have proposed different technological solutions, either based on biotechnology or facilitating technologies to minimise or eliminate plastic. Breweries, for example, have begun using alternatives to plastic ring units (Figure 16). The Carlsberg Group has replaced these rings with a biodegradable adhesive that keeps the beer cans attached to one another, allowing them to be disengaged easily by applying moderate force. According to the company, this change supposes a decrease of more than 1,200 tonnes of plastic per year around the world, equivalent to 60 million plastic bags.

Figure 16. Solutions by beer companies for elimination of plastic from beer packaging



Source: Beer companies' official websites.

Figure 17. Advertising by SaltWater Brewery company for new biodegradable and edible packaging

Source: SaltWater Brewery website

The company Corona is pursuing two strategies regarding this problem. The first involves replacing plastic rings with a biodegradable material that keeps the cans together and, in the case that this material reaches the marine environment, it can serve as food for marine organisms. Another non-biotechnological strategy, called 'fit-packs', involves modifying the ends of cans so that they can be thread together without any additional element. DAMM has proposed a solution based on biodegradable adhesives, which can reduce plastic waste by 260 tonnes annually, an amount equivalent to 89 million plastic rings.

There are many companies in the beer sector seeking to replace plastic rings with biodegradable materials, but the pioneer in implementing this type of solution was SaltWater Brewery, an American company whose main consumers are members of fisherman collectives and sea workers, who are thus very interested in preserving their own lifestyle and working environments.

The European Commission promotes the realisation of biotechnological research projects whose objectives are to develop new materials applicable to the food sector. One example is the BioBarr project (*New Bio-based Food Packaging Materials with Enhanced Barrier Properties*[13]), co-financed by the Horizon 2020 program and the Bio-Based Industries Public-Private Partnership, with the objective of developing a bioplastic alternative based on polyhydroxyalkanates for application in the agro-food industry.

4.3. Human food sector applications

MBT can provide products in different areas of human nutrition such as functional ingredients like prebiotics or omega-3 supplements, and other food ingredients such as stabilisers, thickeners, and preservatives. One functional food, fucoidan, an extract with antioxidant properties that improves the health of the intestinal tract, is obtained from the alga *Fucus vesiculosus* (Figure 18). Fuccoxanthin, obtained from various species of brown algae, is used as a dietary supplement for weight-loss diets, but also as a food colouring. Another example of a functional ingredient is astaxanthin, which has antioxidant properties and is obtained from the microalga *Haematococcus fluvialis*.

Figure 18. Fucoidan extract. Swanson

Source: Swanson vitamins

[13] Project website: *http://www.biobarr.eu/*

Some macroalgae such as *Laminaria sp.*, *Macrocystis sp.*, *Lessonia sp.*, and *Ascophyllum sp.*, among others, contain high levels of alginate, a common ingredient used in the bakery industry. Mannitol extracted from some brown algae is used as a substitute for sucrose, while alginate, carrageenan, and agar obtained from different algae are used as food stabilisers E400-E407 (Ecorys, 2014).

Innovation in functional food opens the door for new market opportunities. Numerous companies are working along this line, such as the Spanish company Fitoplancton Marino [14], which has requested a patent (EP3091069A1) for a production methodology of *Tetraselmis chuji* enriched in the superoxide dismutase enzyme (SOD) based on its antioxidant and anti-inflammatory properties. These characteristics also make it suitable for use in the pharmaceutical and cosmetic industries.

4.4. Cosmetic industry applications

One avenue for the valorisation of marine resources is in the development of cosmetic products, as explained previously in sections 3.1-3.3 of this report.

Figure 19. Cosmetic products made from microalgae extracts

Source: Fitoplancton Marino

There are other marine resources, such as algae, jellyfish, or coral that can be valorised. *Ascophyllum nodosum*, *Fucus vesiculosus*, and *Laminaria saccharina* algae are used in cosmetics for treatment of cellulite. Alginates, agar-agar, and carrageenan obtained from various algae help to control viscosity in cosmetic products. *Porphyra umbilicalis* (red algae) is used to make sun-protection lotions, while *Laminaria saccharina* is used in the manufacture of moisturising creams. Collagen obtained from some jellyfish species is used in the production of moisturising products, while some soft corals such as *Pseudopterogorgia elisabethae* are used in dermatological lotions (Ecorys, 2014). These examples, along with those described in section 3, provide a broad overview of the potential of MBT in the cosmetics sector.

[14] More information: *http://www.fitoplanctonmarino.com/*

4.5. Aquaculture sector applications

MBT has played a major role in the development of aquaculture as it is known today. Section 3.1 described different innovations in the composition of fish feed made from fish meal and oils. There are other organisms that can contribute to the improvement of this type of feed, such as *Haematococcus pluvialis*, which has a high astaxanthin content, or other species of algae which are rich in proteins and lipids. Microalgae such as *Chlorella sp*., *Espirullina sp*., *Schizochytrium sp*., and *Porphyridium sp*. are also being used in feed preparation.

Figure 20. Aquaculture fish feed

Source: Biomar

The aquaculture sector is also dealing with challenges related to human healthcare. The design of drugs and vaccines is a high priority, but it must be done under non-polluted conditions. Thus, techniques such as genetic broodstock selection and epigenetics for improving farm management are very relevant. Further on, a good practice focused on the application of genetic engineering in salmon farming is described in section 6.2.

4.6. Other industrial applications

Apart from the aforementioned industrial applications, there are some other applications for MBT. The joint venture formed by French companies Le FabShop and Algopack has developed a project focused on the use of algae as a sustainable raw material in the production of biofilaments for 3D printing (Atalante 2012).

Figure 21. Researchers from the ECOWAL group at Pablo de Olavide University (Seville, Spain).

Source: Pablo Olavide University

Pablo de Olavide University (Andalusia, Spain) is working on a project aiming for the sustainable production of paper and/or cardboard based on the use of tide seaweed as a source of cellulose which is alternative and complementary to the typical terrestrial vegetable biomass. The seaweed and marine plants that are used are *Posidonia sp*., *Ulva sp*., and *Cladophora sp*. These algae and marine plants are those that, in summer seasons, are removed from beaches due to tourism, thereby becoming a residue. In comparison to the use of terrestrial vegetation, the use of algae in paper production implies a decrease in the chemicals used in the paper manufacturing process and, therefore, a decrease in the associated contamination, with a simultaneous increase in the use of the cellulose present. Countries like Chile and Spain have already been successful in developing these technologies at pilot scale.

Some companies, such as the Norwegian ArctiZymes[15], have used products of marine origin to improve laboratory techniques such as the polymerase chain reaction (PCR). In this case, various enzymes from the Nordic prawn *Pandalus borealis* are used to eliminate DNA contamination in the samples to be treated by PCR. Section 6.1 of this report describes a good practice based on the use of various components of the blood of a marine arachnid species to improve and refine a laboratory diagnostic test.

Another notable industrial application is the use of algae as a possible source of renewable energy. Extracts of the alga *Laminaria hyperborea* can be fermented to obtain ethanol. *Laminaria sp.* is more competitive than terrestrial biomass in this process, in terms of the cost-benefit ratio due to the rates of conversion into methane. (Sayadi, Ghatnekar, and Kavian 2011).

[15] More information: *https://arcticzymes.com/*

5. Biotechnological potential of alien species

According to the World Organization for Nature, invasive alien species are alien species introduced artificially, accidentally, or intentionally, which after a while manage to adapt to the environment and colonise it. The native species usually cannot compete against these species and are displaced or even disappear from the area due to the dominance exerted by the invasive species. According to the UN, invasive species are the second leading cause of loss of biodiversity in the world, and one in three species in Europe is in critical danger of extinction due to this phenomenon. Aside from the ecological impacts, these species suppose an annual cost of 12.5 billion euros per year in the European Union alone (Scalera, Genovesi, Essi, & Rabbitsch, 2012). Regulations imposed in some countries prohibit economic profit of species catalogued as invasive species, preventing the implementation of management measures for their commercial exploitation in order to alleviate their negative impacts, and economic or technical investments by companies, thereby also affecting the development of solutions based on biotechnology.

Due to the serious problems caused by invasive alien species, there are regulatory and legal frameworks at both the European and regional levels. At the European level, the law in consideration is the Regulation (EU) n. 1142/2014 of October 22, 2014, on the prevention and management of the introduction and spread of invasive alien species[16]. This legislation establishes rules to prevent, reduce, and mitigate the adverse effects of invasive alien species on the biodiversity of the European Union. It contains a list of species for which certain restrictions are applied. Some alien species found in the Mediterranean region listed as invasive species by the EU are the fish *Perccottus glenii* and *Pseudorasbora parva* and the crustaceans *Procambarus clarkii* and *Pacifastacus leniusculus* (European Commission, 2019). Among other considerations, invasive species that are troubling for the European Union (those listed) cannot be introduced into any territory of the European Union, and their transport, breeding or reproduction in captivity, commercialisation, and release are all prohibited.

In the next section, the harmful impacts caused by two allochthonus species of the Mediterranean, the blue crab (*Callinectes sapidus*) and the apple snail (*Pomacea sp*), are explained. The criteria for selecting these two species were that both species produce a high impact on biodiversity and on human activities in the areas of the Mediterranean in which they are present, and that they are in different states of propagation, with the expansion of the apple snail being less extensive than that of the blue crab.

Neither the blue crab nor the apple snail are included in the list of invasive alien species of the EC (European Commission, 2016), however, the apple snail is part of the Spanish Catalogue of Exotic Invasive Species, which prohibits possession, breeding, transport, and domestic and foreign trade of the species (Spain Ministry of Agriculture and Fisheries, 2013).

[16] Available at: *https://eur-lex.europa.eu/eli/reg/2014/1143/oj*

5.1. Blue crab, *Callinectes sapidus*

The blue crab (*Callinectes sapidus*) is a decapod crustacean from the Atlantic coast of Americas which is found in the territory between Nova Scotia (Canada) and Argentina.

Figure 22. Blue crab, *Callinectes sapidus*

Source: The Children's Museum of Indianapolis

The blue crab was introduced to Europe at the beginning of the 20th century from the French coast. It is now ubiquitously distributed all around Europe, but its population has recently increased in some Mediterranean countries such as Italy, Greece, and Spain. The rapid expansion in population has occurred in both hypersaline and freshwater areas. In fact, stable populations of this species can be found in rivers such as the Bolbe in Greece. Its presence, however, is not limited to the Mediterranean basin, also being present in waters of the Adriatic Sea, the Ionian Sea and the Black Sea (Mancinelli et al., 2017). The literature describes several theories that explain the arrival of this crustacean to European shores. The theory that is most widely accepted by the scientific community suggests that the species was transported from its native habitats with the ballast waters of ships and boats. The ongoing globalisation of both people and goods has made this type of transport the most common way by which aquatic flora and fauna are dispersed. When an alien species reaches a new location, the environmental conditions of the new site are usually not the most suitable for their development, making it difficult for them to settle. However, the opposite may happen as well, where the alien species finds optimal and favourable conditions with no predators to regulate its proliferation. This was the situation of the arrival of the blue crab in the areas of the Mediterranean in which it is currently present.

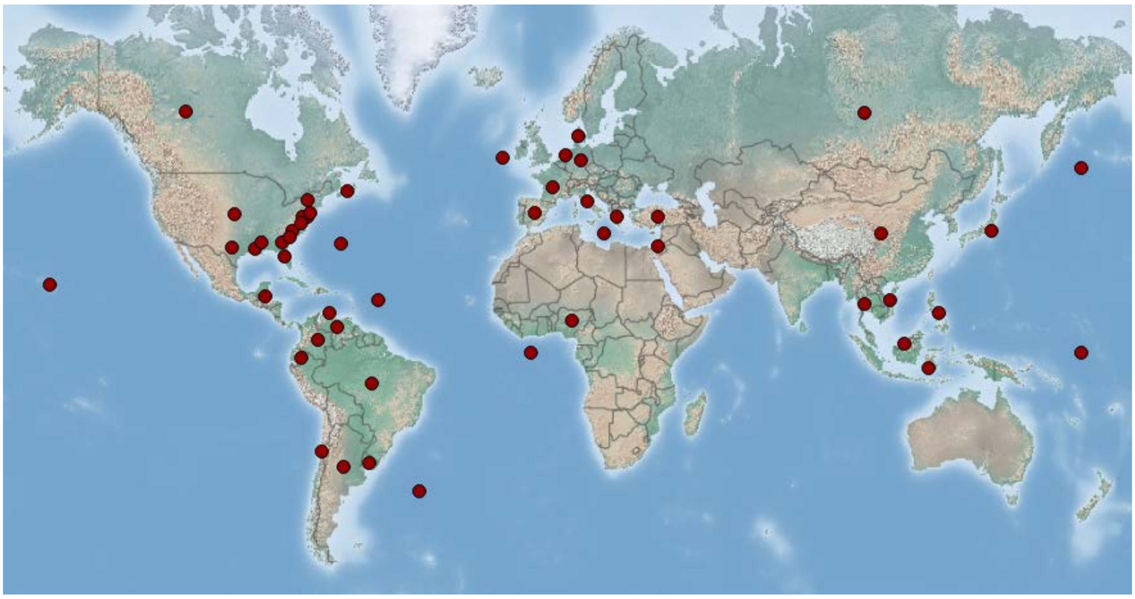
The temperature around the Mediterranean favours the growth and development of the blue crab, which has difficulty feeding and reproducing in waters below 10 °C. Due to climate change, the average temperature of the Mediterranean Sea has decreased, causing some areas to become optimal for the blue crab's reproduction, improving its ecological efficiency and therefore its dispersion. In its original habitats, winter conditions are harsher, representing the period wherein the crab slows down its activity or even dies. In addition, different predatory species are present, such as sharks, rays, eagles, octopuses, caimans, bugs, and certain fish. On the other hand, these conditions do not characterise the Mediterranean, and the crab is found as a foreign species, proliferating without control and causing serious economic and environmental impacts. In the western part of the Mediterranean, the common octopus (*Octopus vulgaris*) is a natural predator of blue crab, although the presence of this type of octopus is very minor due to the fishing pressure derived from its commercial value. The absence of predators and the high rate of reproduction of the blue crab in the Mediterranean are two factors that favour their dispersal.

The presence of blue crabs exerts negative impacts on different economic sectors at the local level. Professional and recreational fishing, both in rivers and seas, are affected in different ways. On the one hand, the blue crab feeds on native fauna, and therefore causes decreases in the capture of these resources. On the other hand, a large amount of fishing gear is wasted due to the action of the defense structures of the blue crab's body, which are capable of breaking the fishing nets and other equipment.

The blue crab also causes a serious negative impact on the aquaculture sector. This crab is a great swimmer, and uses this ability to move and capture food. Therefore, it can feed on clams, mussels, and other molluscs reared in aquaculture facilities, both on land and in the water column.

The ecological impact caused by the presence of the blue crab is very important since it is a general predator which feeds on a wide range of catches, therefore resulting in a drastic decrease in different prey species and competitors. This leads to very low species diversity in the environment, and therefore more fragile and less-resilient ecosystems. In addition, it should be noted that both blue crabs and other species of crustaceans such as lobster are transported live with their pincers tied with flanges or other plastic elements, which can potentially result in waste residues in the natural environment.

Figure 23. Geographic distribution of the blue crab, *Callinectes sapidus*



Source: Cabi (2018)

The existence of a large population of blue crabs in the Mediterranean has boosted a specific blue crab fishery, transforming this problem into a commercial opportunity. However, due to the high variability in its price, its value as commercial opportunity is still early to evaluate. In Catalonia, for example, prices ranged between 2 €/kg and 8 €/kg in June of 2019. Other European countries also sell blue crab for human consumption, but some such as Greece have decreed a fishing closure to preserve the species. Biotechnology may be an effective tool for valorising this resource and increasing its economic value.

In 2018 the General Fisheries Commission for the Mediterranean, the management body dealing with fisheries management in the Mediterranean and Black Sea and depending from the UN FAO, adopted a Recommendation (GFCM 42/18/7) on a regional research programme on blue crab in the Mediterranean Sea, which is binding for its 22 Mediterranean Contracting Parties and the European Union, aiming at its sustainable exploitation.

In Catalonia, the fisheries administration designed, jointly with the fisheries sector, a strategy for their commercial exploitation through the "blue crab co-management committee" created in November, 2018 with this purpose.

The increasing amount of catches in the region, makes blue crab a good candidate as an object of research in recovery studies carried out by the industrial sector. Some biotechnological studies on this crab have shown positive results regarding their use in water bioremediation, as it is able to capture contaminants from the environment such as cadmium, nickel, and lead (Foroutan et al., 2019). Research has also been carried out on the recovery of the bioactive components of its shell, such as astaxanthin, a pigment with antioxidant properties (Félix-Valenzuela, M Goycoolea, IHiguera-Ciapara, & I.M. Argüelles-Monal, 2007). Other projects have been carried out to evaluate the viability of chitosan from the shell of the blue crab and pectin from the peel of oranges, both of which are food residues, in the production of biodegradable films for the food industry (Baron, Pérez, Salcedo, Córdoba, & Sobral, 2017). All of these examples demonstrate promising results, but more research needs to be carried out.

5.2. Apple snail, *Pomacea sp.*

The apple snail (*Pomacea sp*) is a gastropod mollusc native to the Amazon basin. In Spain, it is widely present in the Delta del Ebro (Catalonia and Aragon), where it exerts great environmental, economic, and social impacts. The specific species of concern of this type of snail are *Pomacea maculata*, *Pomacea canaliculate*, and the hybrid between the two. It is present in crop areas, especially rice fields, where it causes damage to the phenolic states of seedlings, resulting in losses ranging from 60% to 90% of the total crop. The apple snail lays its eggs out of water, over aquatic vegetation or on hard surfaces such as concrete or stones. The eggs are reddish or bright pink and can be found in groups of between 300 and 800 eggs, although a group may reach over 2,000 eggs (Rodríguez, Sorolla, Nuñez, García, & Hernández, 2014). The offspring are born with the same appearance as that of an adult and are sexually mature in 2-3 months, a short period of time that showcases their high reproductive efficacy.

The impacts caused by *Pomacea spp*. are different First, it causes direct damage to rice and, in general, on the vegetal biomass found along the sides of the Ebro River, reducing biodiversity both in terms of species and abundance, and thereby weakening the ecosystem. The species that depend on the rice for survival, like other gastropods and some species of fish that use the vegetation to lay and hide their eggs, are very threatened by this snail species. On the other hand, *Pomacea spp*. also produces economic damage at the local level in areas where rice cultivation is the main source of economic income.

Figure 24. Apple snail

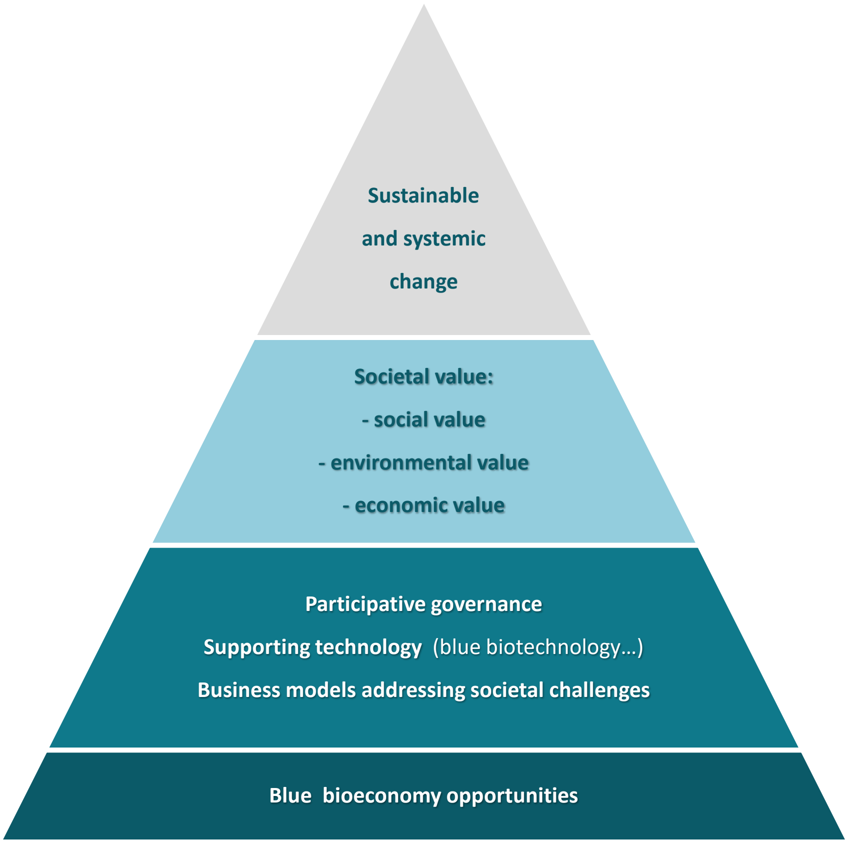
Source: Jess Van Dyke, Snail Busters, LLC, Bugwood.org

Due to the impacts it generates around the Delta del Ebro, the apple snail has been part of the catalogue of invasive species in Spain since its presence was detected in August of 2009. This catalogue prohibits its commercialisation, and it is therefore difficult to find biotechnological solutions to the problems caused by this species.

6. Potential impacts in terms of shared value creation (SVC)

The governance platform of the PANORAMED project establishes the conceptual framework (Figure 25) that should allow conversion of the opportunities offered by blue bioeconomics into global and sustainable changes. This transformation is carried out through different systemic innovations which go beyond the technological dimension treated in the previous sections, and which must be addressed from a holistic point of view. Systemic approaches are needed which promote synergism between the various agents and economic activities, maximising SVC in an equitable manner without compromising the sustainability of the ecosystem, and contributing to social and technological transformations. Thus, it is necessary to develop new governance models that focus on responsible research and innovation and which integrate public commitment, gender equality, scientific education, open research, and ethics in order to address the Sustainable Development Goals (SDG) more efficiently.

Figure 25. PANORAMED conceptual framework.

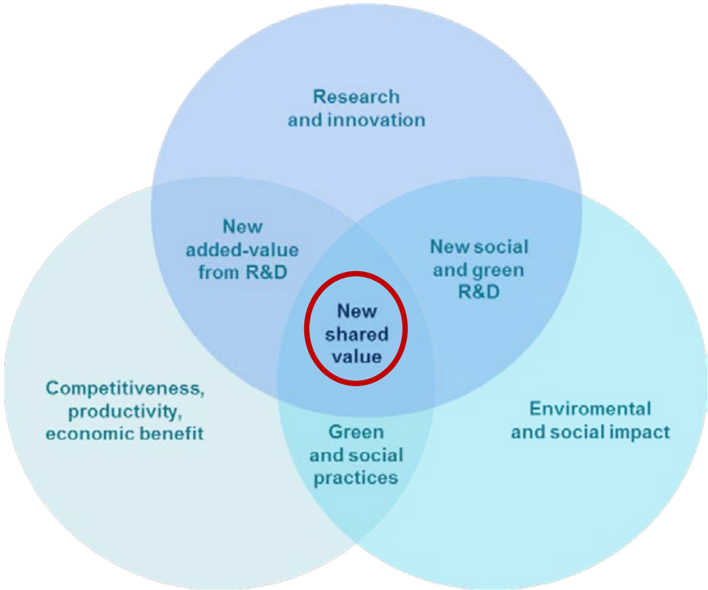


Source: Panoramed

Systemic innovations must be produced by entities that impart value to their environment beyond that related to their own economic performance, according to the theory of SVC. The following paragraphs describe the economic theory of SVC (Porter & Kramer, 2011), its relationship with the SDGs, and the potential impacts of MBT in terms of contributing to some of these objectives, and therefore its potential for generation of shared value.

In 2011, professors Mikel Porter and Mark Kramer proposed a new conceptual approach to business management which they called shared value creation (SVC). This theory goes beyond the reaches of the concept of corporate social responsibility (CSR) and has been widely accepted in the business world. It proposes a management model in which the company must aim for more than just their own economic benefit and must generate shared value, which means that it must generate benefits for both the company and its environment, on economic, social, and environmental aspects. It is, therefore, in the confluence of the realms illustrated in Figure 26 where the concept of shared value is described.

Figure 26. Shared Value Creation



Source: PANORAMED project

According to the theory, there are three levels in the creation of shared value:

1) **Redirection or re-conception of products and markets.** The organisation must be active in reading the needs of society, including both current and potential users, in order to make their solutions accessible to most of society. Economic development is not complete if it is not inclusive.

2) **Re-definition of the productivity of the value chain.** It is necessary to modify practices along the value chain and thus fortify it by improving the use of resources, employees of the organisation, and business partners.

3) **Facilitate the development of local clusters.** It is necessary to improve the available skills and the supplier base, and support the institutions and communities amidst which the organisation operates in order to boost productivity, innovation, and growth[17].

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[17] For a more detailed approach to SVC and its relation to cluster strategies, it is interesting to consult the report '*How clusters can contribute to the social and environmental challenges through the creation of shared value*', prepared by Dr. Xavier Amores, an expert in the theory and management of business clusters, within the framework of the PANORAMED project.

In order to move towards the creation of shared value, organisations should undertake the steps described below:

1) **Identify non-covered social opportunities or needs**, as framed in the SDGs defined by the UN (Figure 27).
2) **Introduce a business strategy** based on the needs detected, and define and execute an action plan responding to these needs.
3) **Measure the results,** assessing whether they bring value to the organisation at the internal level or if they add value externally. It is necessary, therefore, to define and establish a measurement and monitoring system**.**
4) **Commit seriously at the management level.** The vision for the SVC must be shared by the entirety of the management and actors of the organisation and its shareholders.
5) **Adapt the organisation to the new business model.** It is necessary to implement all of the organisational and logistical changes necessary in order to adapt the organisation to the new paradigm.
6) **Generate strategic alliances.** The relational framework with other agents is a key element in the generation of an ecosystem favourable for the implementation of the SVC strategy. It is very difficult to achieve the goals of a single organisation if it does not have strategic allies committed to the same philosophy.

MBT contributes to various SDGs, and therefore can potentially play a relevant role in SVC strategies, since each SDG refers to at least one of the areas considered within the concept of shared value (namely social value, economic value, and environmental value). Figure 27 shows the SDGs, and Table 4 lists some of the SDGs toward which MBT has a significant impact, further specifying in which ways MBT can bring shared value.

Figure 27. Sustainable development goals

Source: United Nations (2015)

Table 4. Contributions of MBT to the sustainable development goals (SDGs)

SDG	Created value	Contribution to the SDG achievement
SDG 1. No poverty	Social Economic	MBT is a growing sector, with estimated creation of more than 10,000 new jobs by 2020 (Ecorys, 2014).
SDG 2. Zero hunger	Social Economic	MBT improves food production sectors such as fishing and aquaculture, making them more accessible to the whole of society. The fishing sector uses, among other techniques, population genetics for the sustainable management of fisheries. In aquaculture, biotech tools are used to improve productive processes such as the genetic selection of breeders, in vaccine production, and in nutrition design to improve the health of cultures and food safety.
SDG 3. Good health and well-being	Social	The MBT provides new drugs, surgical materials, and diagnostic tools for human health. It also contributes to the production of functional foods for diets designed for people with special dietary needs.
SDG 6. Clean water and sanitation	Social Environmental	MBT encompasses the bioremediation processes carried out in marine waters which employ microorganisms to eliminate plastic waste, as described in the good practice of section 7.3.
SDG 7. Affordable and clean energy	Economic Environmental	Production of bioethanol, biodiesel, and biofuel through processes involving microalgae (Ecorys, 2014).
SDG 9. Industry, innovation and infrastructure	Economic	MBT is a discipline that promotes and provides innovation in a transversal way across various industries such as food, cosmetics, pharmaceuticals, and energy. To promote such interaction between disciplines, some entities such as the University of California of Santa Barbara (UCSB) have built centres such as its MBT Center which is equipped with cutting-edge technological equipment needed to carry out experiments.
SDG 10. Reduced inequalities	Social	Inclusion of people from disadvantaged groups in the value chains of MBT.
SDG 14. Life below water	Environmental	Sustainable management of fisheries (related to SDG2) and improvements in rearing techniques, decreasing the pressure on wild populations.
SDG 17. Partnerships for the goals	Economic	The value chains and initiatives within MBT tend to have a transversal character between disciplines and across the different actors in the quadruple helix. The best practices selected and described in section 6 are an example of a strategic alliance towards a common goal.

7. Identification of best practices in blue biotechnology

As mentioned in section 5, the good practices identified in this report can be used to create shared value, and thereby act as the main sources for systemic and sustainable change in society. The identification and analysis of these best practices provide insights into the existence of barriers against and opportunities for their implementation in the MBT sector. This report describes several initiatives impacting different industries and using various raw materials and technologies.

This section of the report provides a detailed analysis of a series of cases that can be considered best practices for SVC. The selection of the cases highlighted as best practices was based on their capacity to contribute to systemic change, their potential impacts in the Mediterranean region, the participation of different agents of the quadruple helix, and their responses (or lack thereof) to non-technological challenges.

Table 5. Selection criteria for best practices (BPs)

Selection criterion	BP1	BP2
Characteristics of the implemented solution:		
Create shared value		
Exert impact globally		
Applicable in the Mediterranean		
Participation by agents of the quadruple helix		
Impact of the solution in economic sectors:		
High added value sectors		
Primary sector		
Typology of the challenges faced:		
Legal challenges		
Social challenges		
Environmental challenges		
Sustainability of the techniques used:		
Applies principles of circular economy		

Source: Bou, unpublished data

Table 5 lists the selection criteria and illustrates which are met by each of the three best practices selected. The best practices identified, which respond to at least one of the selection criteria, are the following:

- BP1: Use of horseshoe crab blood;
- BP2: Production of fast-growing transgenic salmon;

- BP3: Use of plastic-consuming microorganisms.

The high added value sectors considered are human health, animal health, and cosmetics. As a primary sector, fishing and aquaculture are considered.

7.1. Best practice in the pharmaceutical sector: Use of horseshoe crab blood

7.1.1. Technological challenge

Healthcare professionals need to administer injectable substances to patients, such as vaccines, anaesthetics, or antibiotics. These substances can easily be contaminated by endotoxins of bacterial origin which, upon contact with blood, are harmful to human health and can even cause death. For this reason, such substances require prior certification of their pathogen-free status by official authorities such as the American Food & Drug Administration (FDA).

From the 1940s until the 1970s, the pharmaceutical industry used mouse blood for the detection of bacterial endotoxins in injectable substances destined for human use. Since the 1970s, the blood of horseshoe crabs (mainly *Limulus polyphemus*) has been used due to the high sensitivity of the immune systems of these species toward endotoxins. Amoebocytes present in the haemolymph crab are very sensitive to endotoxins, and upon contact with an endotoxin, a blood-clotting reaction occurs, which is the base of the Limulus Amoebocyte Lysate (LAL) test, in which an extract of crab blood is used to verify the presence of endotoxins in the injectable products. The extract contains proteins that specifically recognise endotoxins and bind to them. The LAL test is the reference test most widely used for the detection of endotoxins, alongside the rFC test that is described in section 7.1.2.

Figure 28. Horseshoe crab bleeding in laboratory.

Source: Timothy Fadek

The species of horseshoe crab used for these tests are: *Tachypleus tridentatus* (Asia); *Tachypleus gigas* (Southeast Asia); *Carcinoscopy rotundicauda* (Southeast Asia); and *Limulus polyphemus* (Atlantic Ocean of North America). To obtain the blood extract, bleeding of one-third of the crab's total blood capacity is induced. After this operation, 13% of processed crabs are sold to the fishing industry as bait and the rest are returned to the wild. The crabs released are in a state of such weakness that approximately 30% of them end up dying. It is estimated that around 130,000 crabs worldwide die annually as a result of these blood extraction procedures. This mortality rate not only impacts the natural populations of horseshoe crabs but also those of other animal species along the trophic chain, such as some bird species that feed on horseshoe crabs.

Beyond the ecological impacts described, the usual practice of blood extraction from horseshoe crabs makes the production of the LAL test dependent on a natural resource which is non-sustainable in the long term. The economic cost of its manufacturing further demands the search for alternative solutions.

7.1.2. Implemented solution

The cascade of reactions that take place in the LAL test was the subject of scientific research in the 1990s. It was noticed that one of the proteins involved in the cascade is factor C. In 1997, a research group from the National University of Singapore managed to synthesise the recombinant form of factor C, the rFC, which formed the basis for the design of a new endotoxin-detection test (Maloney, Phelan, & Simmons, 2018). This test was not initially adopted by the pharmaceutical industry because of its lower efficacy in comparison to the LAL test. However, subsequent studies showed that the rFC test was equally or more effective than the LAL test, even preventing the appearance of false positives. The rFC test was marketed until 2003, at which time the pharmaceutical industry still showed reluctance to use this method, claiming possible risks to human health despite the existence of scientific evidence showing otherwise.

Another reason for the resistance against the use of the rFC test lies in legislative aspects. The pharmaceutical industry operates in a globalised market and is subjected to different regulations, requiring legislative harmonisation that allows the commercialisation of the test worldwide. The use of rFC as an alternative to the LAL test was accepted by the FDA in 2012, but the lack of harmonisation at the European level has delayed the adoption and commercialisation of the test in Europe. Currently, the rFC test is a standardised and widely used method in the pharmaceutical industry, replacing the LAL test in 90% of cases. It is estimated that the annual mortality of horseshoe crab species in North America has decreased by more than 100,000 crabs thanks to the adoption of the rFC test for the detection of endotoxins in injectable healthcare products.

In this case, the best practice is based on the in vitro synthesis, through biotechnology, of an alternative to the natural, scarce, and finite resource which was previously used for the detection of endotoxins in injectable healthcare products.

7.1.3. Shared Value

The described practice exhibits social, environmental, and economic value. The use of a product obtained by in vitro techniques guarantees the safety of the injectable product for human use. Therefore, the social value of this best practice is related to public health guarantees.

A laboratory-produced substance can replace the use of blood from horseshoe crabs, which implies a drastic reduction in the fishing of these crab species, and by extension the recovery of wild populations, generating environmental value.

The economic value of this best practice is determined by two key aspects. On the one hand, the adopted solution guarantees long-term sustainability in the production of the endotoxin-detection test, encouraging its commercialisation. On the other hand, the solution adopted reduced the production costs of the test by making it independent from the use of a limited natural resource (Maloney et al., 2018).

7.2. Best practice in the environmental services sector: Plastic-consuming microorganisms

7.2.1. Technological challenge

The good practice identified in this section responds to three different challenges. One of them is the elimination of marine plastic litter, which is one of the most important environmental challenges in current society. The presence of microplastics affects marine flora and fauna, and ultimately human health. A more detailed analysis of this problem in the Mediterranean region was given in section 4.2 of this report.

Figure 29. Plastic-consuming microorganisms

Source: Biocellection

On the other hand, the aquaculture sector often faces problems associated with diseases occurring under rearing conditions. Vaccination and nutraceutical ingredients are the solutions most frequently adopted by this industry.

Much of the protein used as a source of food in the aquaculture sector comes from flours made from caught fish. Thus, an important part of the captures of extractive fishing is destined to the production of fish feed. As discussed in section 4.5 of this report, several research lines are focused on the search for alternative protein sources and thereby decreasing the environmental impacts of the manufacture of fish feed.

7.2.2. Implemented solution

Biocellection[18] has selected bacterial strains that consume plastics as a source of nutrition for their growth and multiplication. The same strains have other industrial applications, such as in the production of vaccines for farmed fish. They can also be used as a protein-rich ingredient in feed used in aquaculture, partially or totally replacing fishmeal. This new product has become a very interesting nutraceutical compound for the aquaculture industry.

When cultivating this bacterial strain in a bioreactor, the consume plastic to support their growth and multiplication. This bacterial biomass is the basis for the biosynthesis of the vaccines for diseases in cultured fishes and, on the other hand, is also the basis of a protein-rich ingredient for the manufacturing of fish feed. The technology developed by Biocellection has been experimentally validated in the real-world environment, and was able to reduce the time required for bacterial growth from months to days. In this way, the company offers its technology as a service platform for other biotech companies.

7.2.3. Shared value

The accumulation of plastics in animals and marine organisms destined for human consumption is one of the main threats to human health arising from marine litter. The best practice identified provides a solution for reducing the amount of plastic waste in the sea, and thereby the presence of such pollutants through food chains, contributing social value.

Plastic waste present in the sea has a large dispersion capacity, with very long degradation times and extreme toxicity to marine flora and fauna. The use of the technology developed by Biocellection can help in reducing the amount of plastic present in the sea, creating environmental value. On the other hand, the use of these bacterial strains as a source of protein in fish feed can reduce fish captures for the purpose of fish feed production.

The emergence of this best practice confers economic value to the MBT sector, as it implies the emergence of new business opportunities based on the availability of raw materials at low prices. Service platforms and tests that Biocellection offers to other companies and agents of the MBT ecosystem support harmonious growth based on technological innovations applicable to the utilisation of pollutants and waste.

[18] More information: *https://www.biocellection.com/*

8. Recommendations and proposals for research, innovation, and technology transfer in MBT for public administrations

This report analyses the main marine resources with biotechnological potential in the Mediterranean region, possible industrial applications in high added value sectors, and three cases considered as best practices. The analysis of these elements and a literature review have allowed detection of the barriers against and opportunities for the implementation of MBT in the Mediterranean, from the perspectives of SVC and creation of blue oceans which were described in section 2 of this report. Table 6 presents a SWOT analysis on which the recommendations for public administrations are based.

Table 6. SWOT analysis on MBT, including correspondence of each point with the recommendations given in the following sections.

Weakness	
Lack of key performance indicators (KPI) for SVC initiatives	Recommendation 3
Lack of MBT cluster organisations as SVC facilitators	Recommendation 6
Low research-company collaboration (Organisation for Economic Co-Operation and Development 2013)	Recommendation 6
Lack of identification of agents (research, industry, civil society, and government) in the blue biotechnology sector in the Mediterranean	Recommendation 7, 6
Lack of technological centres and specialised infrastructure in MBT	Recommendation 8
Threats	
Current legislative framework hinders exploitation of the potential of MBT	Recommendation 1
Existence of harmful subsidies that decrease potential progress in MBT	Recommendation 2
Strengths	
Discipline in permanent growth (Collins, Broggioato, and Vanagt 2018)	Recommendations 6, 7, 8
Culture of collaboration with other disciplines (e.g. engineering and robotics)	Recommendations 4, 6, 7
Impacts in at least 9 of the 17 SDGs	Recommendation 3
MBT impacts in sectors with high economic potential (e.g. pharmaceutical industry)	Recommendation 10
MBT is linked to many other mature biotechnologies, improving its technological development (Kafarski 2012)	Recommendation 6
Successful MBT projects with potential to be translated to other Mediterranean regions facing similar issues	Recommendation 11
Opportunities	
Increased orientation of public subsidies from harmful to beneficial impacts	Recommendation 2
Large size of unexplored marine areas	Recommendation 4
Aquaculture techniques able to rear organisms with biotechnological purposes without affecting their natural populations	Recommendation 5
Existence of collection systems for marine wastes to use them for blue businesses	Recommendation 9

Source: Bou, unpublished data

This section lists a series of recommendations to public administrations for improving the implementation of MBT as a generator of shared value in the Mediterranean, which were elaborated from the analysis of the barriers and opportunities detected.

Recommendation 1. Adaptation of legislative frameworks

Like any other industrial sector, the blue economy is subject to national and European legislative frameworks, which occasionally constitute an obstacle in its development and consolidation as an economic engine. This situation can be minimised via three possible legal adaptations:

- **Authorisation of the commercialisation of invasive exotic species under specific circumstances.** In certain cases, such as that presented in section 5 of this report, the commercial exploitation of such species is an effective method to control the expansion of the species at the same time that it opens opportunity for economic benefit. Prior cases with species of the marine ecosystem, such as the horseshoe crab (section 6.1), demonstrate that pressure on a specific species results in its population decline.
- **Legal harmonisation between different public authorities (FDA, EMA, etc.)[19] on commercial products and services.** The blue economy has a global scope, and companies therefore face different regulatory and legislative frameworks depending on the country in which they want to commercialise their products and services. The best practice described in section 6.1 is an example of how the diversity of legislative frameworks can slow the commercialisation of technology.
- **Establish equal business competition conditions for European companies.** The European Commission must ensure that all agents of the blue economy ecosystem, and therefore all agents related to MBT, can access the Mediterranean market under the same conditions and opportunities. All products and services that are commercialised in this region must meet the same requirements, regardless of whether they come from member countries of the EU or from third countries, in order not to harm companies based on their geographic origin.

Recommendation 2. Orientation of the subsidy system towards initiatives that generate shared value

Different experts on subsidies have studied their characteristics from theoretical and practical points of view, and have established a classification system based on the resultant benefits or harms (Sakai, Yagi, & Sumaila, 2019). Beneficial subsidies drive economic growth through research and innovation. Pernicious subsidies cause negative situations in the environment of their own activity in the medium and long term. Examples of negative subsidies are the abolition of fuel taxes or the replacement of fishing boat engines with more powerful ones. These subsidies, rather than attacking the true cause of the reduction in catches, which is the lack of living resources in the environment, increase the fishing pressures on these populations, aggravating the problem. Several conversions have been made in this regard within the framework of the Common Fisheries Policy[20], however, there is still progress to be made.

[19] FDA: Food & Drug Administration; EMA: European Medicines Agency
[20] Available at: *https://ec.europa.eu/fisheries/cfp_en*

Recommendation 3. Design Key Performance Indicators (KPI) that allow measurement of the real impacts of actions in terms of shared value creation for all agents of MBT value chains

The actions developed must have a transformative effect and impact from the perspective of SVC. This impact assessment requires the design of KPIs that measure the progress and effectiveness of the actions and the achievement of the objectives set initially, paying special attention to the SDGs (Section 6). These KPIs must include aspects related to the social, economic, and environmental impacts.

Recommendation 4. Search for marine species with MBT potential in under-explored regions and/or hotspots

Seas and oceans are sources of organic and inorganic resources, which we must continue exploring in order to maximise the possibilities they offer. To achieve this goal, we must focus on new and improved technologies that allow the exploration of new areas of the seafloor, such as the technological development of remote submarine vehicles for the detection and harvesting of marine resources in regions, which are currently inaccessible. Mechanisms to ensure that prospection and harvesting of marine resources effectively avoid any potential negative impact on the target species and its surrounding ecosystem will be needed.

Recommendation 5. Improvement of aquaculture and in vitro laboratory techniques as sustainable alternative sources of marine resources without affecting wild populations

The MBT developments should not adversely affect the environment due to the collection of individuals or compounds. Therefore, the improvement of alternative methodologies like aquaculture and laboratory techniques is necessary.

Recommendation 6. Promotion of collaborative projects between clusters and different agents linked to the blue economy, with a holistic vision and international projection

The study '*How clusters can contribute to social and environmental challenges through the creation of shared value'* (Amores 2019), underlined in the framework of the Panoramed project, highlights the role of clusters as shared value generators, and the author recommends the implementation of collaborative programs/platforms among Mediterranean clusters.

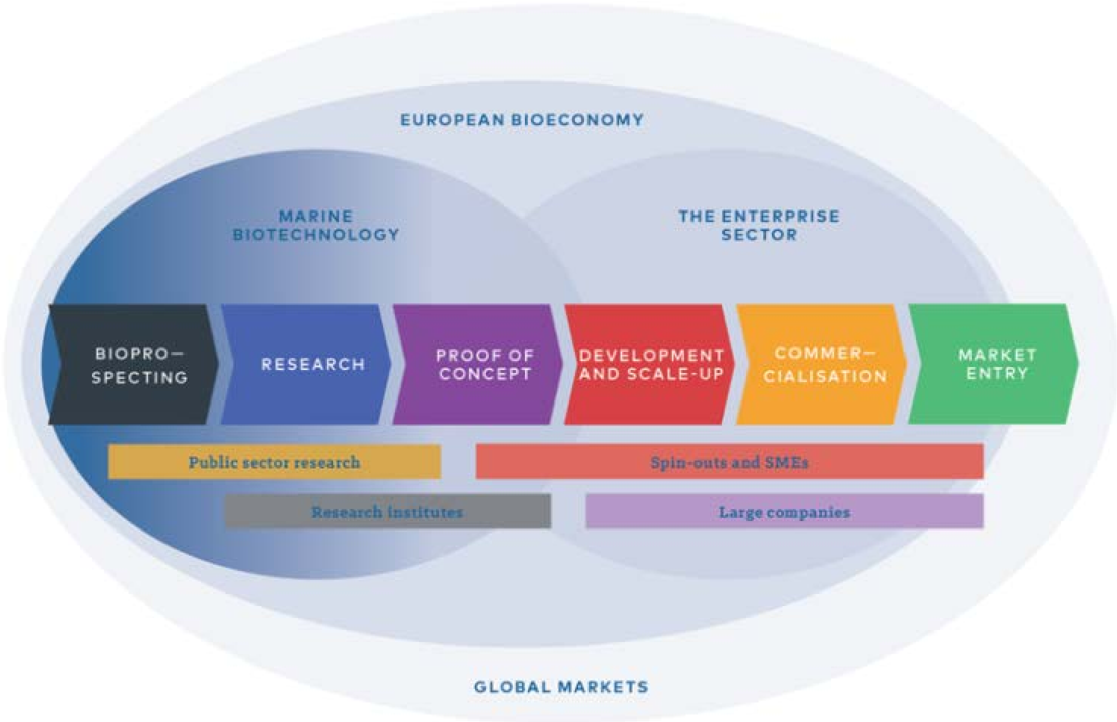
Recommendation 7. Establishment of local and/or regional MBT networks on blue growth in the Mediterranean

Innovation and technological developments in blue growth, in general but in particular in MBT, must be structured within stable and multidisciplinary networks that are capable of generating systemic changes with a multiplier effect. The financing of these structures, in the long term, is essential for the development of blue growth in the Mediterranean region and in the rest of Europe.

Recommendation 8. Creation of a European maritime network of biotechnological infrastructure to promote sustainable business models, such that the agents of the MBT value chain in the Mediterranean can access high-quality biotech products and services

MBT is a sector with a wide variety of agents involved in its value chain (Figure 30). One of the bottlenecks detected is a difficulty in accessing diverse and high-quality biological material at various nodes along the MBT value chain, especially for research groups and private companies. This problem can be solved by creating a network of biobanks where these collections of biological material are available, with high-level scientific and technical services attached. This network can function as a scientific knowledge campus and a physical meeting point for public administrations, research groups, companies, and other agents in the value chain.

Figure 29. Agents involved in the MBT value chain.



Source: Hurst et al., 2016

Recommendation 9. Creation of structures and mechanisms to optimise waste and by-product management for reuse, employing MBT techniques

This report has mentioned the use of biotechnology as a facilitating technology to solve environmental problems related to the management of biological wastes and plastic litter. To make this solution effective, it is necessary to design a network for the collection and redistribution of wastes and by-products, as well as centralised management mechanisms, or alternatively in a decentralised manner through local nodules.

Recommendation 10. Organisation of working sessions in the Mediterranean with all countries and the entire value chain represented, in order to develop transnational projects with a multi-actor approach

The EU supports meetings with multi-actor approaches under the framework of the blue economy, such as the Blue Bioeconomy Forum[21]. However, structuring of these meetings at the country or regional level is recommended such that the value chain of each country/region can be structured and each country/region can be represented in the working meetings organised at the European level.

[21] More information: *https://ec.europa.eu/easme/en/final-stakeholder-event-blue-bioeconomy-forum-take-chance-have-your-say*

Recommendation 11. Promotion of scalability and replication of pilot projects previously validated in other Mediterranean areas with similar issues

There are several European funding instruments supporting the execution of pilot research projects in specific areas with specific problems, and this also applies to MBT. It is common for these initiatives to be abandoned once the relevant project has been completed, and for the generated knowledge not to produce the expected impact. In this situation, technical and economic means must be specified, with the goal of realising two strategies:

- Exportation of knowledge to generate value in other Mediterranean areas experiencing similar problems or situations.
- Scaling-up of validated technologies to make them profitable in the medium and long term and thus attract other agents of the value chain.

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