the University of California a considerable income from licence fees until the patent expired. Estée Lauder remains the main user with 72 products of its various brands and companies.

The starting point to an ABS agreement in this case was an authorisation signed by the Bahamas government for a tripartite experimental coral harvest for the University of California, including training for fishermen. Over time, the demand for the product increased. As the patent did not provide for benefit sharing, the Bahamas government and other local stakeholders sought to reach a proper ABS agreement with the University in the late 1990s, which the University refused. Nonetheless, the experimental permit was extended under an ABS agreement which was eventually reached in 2001 between three parties: the Government of the Commonwealth of The Bahamas, the local company Marsh Harbour Exporters and Importers Ltd. (MH) whose trained fishermen were harvesting the soft coral and the U.S. company Lipo Chemicals Inc. (Lipo) producing Gorgonian Extract® and selling it to cosmetic companies. According to MH, under the agreement's provisions several hundred thousand dollars of royalties and other payments have been received and transferred to the Bahamas government as an interim benefit sharing by MH/Lipo. It was agreed to spend this money for, inter alia, surveys, conservation education, and resource management. Recent publications revealed that although the corals regrow after clipping, their fecundity is reduced, resulting in a prolonged rejuvenation time compared to undisturbed populations.[xxviii] Measures to ensure sustainability are under consideration meanwhile; new environmental research is planned.

Enzymes

Enzymes extracted from hyperthermophile microbes living in marine hydrothermal environments are of high interest for scientific and industrial applications that require high temperatures. Probing such environments led to the discovery of many hyperthermophile strains in the last three decades. In 50 related scientific publications,[xxix] the research teams reported 48 accesses to genetic resources in national waters of eight countries (83 per cent of all accesses); Mexico and Italy attracted the highest interest. Sixteen of these national accesses (33 per cent) were undertaken in deep-sea areas. In only ten cases (17 per cent of all accesses), access took place in deep-sea areas of ABNJ. It is interesting to note that also in the field of investigating hyperthermophile marine microbes, most accesses occurred in national waters and would therefore fall under national ABS regulation.

Consideration for effective national ABS frameworks

- Evidence shows that bioprospecting mostly takes place in national territories, including many accesses in the deep-sea and extreme environments; bioprospecting in ABNJ is still rare
- National ABS frameworks in coastal states need to establish institutional structures that allow for effective access procedures in the marine territory
- Countries need to establish effective monitoring and compliance measures to ensure legal utilisation of marine genetic resources and associated traditional knowledge
- Miniscule concentrations of most MNPs in marine organisms necessitate the establishment of sustainable harvesting and aquaculture or chemical synthesis and fermentation to avoid overexploitation and extinction
- All stages of the value chain – especially those using synthetic MNPs – need to be covered in benefit sharing agreements to enable countries to benefit from the financially significant commercial phase
- The access permit should include all organisms harvested together with the main genetic resource
- Monetary and non-monetary benefit sharing should be specifically targeted to support the protection of marine genetic resources and to establish sustainable ways of sourcing of the raw material

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Relevance of Marine Bioprospecting for ABS Frameworks

The utilisation of marine genetic resources and associated traditional knowledge has long been sidelined in the discussions on access to genetic resources and fair and equitable benefit sharing (ABS). One reason lies in the difficult accessibility of marine ecosystems, especially in greater depths. A second reason is certainly also the historic focus of the ABS debates on terrestrial genetic resources – significantly, the slogan "Green Gold", not "Blue Gold", advanced to be the catchword of the debate. Over the last three decades, research and development based on marine genetic resources and associated traditional knowledge advanced tremendously. As a result, five modern "marine" drugs for six indications were approved since 2004; dozens of marine natural products (MNP) are under clinical tests and many thousand MNPs are under scientific investigations. Enzymes from marine organisms are used in scientific and industrial work, marine ingredients found their way into cosmetics. Through research and development on traditional knowledge about positive health effects of certain seafood, functional foods and nutraceuticals could be brought to the market.

The Convention on Biological Diversity (CBD) states that governments have the right to regulate access to genetic resources. Adhering to the third objective of the CBD, its members shall take measures *"with the aim of sharing in a fair and equitable way the results of research and development and the benefits arising from the commercial and other utilization of genetic resources"*. In 2010, the *Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization* (NP) was adopted under the framework of the CBD. The NP lays down basic provisions for legal ABS frameworks and, noting the 2007 *United Nations Declaration of the Rights of Indigenous Peoples*, includes access to traditional knowledge associated with genetic resources in its scope.

Core provisions of the Nagoya Protocol

Use of Terms – Art. 2

(c) "Utilization of genetic resources" means to conduct research and development on the genetic and/or biochemical composition of genetic resources, including through the application of biotechnology as defined in Article 2 of the Convention;

(d) "Biotechnology" as defined in Article 2 of the Convention means any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use;

(e) "Derivative" means a naturally occurring biochemical compound resulting from the genetic expression or metabolism of biological or genetic resources, even if it does not contain functional units of heredity.

Fair and Equitable Benefit-Sharing – Art. 5 1.

[…] benefits arising from the utilization of genetic resources as well as subsequent applications and commercialization shall be shared in a fair and equitable way with the Party providing such resources that is the country of origin of such resources or a Party that has acquired the genetic resources in accordance with the Convention. Such sharing shall be upon mutually agreed terms.

ABS Governance in Exclusive Economic Zones

The NP applies to genetic resources and associated traditional knowledge accessed in areas under national jurisdiction. Respective ABS legislation covers the terrestrial territory of a country and its marine territory demarcated by the *Exclusive Economic Zone* (EEZ). EEZs expand as far as 200 nautical miles (370 km) from the mean low-water line and comprise the water column, the seabed and the subsea soil.

The global dimensions of EEZs are vast; they cover 36 per cent of the world's ocean area. The issues around bioprospecting in EEZs are of high relevance for countries with long coastlines or many widely spread islands, many of which belong to the *African, Caribbean and Pacific Group of States* (ACP). Its 15 Pacific and 16 Caribbean states as well as 39 of all 54 African states have EEZs, amounting to 24 per cent of the EEZ area worldwide. While only 24 countries worldwide rule over terrestrial areas larger than one million km², 31 countries have EEZs larger than one million km². Within the rank of countries with a ten times larger EEZ than terrestrial territory, ACP-countries form the majority (28 out of 37). For these and other coastal countries, effective ABS regimes with well-functioning access, monitoring and compliance systems in provider and user countries are of utmost importance when it comes to marine bioprospecting.

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An interesting, yet largely underestimated fact is that EEZs cover extensive areas of the deep-sea. For example, almost 84 per cent of the EEZ areas in the Caribbean are classified as deep-sea with depths greater than 200 m, and 74 per cent are even deeper than 1,000 m. Also, 66 per cent of the 521 hydrothermal vent fields discovered until 2009[i] and 47 per cent of the potentially 14,000 seamounts[ii] – both highly interesting deep-sea ecosystems for bioprospecting – are under national legislation. The so far deepest hydrothermal vent was recently discovered in the EEZ of the Caribbean Cayman Islands (UK) in 5,000 m depth.[iii]

It is only bioprospecting in areas beyond national jurisdiction (ABNJ) that is not regulated by national ABS regimes but governed by the *United Nations Convention on the Law of the Sea* (UNCLOS). Marine resources in ABNJ are *"common heritage of mankind"*.

Access is free and feasible for those who have the financial and technical means for their exploitation. The adoption of the NP accelerated discussions within UNCLOS on appropriate benefit sharing mechanisms in the face of unregulated access.

Examples of Utilisation and Commercialisation

This factsheet uses information on research, development and commercialisation with marine genetic resources and associated traditional knowledge contained in selected scientific papers in three fields: drugs, enzymes, and cosmetics.[xii] The following sections present these examples in the ABS context to support evidence-based discussions between governments, parliaments and stakeholders when drafting national ABS legislation in coastal states and to inform the debates about ABS issues in ABNJ.

Table 1: Prescription and over-the-counter drugs based on marine natural products

Product	Active substance & production mode	Indication & year of first drug approval / OTC registration	Organism	Country of origin & year of access	Worldwide sales in 2014 [M USD] (1)
1) Cytosar-U® DepoCyte®	Cytarabine (fermentation)	Leukaemia and lymphoma (USA 1969)	**Cryptotethia crypta** (sponge)	Florida, USA (1945) [iv]	26
2) Vira-A®	Vidarabine (fermentation)	Herpes virus and others (USA 1976)	**Cryptotethia crypta** (sponge)	Florida, USA (1945) [iv]	17
3) Immucothel®	Keyhole Limpet Hemocyanin (non-lethal extraction)	Bladder cancer (The Netherlands 1997)	**Megathura crenulate** (mollusk)	California, USA (1950s)	not stated
4) Prialt®	Ziconotide (synthetic)	Chronic severe pain (USA 2004)	**Conus magus** (mollusk)	Probably Philippines (before 1987) [v]	26
5) Lovaza® Omacor®)	ethyl esters of omega-3 fatty acids (extraction)	Lowering triglyceride concentration in blood (USA 2004)	Oil from various fish species and regions	Traditional diets in the Arctic region and Japan [vi]	851
6) Yondelis®	Trabectidin (semisynthetic after fermentation)	Soft tissue sarcoma (USA 2004) Ovarian cancer (USA 2005)	**Ecteinascidia** (tunicate)	First access: Panama, Colombia, Nicaragua, Honduras, Belize or Mexico (1978) [vii] Access for patent: Florida, USA (before 1986) [viii]	114
7) Carragelose®	Iota-carrageenan (extraction from aquaculture)	Influenza (EU OTC registration 2007)	**Eucheuma & Cnondus spec.** (red algae)	Traditional use in food and cosmetics, especially in Asia [ix]	not stated
8) Halaven®	Eribulin mesylate (synthetic)	Metastatic breast cancer (USA 2010)	**Halichondria okadai** (sponge)	Japan (before 1986) [x]	323
9) Adcetris®	Brentuximab vedotin 63 (Dolastatin 10 derivative & anti-CD30 antibody) (synthetic)	Hodgkin and systemic anaplastic large cell lymphoma (USA 2011)	**Dolabella auricularia** (mollusk) / **Lyngbya & Symploca spec.** (cyanobacteria)	Mauritius (1972) [xi]	388

Drugs

Research and development on MNP in the medical sciences has grown dramatically over the last three decades. As of 2014, eight prescription "marine" drugs and one over-the-counter drug are available.[xiii] Twenty-eight MNPs have been under clinical investigations since 2004. As of 2012, 1,458 MNPs were included in preclinical research and 8,940 published MNPs of medicinal interest were recorded. In 2012, 1,241 new MNPs were described in the literature.[xiv] The worldwide sale of the prescription drugs was worth 1.745 billion USD in 2014 (Table 1). Economic estimations concluded that the pharmaceutical value of new oncology drugs based on MNPs vary in a range between 0.6 and 1.5 trillion USD.[xv]

In four cases (Table 1, nos. 1, 2, 3, 8), the commercialised drug was developed from a genetic resource accessed in industrialised countries. In one case (no. 6), initial research was undertaken with genetic resources accessed in developing countries, but the specimens from which the biochemical compounds were isolated and covered by a patent were accessed a second time in an industrialised country. In two cases (nos. 4, 9), the genetic resource was accessed in a developing country. The commercially most successful marine drug, finally, is a product of investigations in the positive health effects of traditional diets (no.5); case no. 7 also falls into this category. Production of these drugs relies on various supply routes for the active ingredients: Three MNPs are synthesised chemically, two produced by microbial fermentation, one by a combination of both approaches, and three still rely on extracting the genetic resource. In 2011, 15 different MNPs were under clinical anti-cancer trials.[xvi] Using marine organisms as supply for MNPs for clinical trials and industrial production poses questions on the population effects of the harvest; hence, sustainable solutions to avoid overexploitation and extinction are of prime importance.[xvii]

A compilation of preclinical research in the field of HIV reveals that 132 MNPs were tested in laboratory trials from 2002 to 2011. The utilised marine genetic resources are sponges (29 species, 82 MNPs), other animals (12 species, 20 MNPs), plants (22 species, 23 MNPs), and microbes (7 species, 7 MNPs).[xviii] These genetic resources were accessed within the EEZs of 27 countries, while only one access was undertaken in ABNJ. Eight cases utilised commercially available products of marine algae or bryozoans; one case utilised a protein sequence from a data bank. Interestingly, cases accessing derivatives or even mere sequence information represent the most advanced ones in terms of HIV drug development. The analysis of the countries of origin reveals a clear dominance of the Australo-Pacific region (32 accesses). National utilisation of genetic resources occurred in 39 per cent (26) of the cases. Foreign utilisation was undertaken in 41 cases, 28 of them in the USA. National ABS frameworks need to reflect the increasing importance of national access and utilisation and international co-operations when drafting access and negotiating benefit sharing provisions.

Cosmetics

The cosmetic industry uses many marine organisms and their derivatives. The Swiss company Mibelle Biochemistry sells Helioguard 365 / Noriguard nc as UV-filter for sun creams to cosmetics companies, containing a compound from the red algae *Porphyra umbilicalis* collected in France.[xix] The French company Unipex Innovations developed cosmetic ingredients from microbial mats, called Kopara, collected on Moorea Island, French Polynesia.[xx] Kopara is a gelatinous sediment formed by benthic microbial communities, dominated by cyanobacteria. It contains many biomolecules which bear potential for various industrial applications.[xxi]

Access in Areas Beyond National Jurisdiction: Deepsane® / Abyssine® 657

Unipex Innovations, meanwhile merged with Lucas Meyer Cosmetics, also sells Abyssine® 657 containing the anti-inflammatory polysaccharide Deepsane®.[xxii] Since 2003, Abyssine®-containing cosmetics have been marketed by the U.S. company Kiehl's, owned by L'Oréal, and others. Deepsane® is a product of the deep-sea microbe Alteromonas macleodii. The specific strain was isolated from the polychaete annelid Alvinella pompejana which was collected by scientists of the Institut Français de Recherche pour l'Exploitation de la Mer (IFREMER) in 1987 close to a hydrothermal vent located on the East Pacific Rise.[xxiii] The worm was accessed in 2,625 m depth, 315 nautical miles away from the Mexican coast, thus in an area beyond national jurisdiction. Due to its interesting properties for cosmetic purposes, a patent on the bacterium strain, the produced polysaccharide and its use was sought and granted to IFREMER in 1999.[xxiv] This example constitutes the only one among the investigated cases in the fields of medicine and cosmetics in which the genetic resource that was subject to research and development and later successfully commercialised was indeed sampled in ABNJ.

Gorgonian Extract® with ABS Agreement

The most successful case of MNPs in the field of cosmetics is the use of pseudopterosin extracted from the soft coral *Pseudopterogorgia elisabethae*, harvested annually in The Bahamas. This case involves an ABS agreement, covering the initial part of the value chain. Based on samples collected in The Bahamas in 1982, researchers from the University of California discovered the anti-inflammatory properties of pseudopterines[xxv] and received a patent in 1988.[xxvi] While further investigations for medical applications by the company OsteoArthritis Sciences Inc. remained unsuccessful, the substance developed into a major success in the cosmetic industry. In 1995, Estée Lauder began using the coral extract in its brand Resilience. The patent licence fees paid by Estée Lauder to the University of California in 1995 and 1996 alone amounted to 1.5 M USD.[xxvii] According to a recent databank survey, pseudopterosin has been used in 143 products meanwhile, which should have brought

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