UNEP

CBD

CONVENTION ON
BIOLOGICAL DIVERSITY

Distr.
GENERAL
UNEP/CBD/SBSTTA/2/15
24 July 1996
ORIGINAL: ENGLISH

SUBSIDIARY BODY ON SCIENTIFIC, TECHNICAL AND
TECHNOLOGICAL ADVICE
Second Meeting
Montreal, 2 to 6 September 1996

BIOPROSPECTING OF GENETIC RESOURCES OF THE DEEP SEA-BED

Note by the Secretariat

1. BACKGROUND

1. In recent years, there has been a steady increase in public awareness worldwide of the economic, social, environmental, cultural, recreational and other critical benefits derived from marine and coastal biological diversity, including its components. As evidence of the priority now being assigned by governments to this area, at its first meeting the Conference of the Parties to the Convention on Biological Diversity (COP) selected marine and coastal biological diversity as the first major ecosystem "theme" to be addressed systematically under the Convention process, as part of the COP's medium-term programme of work.

2. The Secretariat's report on access to genetic resources prepared for the second meeting of the COP (document UNEP/CBD/COP/2/13) noted, *inter alia*, that, as Article 15 of the Convention (which provides the basis for the Convention's approach to controlling the use of genetic resources) did not apply to areas outside national jurisdiction and, given that it is unclear whether, or how, UNCLOS, or the common heritage principle, applies to the genetic resources of the deep sea-bed, there needs to be an in-depth study on how to best address the use of these resources.

3. The second meeting of the COP, in paragraph 10 of decision II/10, requested the Executive Secretary, in consultation with the United Nations Office for Ocean Affairs and the Law of the Sea, to undertake a study of the relationship between the Convention on Biological Diversity and the United Nations Convention on the Law of the

Sea with regard to the conservation and sustainable use of genetic resources on the deep sea-bed, with a view to enabling the SBSTTA to address at future meetings, as appropriate, the scientific, technical and technological issues relating to the bio-prospecting of genetic resources on the deep sea-bed.

4. This Note presents a brief survey of the issues raised on the bioprospecting of genetic resources on the deep sea-bed in light of the provisions of the Convention and UNCLOS. Its purpose is to enable the SBSTTA to make a preliminary assessment of the areas that it feels it can make an effective contribution to the relationship between the Convention and UNCLOS and to consider how it might make that contribution in a timely fashion. It must be stressed, however, that the consideration of the relevant principles of international law have not been reviewed by either the United Nations Office for Ocean Affairs and the Law or the United Nations Office for Legal Affairs.

5. The Note has been presented to the United Nations Office for Ocean Affairs and the Law of the Sea by way of a preliminary investigation of the nature of the relationship between the Convention and UNCLOS with regard to the bio-prospecting of genetic resources on the deep sea-bed. In this sense it represents no more than a preparatory step for the study requested by the second meeting of the COP.

2. THE INTERNATIONAL LEGAL REGIMES GOVERNING THE USE OF DEEP SEA-BED MARINE GENETIC RESOURCES

6. Marine genetic resources are subject to a set of legal principles that essentially derive from UNCLOS, customary international law and the CBD. These principles basically apply three different regimes to marine genetic resources depending upon their location.

7. Marine genetic resources that are located within the "national jurisdiction" (which effectively means the EEZ), are under Article 22.2 of the CBD and subject to its principles to the extent that this treatment does not conflict with the "law of the sea". UNCLOS, which embodies the "law of the sea", attributes sovereign rights to the coastal State for the purposes of exploring and exploiting natural resources throughout the EEZ. In relation to the exploitation of mineral resources on the continental shelf, however, the coastal State is obliged to make payments or contributions in kind to the Parties to UNCLOS through the International Sea-bed Authority ("ISA"), if any are developed beyond the 200-mile limit.[1] With respect to marine living resources within the EEZ, the coastal State has certain conservation and management obligations[2], including the obligation, in principle, to share under-utilised resources with other States.[3] For sedentary species[4], the continental shelf legal regime is distinct from the living resources conservation provisions of the EEZ found in Article 68. In both cases, however, the general intent of the obligation is to control over-exploitation. As the use of genetic resources is of a non-consumptive nature, these general obligations have little impact or relevance. Consequently, most of the obligations and rights affecting use of these type of marine genetic resources derive from the CBD.

8. Beyond national jurisdiction, the CBD only applies to "processes and activities", and the principal instrument is UNCLOS. Matters not regulated by UNCLOS continue to be governed by general principles of international law.[5] UNCLOS imposes different regimes for the water column and the sea floor. For the water column, UNCLOS maintains that fishing and scientific research are freedoms of the high seas[6]. The freedom to fish is limited by the

rights, duties and interests of coastal states[7], the duty to take measures with respect to a State's own nationals to conserve high seas living resources[8] and to cooperate to conserve and manage high seas living resources[9]. These duties are being increasingly clarified and being developed from broad guiding principles to binding legal obligations. For example, the UN Agreement on High Seas and Straddling Stocks considerably clarifies many of these freedoms and duties. Despite the increasingly normative nature of the legal regime, as with the regime for the EEZ, most of these obligations and duties are generally intended to deal with the over-exploitation of fish stocks and have little relevance to the use of genetic resources. Consequently, the genetic resources of the water column are essentially unregulated.

9. UNCLOS designates the sea-bed, ocean floor and subsoil thereof located beyond the limits of national jurisdiction as "the Area"[10] and designates the Area and its resources as the common heritage of humankind.[11] A special legal regime and institutional structure is established by UNCLOS to control prospecting, exploitation and exploration of the Area's mineral resources. The special regime does not extend to the non-mineral resources of the Area or the water column immediately above the Area.[12]

10. All rights in the mineral resources of the Area are vested in humankind as a whole.[13] In effect, the Area's mineral resources have become international property to be exploited for the benefit of humankind. Neither a State nor a private entity can exercise sovereignty or dominion over any part of the Area or its mineral resources.[14] Title to minerals passes only upon their recovery in accordance with UNCLOS.[15] The International Sea-bed Authority is established to ensure that there is fair and equitable utilisation of the Area's mineral resources.

11. The regime for the Area makes no reference to genetic resources. As a result, it is not clear how UNCLOS may apply to the Area's genetic resources. The most plausible interpretation is that, as with all resources of the high seas other than mineral resources, they are freely accessible, open- access resources[16], appropriable by anyone who collects them. These types of resources are governed by a number of broad principles included under the rubric of the freedom to fish.[17]

12. Article 22.2 of the CBD has the effect that, despite the apparent conflict between UNCLOS's approach of internationalising the Area based on the concept of the common heritage of humankind and the CBD's general approach of conferring sovereignty or nationalising genetic resources, the UNCLOS approach prevails, and marine genetic resources found outside national jurisdiction can therefore effectively be considered as unregulated resources. This situation has arisen, however, by accident rather than design. The potential value of marine genetic resources and their importance in the benefit sharing rubric were not anticipated in the UNCLOS negotiations. Consequently, as these genetic resources appear to promise considerable economic value, the

situation begs the question of whether this approach is correct for these resources both with regard to their sensible exploitation and in the wider sense of the precedent that they provide for other contexts.

13. Marine genetic resources outside national jurisdictions, and especially those in the Area, provide both an opportunity and a challenge. If properly developed, utilisation of these resources could provide an opportunity to implement Article 15 and be an example to countries that a fair and equitable sharing of benefits is possible. There are significant parallels with the current circumstances surrounding the use of these resources and those surrounding the development of the legal regime in Antarctica. The experience in Antarctica suggests that there is a genuine possibility that a regime could be established relatively quickly by international standards. Factors such as an absence of vested economic interest, the absence of dominion by private or public entities, and the fact that the Area comes under the jurisdiction of two newly established regimes are important and propitious in being able to successfully develop an international regime. However, they are factors that will not persist for very long. On the other hand, there is a danger that attempts to develop such a regime will follow a similar path to deep sea-bed mineral resources, which might not only inhibit equitable use of these resources but could also have serious ramifications for the Convention generally.

14. There are a numerous ways that control over the bioprospecting of these resources could be developed. Foreseeable scenarios include:

(a) leaving marine genetic resources unregulated and freely available to those who spend the resources to collect them;
(b) bringing them within the regime governing the Area and the ISA's authority;
(c) bringing them within the CBD regime; and
(d) establishing an entirely new regime to deal with these special and new resources.

15. Each of these options has advantages and disadvantages. The first option, for example, represent a pragmatic approach on the basis that it may well be premature to even consider controlling the exploitation of these genetic resources. Most private entities considering investigating the potential of these genetic resources would take this view. Parallels with the enormous waste of effort involved in controlling exploitation of the Area's mineral resources come to mind. Similar parallels could be drawn with CRAMRA and the mineral wealth of Antarctica. Certainly, leaving exploitation of these resources unregulated has the attraction of providing the most encouragement to opening up the wealth of these resources. Due to the expense of developing these resources, it does, however, effectively bequeath them to large multinational companies or well-resourced government programmes; in other words, to developed countries. Establishing some form of international control prior to the emergence of commercial pressures for the exploitation of these resources would also mean that such a regime could be more easily developed to reflect what is fair and equitable rather than waiting until the resource is being exploited, when the regime would be more likely to reflect existing interests, regardless of whether this was fair or equitable. It would also avoid the problems of equity associated with allowing unregulated exploitation. It may, however, create a bureaucratic weight that industry cannot support, resulting in a situation where the resources are not developed. This, of itself, may be a desirable outcome on the basis that these resources should be protected as common heritage until all can participate effectively and equally in their exploitation.

16. Arguments for an entirely new regime include the fundamentally different requirements and pressures of utilising genetic resources, arising from the fact that it is a non-consumptive process that is quite distinct from the more conventional and consumptive use of marine resources, such as fishing or mining. These distinctions question the applicability of the UNCLOS rubric at all. Furthermore, given that the minerals have been treated separately under UNCLOS, why not do the same with genetic resources? Finally, the fact that the regime originally envisaged by the 1982 UNCLOS was never accepted or applied in practice provides an ominous precedent with regard to genetic resources.

17. On the other hand, the difficulty of establishing a new international authority, along with the unacceptable equitable consequences of leaving the resources in a state of open access and the sensibility of drawing as much as possible on existing structures and regimes, supports an approach that organically develops a regime out of the CBD or UNCLOS. On this basis, even developing a new regime would be best done within the existing structures provided by the FAO, UNCLOS or the CBD. A pragmatic or organic approach would mean concentrating on controlling current and foreseeable uses and not being overly concerned with future uses, which may not eventuate. For the moment, marine genetic resources are largely being used for research purposes. UNCLOS contains a number of provisions dealing with marine research which cover the use of genetic resources of the seas.[18] The organic approach would therefore build upon this existing regime, developing controls and implementing equitable benefit-sharing within UNCLOS. Equitable sharing is ensured under UNCLOS by its requirement that all research be for the "benefit of mankind". How this might be applied in practice has not yet been elaborated, but it is likely to build upon the technology transfer, information exchange and research and training provisions of UNCLOS, which are similar to the CBD provisions and in any event override the CBD's to the extent that they conflict. These provisions do not, however, properly deal with the results of marine research; neither do they touch upon how the benefits of commercialisation of marine genetic resources should be shared equitably.

18. Regardless of which approach is adopted, there are a number of common and familiar legal issues that would need to be addressed in order to ensure that the regime that does emerge governs the use of marine genetic resources in line with the principles of the CBD. Issues such as retaining access for scientific research, avoiding unnecessary obstacles to commercial exploitation whilst at the same time being able to control unreasonable ones, avoiding the political problems that arose with developing the legal regime governing the use of the mineral resources of the Area, and identifying the beneficiaries all need to be resolved before an effective regime that ensures the equitable sharing of benefits can be implemented.

19. At the moment any consideration of these long-term considerations is hampered by a lack of information and knowledge surrounding the use of genetic resources from the deep sea-bed. Without this basic knowledge, decisions about the type of control that is to be preferred, possible or even practical cannot be made. The rest of this report will briefly review existing information on these activities in order to give some guidance to the SBSTTA as to what further studies might be necessary in order to undertake a study of the relationship between the Convention and UNCLOS on this matter.

3. MARINE GENETIC RESOURCES

20. Marine biological diversity is well-known for its extraordinary diversity at the phylum level, or the basic body plan of organisms. Of the 33 known phyla, 32 of these are found in the sea--15 exclusively so, while another five are comprised of species more than 95% of which are marine (Ray 1988). Estimates of species diversity in the sea are growing, and one recent deep-ocean study put this number as high as 10 million, roughly comparable to that of terrestrial species diversity (Grassle 1992). Evidence is growing for high chemical diversity in the sea as well.

21. Molecular diversity from genetic resources is enormous. No reliable estimates exist for the number of marine genetic resources screened to date. Marine invertebrates, usually sessile and/or soft-bodied, have intrigued marine natural products chemists for decades. Scientists have followed a so-called "bio-rational" approach to screening, arguing that, with such seemingly vulnerable body plans, these invertebrates must have evolved effective chemical defenses as a survival strategy (Scheuer 1990). In fact, marine natural products, toxins in particular, are noteworthy for exhibiting highly complex chemical structures.

22. While the potential molecular diversity among marine organisms is high, the potential molecular diversity among microbes, both terrestrial and marine, is probably higher still, perhaps by orders of magnitude (Paleroni 1994). Many microbes, including dinoflagellates, can be cultured directly from the water column. There is also a growing panel of techniques available for culturing symbiotic or commensalist microbes such as bacteria, cyanobacteria and algae from the tissues of fish and other macroorganisms.

23. Substantial circumstantial evidence now exists that chemically interesting natural products previously thought to be produced by marine invertebrates are actually produced by microflora closely associated with host species. For example, a group associated with researchers at the Scripps Institute of Oceanography recently identified novel antibiotics produced by a marine Streptomyces species (Trischman 1994). The bacterium was originally isolated from a jellyfish.

24. As the technology for culturing marine microbes develops, it is likely that interesting organisms will be discovered in a wide range of marine hosts. Thus, conventional predictions about which marine species will yield economically valuable chemicals are probably no longer valid. If it is true that most if not all marine species provide critical microhabitats for microorganisms producing potentially valuable compounds, this would imply a high biodiversity value for all marine organisms, compounding the value of highly diverse ecosystems such as coral reefs.

3.1 Genetic Resources Found in International Waters

25. The bottom of the deep ocean, dark and hence devoid of photosynthetic activity, has been likened to a desert in terms of species diversity. With no source of energy and carbon other than a thin drizzle of debris from above, the ocean floor as an ecosystem exhibits essentially zero primary production (Norse 1993). Two exceptions to this general rule are known, both of which are benthic ecosystems characterized by energy sources other than light.

26. Hydrothermal vents are mineral-rich regions in the ocean floor defined by the borders between continental plates. Deep sea vents are present at depths of 1800 to 3700 meters and are characterized by the ejection of superheated water that is saturated with minerals by the presence of underlying magma. These minerals include hydrogen sulfide, an energy source. An unusual ecosystem has evolved to exploit this energy source, known as the hydrothermal vent community, dependent upon specialized chemolithotrophic bacteria and bacteria-like organisms of the kingdom Archaea for primary production. Archaea represent an extremely old kingdom of life, probably descendants of the original cells to evolve on Earth (Woese et al 1990). Today they are found only in highly specialized niches, such as hydrothermal vent communities that exist as narrow skeins of life strung out along the ocean floor.

27. The only other known exception to the poverty of benthic biodiversity is the as yet poorly characterized communities of bacteria and archaea existing in deep-ocean sediments associated with petroleum seeps (Rueter *et al* 1994). Research expeditions drilling to 5000 meters have discovered the presence of chemolithotrophic microorganisms, apparently living off of the carbon and energy sources provided by the petroleum. These microbes living within deep-ocean sediments may well prove cosmopolitan, though further research is needed.

28. While both of these benthic ecosystems are good examples of the high ecosystem diversity of the sea, neither is particularly rich in species diversity as compared with coastal ecosystems. Hydrothermal vent communities contain bacterial "mats" engaged in autotrophic primary production, as well as a limited number of heterotrophic species including zooplankton such as crustaceans and siphonophores, grazers such as shrimp, and filter feeders such as mussels and tube worms (Jannasch 1995).

3.2 Coastal Genetic Resources

29. Higher marine species diversity is found in coastal ecosystems, and by far the greatest diversity is in the tropics, particularly southeast Asia and the South Pacific, the Indian Ocean, and the Caribbean Sea, making the waters surrounding tropical developing countries the richest marine source in the world for molecular diversity (Norse 1993). Examples of coastal ecosystems include coral reefs (with the highest species diversity), seagrass beds, oyster reefs, mangroves, salt marshes, and the continental shelf.

30. Preferred coastal marine organisms for genetic resources research and development are usually sessile and/or soft-bodied invertebrates such as coelenterates (corals), tunicates, soft-bodied mollusks such as sea hares and nudibranchs, bryozoans, sponges, and echinoderms (sea cucumbers and starfish). These organisms are likely to employ chemical defenses as a survival strategy due to the highly selective pressure of predation existing in coastal ecosystems. Additionally, recent work on culturing microorganisms isolated from the water column, shallow water marine sediments including oil seeps such as those observed in the deep ocean, or from marine animal hosts has yielded a promising array of new chemicals (Fenical 1993). Although known for their prominence in benthic hydrothermal vent communities, microbes of the kingdom Archaea have been discovered in cold water at shallow depths of 100 to 500 meters (DeLong 1992). These microbes may also yield interesting new chemicals as

techniques are developed for culturing them.

4. THE BIOPROSPECTING OF MARINE GENETIC RESOURCES

31. Genetic resources research and development, also known as "biodiversity prospecting" or "bioprospecting," can be defined as the process of gathering information from the biosphere on the molecular composition of genetic resources for the development of new commercial products. Genetic resources, also known as natural products, comprise biological diversity measured at the smallest scale (larger scales being species and ecosystems). Genetic resources can yield either small organic molecules called secondary metabolites, gene-encoding proteins such as enzymes, or metabolic pathways linking enzymatic reactions in a process known as microbial fermentation. Though why organisms produce secondary metabolites is still debated, that these chemicals can have useful properties is well known. These properties have been exploited by humans for millenia as medicines, pesticides, cosmetics, and more.

32. Marine genetic resources are well-known for yielding chemicals exhibiting unusual or highly complex structural diversity (Scheuer 1994). Coral reefs harbour the greatest marine species diversity and, presumably, the greatest chemical diversity as well (Norse 1993). Additionally, harsh marine environments such as deep-ocean hydrothermal vents and the polar oceans are likely to yield valuable "extremophile" microorganisms adapted to living under extreme physiological conditions of heat, cold, pressure, pH, or salt concentration.

33. The use of naturally occurring genes by biotechnology industries has the potential to offer a number of benefits to developing countries. Biodiversity prospecting for genetic resources offers these countries an opportunity to derive income from the process of natural products research and development, creating economic incentives for biodiversity conservation. This process involves extracting economically valuable information (in the form of chemical structures, gene sequences, information on biological activity such as catalytic properties, or fermentation processes in the case of microbial isolates) from naturally occurring genetic resources. The potential economic worth of these processes to developing countries is considered in more detail in the Secretariat's paper on the economic valuation of biological diversity prepared for this meeting of the SBSTTA (see document UNEP/CBD/SBSTTA/2/15).

34. Genetic resources can also be traded for non-monetary benefits, such as biotechnology useful for economic development. Given that monetary compensation for genetic resources is usually modest, trading for technology may be the more potentially rewarding strategy. Because future uses of genetic resources information cannot be known beforehand, what economists call the "option value" of this information is probably high. Option value relates to the amount one is willing to pay to conserve a resource for possible future use. Trading genetic resources for biotechnology may augment, in particular, research on tropical infectious disease, an area consistently underfunded worldwide despite some 600 million sufferers in developing countries (World Health Organization 1992).

4. BENEFITS FROM THE BIOTECHNOLOGICAL USE OF GENETIC RESOURCES

4.1 The Value of Collaborative Genetic Resources Research and Development

35. Genetic resources research and development can be conveniently divided into a series of value-adding processes, beginning with a biological inventory requiring accurate taxonomic identification. Such information-gathering in itself adds value to genetic resources. The taxonomic inventory of marine organisms differs from that of terrestrial organisms in that collection expeditions are costlier and samples must be frozen immediately, with the exception of marine microorganisms that are often cultured. Following inventory, the chemicals or genes are extracted from the genetic resource, and the extracts are tested to detect the desired biological activity. Often these tests for bioactivity involve measuring the manner in which the sample affects living systems such as animals, or individual cells derived from these living systems, or even biomolecules isolated from these cells.

36. For those biotechnology applications requiring the isolation of a pure chemical compound, or enzyme, or microbial strain, these biological assays or "bioassays" are used to guide the purification process. The genetic resources sample is fractionated into several components, each component is tested again for the presence of the biological activity, and the active component is further fractionated until a pure, biologically active principle is isolated. The further development of a biologically active principle into a commercial product is usually the most expensive and time-consuming process. Commercial development often involves extensive animal and/or human testing of a product, especially if it is intended for human consumption.

37. Because genetic resources research and development entails substantial financial risk to private companies seeking to develop commercial products, many firms seek out research collaborations as a risk-reducing strategy to maximize their ability to discover promising new chemicals or genes. Two strategies, outsourcing and in-licensing, are employed here.

38. Outsourcing entails contracting with private firms to supply certain value-adding services, such as sample collection, extraction, bioassay, etc. A sizeable industry has evolved to supply the outsourcing needs of large companies engaged in genetic resources research and development, involving suppliers such as natural products libraries or brokers and middlemen, and specialized companies offering bioassay or chemical purification services. These companies have evolved a market niche to profit from the process of research and development. Many of the highly publicized biodiversity prospecting contracts negotiated in recent years between private firms and research institutes or NGOs in biodiversity-rich developing countries are examples of outsourcing by large research and development firms. Companies that outsource discrete research and development tasks expect to pay the full cost of the research service being provided.

39. By contrast, in-licensing entails acquiring the rights to valuable chemicals, genes or microbes that have been previously identified independently by another research group. Large research and development companies may in-license promising research material from other firms, or, increasingly, from non-profit research institutes, including universities. This is particularly common in the United States and the European Community in the marine genetic resources field, as the cost of collecting expeditions can be high. In these countries, marine collecting expeditions are usually financed by government research grants, as is subsequent basic research on the molecular properties of

the marine organisms brought back to the laboratory. However, private firms sometimes finance a portion of basic research costs (but not the costs of marine collecting expeditions) in return for rights to promising research material.

40. The results of a study performed in the United States in 1991 by the University of Maryland Biotechnology Institute showed that greater than 95% of the funding for marine biotechnology research at academic institutions came not from the private sector but from government (Zilinskas et al 1995). Nevertheless, 52% of academic respondents indicated that they had some form of collaboration with private industry.

41. By contrast, in Japan there is an unusually high degree of cooperation, including financial cooperation, between companies and government and academia. It is not uncommon for private companies to pool their resources with those of the government in financing collecting expeditions and basic research (Sochaczewski 1995, Zilinskas 1995). Up to 80% of marine biotechnology research in Japan is funded by the private sector.

42. Compensation for value-added research material provided to private research and development companies usually includes a balance of up-front compensation and market share (royalties offered as a percentage of sales on commercialized products). Like up-front compensation, market share increases with increasing value added by the provider. Note that, particularly in the United States and the European Community, it is rare for companies that in-license promising new research material from nonprofit research institutes to pay the full cost of the research that led to the discovery. In essence then, it is the governments of developed countries that subsidize the research and development costs of their own biotechnology industries by providing research grants to nonprofit research institutes, including universities, which in turn can generate promising research material for commercial development by industry.

4.2 Collection and Gathering of Marine Genetic Resources

43. Obviously, access to marine genetic resources, especially from the deep sea-bed poses some significant problems that have limited the use of these resources by biotechnology. Currently, there is little reliable information on the collection of these resources, and what does exist is largely unsubstantiated.

44. Both benthic and sedimentary ecosystems of the deep sea-bed are extremely costly to sample. Taxonomic inventories of hydrothermal vent communities must be conducted by scientists encased within deep diving submersibles, of which there are perhaps five worldwide capable of reaching these ecosystems (Walsh 1990). However, some researchers are beginning to experiment now with the use of remote submersibles (Norman Wainwright, personal communication). Typical deep-ocean scientific expeditions can cost up to $30,000 per day, and usually last from one to two weeks. Many benthic microorganisms recovered in this way can be cultured in the laboratory, often at atmospheric pressure (Jannasch et al 1995). Microbes sampled from especially deep locales are sometimes brought to the surface in pressure cells and maintained at high pressure for laboratory study (Jannasch et al 1996). As mentioned previously, governments of industrialized nations heavily subsidize deep ocean collecting expeditions through grants for basic marine science. For example, the European Community funds benthic genetic resources research and development through its Extremophile Biotechnology Programme.

45. A number of private pharmaceutical and biotechnology companies in Japan cooperate closely with the government in funding international marine collecting expeditions. In the United States and the European Community, private companies are more likely to pay for the isolation and culturing of microorganisms collected previously by expeditions funded by government research grants. In some cases, collaborating companies have signed formal agreements with marine biology research institutes, providing money to cover the costs of culturing marine microbes or of isolating useful enzymes, but not to cover the much higher costs of collecting them. Market-share agreements are also usually part of these contracts (F-D-C Reports 1995). The high financial risk of developing new biotechnology products, especially pharmaceuticals, deters private companies from financing their own deep ocean collecting expeditions.

46. Coastal genetic resources are far more accessible than benthic genetic resources, and are generally collected by scuba diving at depths of less than 100 meters or by dredging at depths of between to 500 and 1000 meters on the continental shelf (D'Auria et al. 1993). Sampling methods are relatively cheap, and, combined with the higher species diversity of coastal ecosystems, the result is that there are far more collectors engaged in coastal biodiversity prospecting. Virtually all of the governments of industrialized countries finance coastal genetic resources collecting, whether through academic research grants or by contracting with oceanographic research institutes to collect for government research programs. As well, it has been economical for private companies to employ divers as collectors, either utilizing in-house marine biology expertise or by outsourcing to contractors.

47. Of all the industrialized countries, Japan leads the world in its investment in marine biotechnology. In 1992, Japan's total marine science and technology budget was $457 million, with approximately 80% of this money coming from Japanese industry (Zilinskas et al 1995). In Japan, government-private sector partnerships fund international marine genetic resources collecting expeditions by Japanese research institutes (Sochaczewski 1995). By comparison, the United States government spent some $45 million on marine biotechnology in 1992 (Zilinskas et al 1995). The U.S. National Cancer Institute employs a private marine research institute to collect marine genetic resources, also from the tropics. The European Community also funds international marine genetic resources research.

48. The list of molecules derived from coastal genetic resources that exhibit interesting pharmaceutical properties, some of which are already in human clinical trials, is too long to chronical here. Examples include anticancer compounds (didemnin, halichondrin B, halomon, dolastatin 10, ecteinascidin 743, and bryostatin 1; see Flam 1994 for a review), antivirals (macrolactins), antibiotics (istamycins A and B, mimosamycin), antifungals (swinholide A), anti-inflammatory agents (manoalide), and hormonal modulators (Sternberg 1994). Coastal genetic resources have yielded industrial enzymes such as proteases and collagenases from several marine Vibrio species (Deane et al. 1987) and are also studied for clues for the development of new agrochemicals (Cardellina 1986). Coastal genetic resources are also the source of all marine biomaterials studied thus far, and the source of extremely potent toxins, some of which may have applications as anticancer drugs or as diagnostic and research tools (tetrodotoxin, palytoxin, ciguatoxin, saxitoxin; Swift and Swift 1993). Coastal marine genetic resources are also of interest to the cosmetics industry, and may one day yield new sunscreens and other skin-care products. For example, an anti-inflammatory agent derived from a tropical coral is under development as a skin-care product by a major

cosmetics firm (Jacob 1996). Finally, even higher marine animals have yielded promising new pharmaceutical leads. One example is squalamine, an antibiotic isolated from cartilage of the dogfish shark Squalus acanthias (Moore et al. 1993).

4.3 Biotechnology Use of Marine Genetic Resources

49. The uses of marine genetic resources in the biotechnology industry are many and varied. Although there has been no comprehensive survey of the extent to which industry uses marine genetic resources to develop new products, surveys of other aspects of this use give some indication as to the market size and potential. Further details about the overall contribution of naturally occurring genetic resources to these industries are provided in the Secretariat's paper on the economic valuation of biological diversity prepared for this meeting of the SBSTTA (see document UNEP/CBD/SBSTTA/ 2/15).

1. Industrial Enzymes:

50. Besides investigating small chemical compounds, biotechnology companies also study complex proteins, known as enzymes, which catalyse chemical reactions. The goal of industrial enzyme research and development is to identify enzymes with commercially-valuable properties. Worldwide sales of industrial enzymes exceeds $1 billion (Kelly 1996).

51. Industrial enzymes are used by a plethora of industries as cost-effective and environmentally sensitive substitutes for chemical processing. Examples include those used in detergent formulations, in food processing, for the production of pharmaceuticals, for processing textiles, wood pulp and paper, and for the production of fine and specialty chemicals. For example, proteases, which are enzymes that degrade proteins, are particularly useful in commercial laundry detergents for removing stains containing protein (Deane 1987). The textile industry uses enzymes called cellulases to break down cotton fibers for such processes as "stonewashing", surface polishing, and softening.

52. Industrial enzymes must be stable to extremes of temperature, pH, and salt concentration. For this reason, the isolation and characterization of enzymes from a special class of microorganisms known as "extremophiles" may yield useful new products for this industry. The deep sea-bed provides many example of these extremophiles and consequently may be of interest to companies involved in developing enzymes for this sector.

2. Biotechnology Enzymes:

53. A related application of industrial enzymes is their use as research tools in biotechnology. The goal of biotechnology enzymes research and development is to identify enzymes that are capable of carrying out very specific molecular tasks, usually related to the modification of DNA or RNA, for the creation of genetically modified organisms or for diagnostic procedures. These enzymes go by a variety of names, including restriction endonucleases, RNA and DNA polymerases, alkaline phosphatases, kinases, reverse transcriptases, ligases, and so on. The market for these enzymes has been estimated to be at least $600 million (New York Times 1993).

54. The isolation of enzymes from "extremophiles", bacteria or bacteria-like microbes from the kingdom Archaea that are adapted to living in markedly hot, cold, acidic, basic, pressurized, saline or mineral-rich environments, is of particular interest to biotechnology companies seeking to market new research tools. For example, a ubiquitous and powerful biotechnology process known as the "polymerase chain reaction" (PCR) depends upon an unusually thermostable enzyme known as Taq DNA polymerase to replicate DNA in a test tube. The enzyme must be able to withstand the alternating cycles of heating and cooling inherent to the PCR process.

55. Taq DNA polymerase is derived from a species of thermophilic bacteria, Thermus aquaticus, originally isolated from a hot spring in the western United States. In 1991 Hoffman-Laroche, a Swiss pharmaceutical company, paid more than $300 million to Cetus Corporation, an innovative biotechnology company that invented PCR and the novel use for Taq DNA polymerase, for exclusive world rights to the process. Sales of Taq DNA polymerase in Europe alone reached $26 million in 1991 (Roberts 1992). Worldwide sales of PCR enzymes are in the range of $50-100 million, and the market for biotechnology enzymes derived from extremophiles is forecast to grow at 15-20% per year (Frank Robb, personal communication, and New England Biolabs, Inc., Beverly, Massachusetts, USA).

56. Harsh marine environments, such as deep-ocean hydrothermal vents, polar oceans, and extremely saline bodies of water, have also yielded valuable extremophile microorganisms for this and other biotechnology processes. The identification of new "hyperthermophiles" from deep-ocean hydrothermal vents has generated a modicum of press coverage recently (see for example New York Times 1993, Financial Times 1995, Nikkei Weekly 1995). Due to the high water pressures at the depth at which hydrothermal vents are found, water temperatures can exceed that of the boiling point at sea level. This environment has given rise to some of the most unusual microorganisms on the planet, able to grow at temperatures exceeding 100 degrees Celsius. Enzymes isolated from hyperthermophiles show a corresponding tolerance for high temperatures (Jannasch 1995).

57. There is also a need for extremely heat-sensitive enzymes as biotechnology research tools. Running

biotechnology reactions with heat-sensitive enzymes allows for better control over the reaction process, since reactions can be terminated by heating to destroy the enzyme. Since heating a reaction mixture can also affect the products of the reaction, use of heat-sensitive enzymes allows scientists to stop the reactions at lower temperatures. Heat-sensitive enzymes are derived from cryophiles, organisms living in cold environments. At least one heat-sensitive product, Shrimp Alkaline Phosphatase, is derived from a species of Antarctic shrimp found in extremely cold polar waters (Olsen 1991).

58. Biodiversity prospecting for biotechnology enzymes begins not with proteins, but with cellular DNA. DNA is extracted from the organisms of interest, usually cultured microbes (sometimes it is merely isolated as "environmental DNA" from seawater samples containing recalcitrant organisms not easily cultured), and amplified by PCR to make more copies of the DNA. The purified DNA is next transcribed to RNA and expressed as protein. The proteins are then bioassayed for the presence of the desired activity, for example the ability to polymerize DNA, or to cleave it in a site-specific manner.

59. Along with the industrial enzymes described in the previous section, scientists are studying the structure/function relationships that govern the catalytic properties of enzymes, hoping to understand and to one day actually design particular properties into these enzymes (Borges et al. 1996). By isolating and identifying enzymes derived from organisms living in a variety of environments, scientists are also trying to develop panels of enzymes for industrial applications, each with a different temperature/activity profile.

3. Industrial Microbes:

60. The goal of industrial microbial research and development is to identify microorganisms possessing valuable metabolic processes that can be exploited for industrial use, usually involving biological degradation. Extremophilic microbes are also useful to this industry, as some have been found living on unusual carbon and energy sources, including petroleum. The industrial uses of microbes include industrial wastewater treatment, municipal wastewater treatment, bioremediation of contaminated soils, bioleaching of mineral-rich ores, food processing, and institutional services such as janitorial services. Worldwide sales of industrial microbes have been estimated at approximately $680 million (Perez 1995).

61. Environmental biotechnology requires microbes capable of degrading or sequestering synthetic compounds or heavy metals for the bioremediation of contaminated soils, or petroleum for the bioremediation of oil spills (Leahy and Colwell 1990). A related application is the bioleaching of copper, uranium and gold-bearing ores, in which microbes are used to solubilize metal ions present in mined rock (Rawlings and Silver 1995).

4. Pharmaceuticals:

62. The goal of pharmaceutical research and development is to identify small chemical compounds that are non-toxic to the patient yet effective against disease. Of all the markets for genetic resources-derived commercial products, the world pharmaceuticals market is the largest, with 1994 sales of $256.2 billion (Scrip 1996). Some have estimated that as much as 40% of prescription drugs are derived from natural sources, though it is clear that

the majority of these come from microbial sources, rather than botanical or marine organisms. For example, terrestrial actinomycetes, a class of gram-positive bacteria, have yielded the majority of antibiotics discovered in the last half-century (Okami 1988). Fermentation broths, prepared by culturing the microbes under diverse conditions to induce them to produce unusual secondary metabolites, are the key starting material for antibiotic drug discovery. There is growing evidence that substantial actinomycetes diversity exists in marine environments as well (Takizawa 1993). Another area of commercial use of marine genetic resources is the application of well-known toxins, derived from marine genetic resources, to potential pharmaceutical applications (Zilinskas, et al 1995).

5. Biomaterials:

63. Other markets for marine natural products include marine industrial or biotechnology products based on such marine polymers such as chitin, carrageenan, or other polysaccharides (Harvey 1988, Abu 1992, Singleton 1988). Marine natural products may also offer clues to the "bioengineering" of surfaces to reduce or prevent biofouling of ship hulls and other submerged structures by sessile marine organisms (Curtin 1985).

5. CONCLUSION

64. For the moment it appears that the commercial potential of coastal genetic resources is much greater than the commercial potential of benthic and polar genetic resources. In addition, benthic and polar genetic resources are far costlier to sample, further increasing the risk involved in their commercial development. Without heavy government subsidy, it is unlikely that there would be any private-sector development of these genetic resources. By contrast, the financing of coastal genetic resources research and development is within the acceptable risk limits for private-sector investment.

65. Research on extreme ecosystems has yielded valuable new extremophiles capable of living at a variety of temperatures, pressures, and on a number of carbon and energy sources. The extent to which new, commercially useful extremophiles may come from the deep sea-bed is not known. Consequently, the economic value of this market is entirely speculative and, to date, unrealised.

66. Although public scrutiny has highlighted the contribution of benthic and polar genetic resources to this field, extremophiles are also derived from both coastal and terrestrial ecosystems. Developing countries in particular are blessed with a number of unusual and extreme habitats, including regions of high vulcanism characterized by high temperature, extremes of pH and salinity, anaerobic conditions, or saturated mineral solutions. Other unusual habitats include subsurface petroleum reserves, which may contain hydrocarbon-metabolizing microbes, or cold alpine environments likely to harbour cryophilic organisms. Extremophile research is still in its infancy. Scientists from developing countries are in a position to learn a great deal from their counterparts in developed countries. Indeed, the equitable sharing of this benefit may be the only profit that can realistically be expected from the genetic resources of the deep sea-bed for many years to come.

67. What is clear from the survey is that the collection, use and control of the genetic resources of the deep sea-

bed is quite different to that of genetic resources found within the national jurisdictions of states. The lessons of other regimes, such as the regime governing Antarctica, point to the benefits of considering these types of issues before strong commercial interests are developed and of considering them on the basis of best-available knowledge. On the other hand, developing complex international regimes for governing the use of potentially "valuable" resources has rarely proven to be a successful strategy for their equitable use or a valuable use of international resources. Furthermore, the knowledge base on which to make informed and appropriate decisions about how this area might be controlled is almost non-existent. Such a situation points to the clear need for more research from all relevant parties. The SBSTTA, as the only scientific, technical and technological authority under the Convention to provide advice to the Conference of the Parties, obviously has an important role in developing the necessary understanding of the area to make the appropriate decisions.

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Notes

1. Article 82.

2. Article 61, which, for example, imposes an obligation to "ensure through proper conservation and management measures that the maintenance of the living resources in the EEZ is not endangered by over exploitation". States must also cooperate with other states in the conservation of management of shared stocks (article 61(2)).

3. Article 62.

4. Defined in Article 77(4) as living organisms that, "at the harvestable stage, either are immobile on or under the sea-bed or are unable to move except in constant physical contact with the sea-bed or sub-soil".

5. Preambular Paragraph 6 of UNCLOS.

6. Article 87(1)(e) and (f).

7. Article 116.

8. Article 117.

9. Article 118.

10. Article 1(1).

11. Articles 133(a) and 136.

12. Article 135.

13. Article 137(2).

14. Article 137(1).

15. Annex III, Article I.

16. An alternative interpretation which results in the same conclusion is to consider them as coming within the rubric of "living resources" which is defined in wide enough terms to include genetic resources. As such, they would be outside the special conditions which apply to mineral resources and freely accessible.

17. Article 87(1)(e).

18. See Article 143(1) (Promote international cooperation in marine scientific research in the Area) and Article 242 (Promote international cooperation in marine scientific research).