Marine bioprospecting

key challenges and the situation in South Africa

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The African Centre for Biosafety (ACB) is a non-profit organisation, based in Johannesburg, South Africa. It provides authoritative, credible, relevant and current information, research and policy analysis on genetic engineering, biosafety, biopiracy, agrofuels and the Green Revolution push in Africa.

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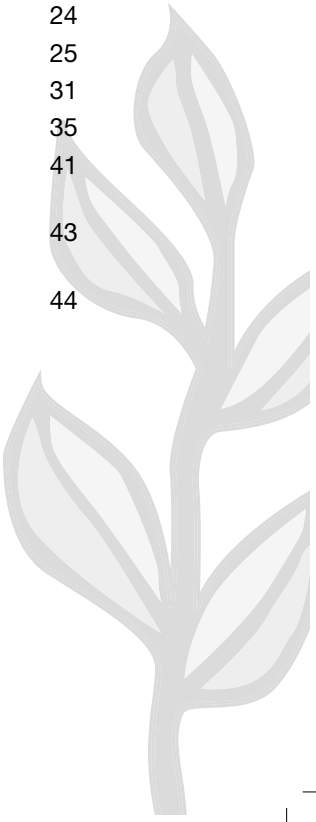

Acronyms

ABS	Access and Benefit Sharing
ACB	African Centre for Biosafety
BSA	Benefit Sharing Agreement
CBD	Convention on Biological Diversity
Consultative Process	United Nations Open-Ended Informal Consultative Process on Oceans and the Law of the Sea
CSIR	Council for Scientific and Industrial Research
DEAT	Department of Environmental Affairs and Tourism
ECA	Environmental Conservation Act
EEZ	Exclusive Economic Zone
IP	Intellectual Property
IPR	Intellectual Property Rights
LoC	Letter of Collection
MCM	Marine and Coastal Management (one of four branches of DEAT)
MLRA	Marine Living Resources Act
MoU	Memorandum of Understanding
MAT	Mutually Agreed Terms
MTA	Material Transfer Agreement
NCI	National Cancer Institute (USA)
NEMA	National Environmental Management Act
NEMBA	National Environmental Management Biodiversity Act
NIH	National Institutes of Health (USA)
NRF	National Research Foundation
R & D	Research and Development
PIC	Prior Informed Consent
SA	South Africa
SBSTTA	Subsidiary Body on Scientific, Technical and Technological Advice
SCRIPPS	SCRIPPS Institution of Oceanography, Graduate School of the University of California, San Diego (USA)
TRIPS	Trade Related Aspects of Intellectual Property Rights
UNCLOS	United Nations Convention on the Law of the Sea
UNU	United Nations University

man, in his typical wasteful
way, has managed to
consume his natural resources
on land at a rate that is already
making him turn to the sea
as his last great relatively
untapped resource on earth.

Stewart, HB. 1966. In Deep Challenge. 14.

Structure of booklet

This booklet is comprised of three main sections. In section 1, we provide the context in which marine bioprospecting takes place and introduce the following: the concept of marine bioprospecting, the unique genetic wealth of the oceans, the imperatives underpinning commercial interest in marine genetic resources and information on product development of marine resources.

In Section 2, we discuss some of the key problems associated with marine bioprospecting, including adverse impacts on marine biodiversity, intellectual property rights and the absence of regulatory systems. In particular, this section provides insight into the problems associated with public-private partnerships, a phenomenon that is fast becoming a characteristic of marine bioprospecting.

Section 3 introduces the current legal situation concerning marine bioprospecting internationally as well as in South Africa, and discusses the lacunae in these legal systems. We also present two case studies of marine bioprospecting in South Africa to illustrate the relationships inherent in public private partnerships, where heavy reliance is placed on bioprospectors to ensure fairness in contractual agreements and compliance with available laws.

Some terms

Abyssal slopes and plains:	Relatively flat area of ocean floor adjacent to the continents, and depths >2000m.
Hydrothermal vents:	Fissures from where hot water emerges, often located near volcanically active areas
Seamounts:	Undersea mountains that do not break the surface of the water

Introduction

The African Centre for Biosafety (ACB) is a newcomer to the discourse on bioprospecting and biopiracy, and in particular, the cutting edge and emerging arena of marine bioprospecting. Nevertheless, we present the research in this booklet in the hope that it will contribute to debate, public awareness and improved policy, legal and administrative reform in South Africa.

As an activist organisation, we are particularly interested in interrogating the impact of marine bioprospecting on the environment and the problems associated with public-private partnerships. In this regard, we advocate for adequate international and national regulation in order to protect the rich, unique and astonishingly fragile marine biodiversity.

Marine bioprospecting is a relatively new field, with some of the earliest exploration only occurring in the 1940's.[1] World wide, most marine bioprospecting takes place in sensitive areas such as coral reefs, hydrothermal vents, abyssal planes and seamounts – mostly areas described as the common heritage of mankind. These richly diverse marine ecosystems are inhabited by organisms possessing unique chemical compounds, and thus open new pathways for marine research and development. This natural wealth is up for grabs in the commercialisation of pharmaceuticals, cosmetics, nutritional supplements, molecular probes, enzymes, and agrochemicals. Indeed, marine biological resources have wide application, ranging from their use in HIV medicines, to anti-aging skincare products and nutritional additives.

The private sector is heavily involved in marine bioprospecting, with the pharmaceutical sector reaping considerable financial benefit. In 2006, the market value in the pharmaceutical sector was estimated to be $643 billion.[2] Pharmaceutical giants such as Johnson & Johnson, GlaxoSmithKline and Bristol-Myers Squibb, provide significant funds for marine bioprospecting. A number of health agencies such as the United States National Institutes of Health and the National Cancer Institute are also heavily involved in the funding of marine bioprospecting.

Marine bioprospecting is typically associated with public-private partnerships, due to the astronomical expenses, state of the art technology and specialised expertise associated with marine exploration. It is estimated that marine exploration costs at least $30 000 per day and $1 million for 30 days,[3] expenditure well beyond the means of public institutions. Such partnerships are protected from public

oversight by the cloak of private contractual and confidentiality agreements, and are thus largely unregulated. Whilst generally speaking, public institutions are geared towards utilising public funds for the purposes of research and development for public benefit, private institutions are principally interested in making a profit. This inherent tension has given rise to some disturbing trends including non-disclosure of research findings; monopolisation of intellectual property rights; non-reciprocal sharing of benefits from drug development; unequal technological transfer; and lack of transparency about both the partnerships and the projects themselves.[4,5] Public-private partnerships are even more common between developed and developing nations, since the former provides the funds and expertise, whilst the latter opens its doors to its rich genetic marine biodiversity.

South Africa has 2500km of coastline with three distinct marine biogeographic areas, namely the temperate west coast with the cold Benguela current, the warm temperate south east coast and the subtropical Agulhas east coast current.[6] This makes South Africa a prime location for marine bioprospecting as its oceans are teeming with marine biodiversity. However, South Africa does not have a long history in the field of marine bioprospecting, due to a range of factors, including lack of technology, expertise and funding available to their counterparts in developed countries. Research institutions, such as Rhodes University have therefore entered into marine bioprospecting collaboration with leading marine bioprospectors such as the SCRIPPS Institution of Oceanography (USA) and the National Cancer Institute (USA).

The two case studies in South Africa reveal that as with most developing nations, South Africa has barely caught up with the challenges associated with bioprospecting. The focus has been almost exclusively on terrestrial bioprospecting, and as a result marine bioprospecting has been a free-for-all as there are almost no legislative frameworks in place to deal specifically with marine bioprospecting.

The regulation of marine bioprospecting is complex, involving a range of issues. These include grappling with the challenges of ownership of common property, intellectual property rights and benefit sharing; conservation and protection of marine biodiversity; technology transfer and capacity building; jurisdictional issues in monitoring and enforcement; as well as the difficulties inherent in regulating marine over-exploitation and activities that occur beyond national jurisdictions. These issues have been discussed in various international meetings including those held under the auspices of the Convention on Biological Diversity, the United Nations Convention on the Law of the Sea, the International Seabed Authority and the United Nations General Assembly on Oceans and Law of the Sea.[7]

In this booklet we focus on the recent interest in marine biodiversity for commercialisation and the grappling by the international community in coming to terms with genetic resources beyond areas of national jurisdiction. Further, we provide examples from South Africa to illustrate the lack of streamlined regulatory approaches to marine bioprospecting including the lack of monitoring and enforcement capacity.

section 1

Background

Marine bioprospecting

Marine bioprospecting, also known as marine natural products research, is concerned with the exploration and exploitation of the rich biological and chemical diversity found in marine organisms which inhabit the oceans.

Marine bioprospecting is a relatively new endeavour, having its origins in the late 1940's,[8] when Werner Bergman 'discovered' arabinoside sugar in marine sponges, a substance which does not occur on land.[9,10] This discovery led directly to the development of several anti-viral (ara-A) and anti-cancer (ara-C) compounds.[11] Marine bioprospecting gained momentum in earnest during the 1970's and 1980's due to improved deep sea collection methods and analyses.[12,13] Until then, marine bioprospecting was limited to places of high biodiversity and easy accessibility, such as the tropical seas and coral reefs.[14]

Blue gold: the oceans' genetic wealth

Until recently, the oceans and seas were misjudged as being poor habitats for flourishing biodiversity, due to the voluminous salt content and seemingly infertile environment.[15, 16] However, advances in technology have made marine exploration possible and it has become apparent that the oceans are thriving with the greatest diversity of life forms on earth.

Life began in the oceans, and therefore it is not surprising that the 2,7 billion years head start on evolutionary process has resulted in the oceans having a more unique, and diverse life forms than on land.[17] Of all of the earth's life forms, 36 out of 38 animal phyla are represented in the marine environment.[18] Marine plants, such as seaweed, phytoplankton, macro-organisms, are also incredibly diverse, with algae alone having over 100 000 species.[19] Novel and previously undiscovered marine biodiversity is concentrated in coral and temperate reefs, seamounts, hydrothermal vents, abyssal slopes and plains.[20] Over 67% of marine

based products have come from the Caribbean, the Indian and West Pacific Oceans, the Mediterranean and the oceans of Australia, Japan and China.[21]

Some areas of the ocean contain more biological diversity than any tropical rain forest, and therefore have more potential for natural product discovery.[22] This marine genetic wealth has resulted in the ocean being aptly described as 'blue gold'.[23]

To date, approximately 300,000 marine species have been documented,[24] constituting only a minute fraction of the oceans species. It is anticipated that more than 2 million species will be discovered in the future,[25] as a result of the scientific community's appetite for researching undocumented marine biodiversity and the private sector's relentless search for novel sources for the development of new products.

Commercial interest

Marine organisms have evolved to possess complex chemical compounds, which are different to their terrestrial counterparts. The reason for this is twofold. First, marine life has evolved over a long period of time in severe and hostile marine environmental conditions. These include freezing temperatures, high pressures, intense heat from hydrothermal vents, low energy and perpetual darkness due to lack of sunlight.[26,27] Second, marine life forms have unique and highly developed chemical defence systems to ensure their survival. Unlike terrestrial life forms, many marine organisms have soft exteriors, making them vulnerable to attack. They may also lead a fairly slow or inactive lifestyle, making it difficult for them to escape speedily from danger or to compete for space.[28, 29, 30] Examples of creatures with highly developed chemical defence systems range from bryozoans, sponges, ascidians, sea hares, molluscs, marine plants, algae, soft corals to certain shrimps.[31] In order to survive attacks from predators and successfully compete for territory, marine organisms use chemical defence mechanisms to defend territory and incapacitate or eliminate predators and competitors. They do so by emitting highly toxic chemicals, which are highly active and concentrated in order to withstand dilution by the surrounding water.[32]

An example of a toxic defensive mechanism is the cone snail *Conus magus* from the Pacific Ocean (see Table 1), which shoots venom to paralyse the fish they feed on. This paralysing poison has been used to manufacture a painkiller more potent than morphine. It is marketed under the brand name, Prialt®.[33] Other organisms with unique characteristics include thermofiles, which have the ability

to withstand extreme temperatures; and barophiles, which can withstand great pressure.

Marine organisms that possess these complex chemical characteristics have attracted the attention of a variety of industry sectors, including the pharmaceutical, cosmetics, nutraceutical, agrochemical and biotechnology sectors.[34]

The pharmaceutical industry is especially interested in the natural defence mechanism of marine organisms. There are over 30 000 diseases described in the world, of which, less than a third of their symptoms are treatable, and even fewer curable.[35] Recent trends indicating that humans and animals are developing resistance to existing antibiotics have spurred the pharmaceutical industry on to search for bacterial resistant properties in marine organisms.[36] This makes the chemical defence systems of marine organisms highly sought after because of their anti-viral, anti-bacterial, anti-biotic, anti-cancer, anti-tumour and anti-inflammatory properties,[37] and as pain inhibitors and anaesthetics.[38] It is estimated that the success in finding novel compounds and the subsequent novel drug development from marine biological resources is 1000 times greater than terrestrial biological resources.[39] Furthermore, the margin of profit and the market value in the pharmaceutical sector makes marine bioprospecting especially attractive. As David Newman of the National Cancer Institute (NCI) aptly describes, "…with drugs, when you hit it, you hit it big."[40] Of all the industries producing marine based products, the pharmaceutical industry is likely to reap the most profit, followed by the cosmetics industry. [41]

Marine bioprospecting: profits or public interest?

Probing the oceans' depths to search and collect samples from its harshest environments demands the employment of cutting edge technology, expertise, and huge capital investment. For instance, the Harbor Branch Oceanographic Institution charges $12 000 per day for marine bioprospecting and an additional $4 500 per day for the diving itself.[42] The collection of one tonne of the sponge *Lyssodendorix* sp. is needed to produce a mere 300mg of pure halichondrin B costs around US $500 000.[43] Due to the high costs involved (an estimate ranging between $200 million to $2 billion), [44] the long term nature of the endeavour (15-20 years) and risks associated with bringing a product to the market successfully, it is assumed that marine bioprospecting is altruistic – for scientific advancement and benefitting humankind.

This view is most vociferously advocated by the United States government.

At the international Conference on Oceans and Law of the Sea held at the UN General Assembly in June 2007, the Head of the U.S Delegation, Ms Constance C. Arvis said the following:

"[T]he greatest benefits to humanity from marine genetic resources will not be the profits that may arise from products that are developed. Rather, the greatest benefits will come from expanding our knowledge and increasing the number and nature of products that enhance our lives, health and livelihoods... we remain unconvinced of the need or desirability for a new international regime to protect marine genetic resources in areas beyond national jurisdiction… [such] regime is likely to inhibit research; research that not only improves our fundamental understanding of the world's oceans but also produces valuable, even in some cases critical, products for all of mankind." [45]

Nevertheless, marine bioprospecting is an extremely lucrative business. In 2006, the market value of marine genetic resources in the pharmaceutical sector was estimated to be $643 billion, and worth $231 billion in 2005 to the cosmetic industry. The enzyme market is estimated at least $50 billion per annum.[46] The combined revenue of the four largest US companies (Pfizer Inc., Johnson & Johnson, Merck & Co., Abbott Laboratories) in 2003 amounted to a staggering $129 billion.

Numerous commercial products based on marine organisms have been brought to the market, including the following:

Ara-A (Vidarabine®, Vidarbin Thilo®) and anti cancer drug Ara-C (Cytosar-U®, Cytarabine, Alexan®, Udicil®) sold by Pharmacia & Upjohn (now Pfizer), both with estimated sales figures of $93 million in 2007 each[47]

Acyclovir (Zovirax®) prescription drug for herpes with estimated sales figures of $237 million in 2006[48]; and AZT (Retrovir®) for treating HIV sold by Glaxo-SmithKline[49], with estimated sales figures of $23 million in 2005.[50]

Vent™, VentR®DNA, DeepVentR®DNA by New England Biolabs[51]

Pyrolase™, an enzyme used for industrial processing, by Diversa (now Verenium)[52]

Skincare protection Venuceane™ by Sederma[53,]

http://www.esteelauder.com/templates/products/product_popup.tmpl?PRODUCT_KEY=CATEGORY5862!PROD9423 (accessed 23 September 2008).

Estee Lauder's Resilience™ Face lift Cream, described as "University of California's top ten most valuable royalty generating inventions" with a market value of $3-4 million[54];

Formulaid®, a nutritional additive for infant formula produced by Martek Biosciences[55]

Prialt®, a potent drug for severe pain management which is manufactured by Elan Corporation.[56]

Private capital has successfully managed to commercialise marine resources and is generating massive profits from the marine bioprospecting ventures. Aside from marine based products already on the market, several products are in various stages of clinical and advanced clinical trials (see table 1).

Table 1: List of Important Marine Organisms in Clinical Trials

Chemical Compound	Source	Origin	Activity	Development Status	Company / Research Institution
Anabaseine (Hoplonemertine toxin)	Various nemertine worms esp. *Paranemertes peregrina* (NEMERTEA)	Friday Harbour, Washington	Anti-Alzheimer	Phase I clinical trials	Taiho
Aplidine (Aplidin®) (Dehydrodidemnin B)	Tunicate *Aplidium albicans* (CHORDATA)	Mediterranean	Anti-cancer	Phase II clinical trials	PharmaMar
Bryostatin 1	Bryozoan *Bugula neritina* (ECTOPROCTA)	Gulf of California, Gulf of Mexico	Anti-cancer	Phase II clinical trials	Arizona State University, GPC Biotech (Licensee), Stanford University (Licensee), National Cancer Institute, Bristol-Mayers Squibb, CalBioMarine
Contignasterol (IZP-94005, IPL576,092)	Sponge *Petrosia contignata* (PORIFERA)	Papua New Guinea	Anti-asthma	Various phases of clinical trials	Aventis Pharma, Inflazyme Pharmaceuticals
Curacin A	*Lyngbya majuscula* (CYANOPHYTA)	Caribbean, Curaçao	Anti-cancer	Preclinical	Oregon State University
Debromo-hymenialdisine (DBH)	Palauan sponge *Stylotella aurantium* (PORIFERA)	Palau	Anti-Alzheimer; treatment against osteoarthritis	Phase I clinical trials	Genzyme Tissue Repair (Licensee)
Diazonamide A	Tunicate *Diazona angulata* (CHORDATA)	Phillippines	Tubulin interactive	Preclinical	Scripps Institution of Oceanography
Dictyostatin	Unidentified Jamaican sponge of Family Corallistidae (PORIFERA)	Jamaica	Tubulin interactive	Preclinical	Arizona State University, Harbor Branch Oceanographic Institution, Cambridge
Discodermolide	Deep-sea sponge *Discodermia dissoluta* (PORIFERA)	Bahamas	Tubulin interactive	Phase I clinical trials	Harbor Branch Division of Biomedical Marine Research, Novartis Pharma AG (Licensee)
Dolastatins	*Dollabella auricularia* (MOLLUSCA)	Coromos Islands, Indian Ocean	Tubulin interactive	Phase I & II clinical trials	National Cancer Institute, Knoll, and other groups

Chemical Compound	Source	Origin	Activity	Development Status	Company / Research Institution
Ecteinascidin 743 (Yondelis®)	Tunicate *Ecteinascidia turbinata* (CHORDATA)	Caribbean	Anti-cancer	Phase II clinical trials	PharmaMar, Johnsons subsidiary Ortho Biotech, National Cancer Institute
Eleutherobin	Octocorals *Eleutherobia* sp., *Erythropodium caribaeorum* (CNIDARIA)	Australia, Caribbean	Tubulin interactive	Preclinical	University of British Columbia
Halichondrins	Sponge *Halichondria okadai* (PORIFERA),	Japan, New Zealand	Tubulin interactive	Preclinical	National Cancer Institute, Eisai Research Institution, Kishi Group and others
Hemiasterlins (H-286)	Sponges of genus *Auletta, Siphonochalin* (PORIFERA)	South Africa, Papua New Guinea	Cytotoxic and tubulin interactive	Phase 1 clinical trials	University of British Columbia,
Kahalaide F	Sea slug mollusc *Elysia rufescens* (MOLLUSCA)	Hawaii	Cytotoxin; gene inhibitor	Phase II clinical trials	PharmaMar
KRN7000	Sponge *Agelas mauritianus*. (PORIFERA)	Okinawa, Japan	Anti-tumor, immunosti-mulatory	Phase I clinical trials	Kirin Brewery, University of the Ryukyus
Lasonolides	Deep-sea sponge *Forcepia* sp. (PORIFERA)	Gulf of Mexico	Anti-cancer	Preclinical	Harbor Branch Division of Biomedical Marine Research
Latrunculins	Sponge *Latrunculia magnifica* (PORIFERA), sponge *Negombata magnifica*	Red Sea	Actin interactive	Preclinical	National Cancer Institute and other groups
Laulimalide (and Synthetic Analogs)	Sponge *Cacospongia mycofijiensis*; also *Hyatella* sp., *Fasciospongia* sp., and *Dactylospongia* sp. (PORIFERA)	Pacific Ocean	Tubulin interactive	Preclinical	Various groups
Manzamine A	Sponge *Haliclona* sp. (PORIFERA)	Okinawa, Japan; Indonesia	Activity against malaria, tuberculosis, HIV and others	Preclinical	Various groups

Chemical Compound	Source	Origin	Activity	Development Status	Company / Research Institution
Neovastat® (AE-941)	Shark	Various temperate oceans	Anti-tumor; anti-angiogenic	Preclinical & Phase III	National Cancer Institute, AEterna Zentaris, Atrium Biotechologies, and other groups
Peloruside A	Sponge *Mycale hentscheli* (PORIFERA)	New Zealand	Tubulin interactive agent	Preclinical	University of Victoria, University of Texas Southwestern Medical Center, Reata Pharmaceuticals Inc. (Licensee)
Pseudopterosins	Soft coral / sea whip *Pseudopterogorgia elisabethae* (CNIDARIA)	Caribbean	Anti-inflammatory and analgesic agent	in use as a commercial skin cream additive (Estee Lauder's Resilience cream); in preclinical development for medical applications	Estèe Lauder, and various other groups
Salicylihalamides	Sponge *Haliclona* sp. (PORIFERA)	Western Australia	Vo-ATPase inhibitor	Preclinical	National Cancer Institute, University of Western Australia, and others
Sarcodictyins	Corals *Sarcodictyon roseum*, *Eleutherobia aurea*, and others (CNIDARIA)	Mediterranean	Tubulin interactive	Preclinical	Pharmacia-Upjohn
Spisulosine	Arctic surf clam *Spisula* (=*Mactromeris*) *polynyma*	Canada	Anti-tumor	Phase I clinical trials	PharmaMar
Squalamine	dogfish, *Squalus acanthus*,	New England	Anti-tumor; anti-angiogenic	Phase I/Phase II clinical trials; also sold as a non FDA-approved dietary supplement	NIH, University of Pennsylvania, Genaera Corporation (Licensee)
Thiocoraline	*Micromonospora marina* (Actinomycete bacteria)	Mozambique	DNA polymerase inhibition	Preclinical	PharmaMar

Chemical Compound	**Source**	**Origin**	**Activity**	**Development Status**	**Company / Research Institution**
Topsentins	Sponges *Topsentia genitrix*, *Hexadella* sp. and *Spongosorites ruetzleri* (PORIFERA)	Caribbean and other areas	Anti-inflammatory	Preclinical	University of California, Harbor Branch Oceanographic Institution
Vitilevuamide	Ascidians *Didemnum cuculiferum*, *Polysyncraton lithostrotum* (CHORDATA)	Fiji	Tubulin interactive	Preclinical	University of Utah, and other groups
Ziconotide (Prialt®)	Cone snails *Conus geographicus*, *Conus magus* (MOLLUSCA)	Philippines, Great Barrier Reef	Analgesic	Drug Developed FDA-approved Dec. 2004 for the management of severe pain in the US and 2005 in EU (Prialt®)	University of Utah, Elan Corporation, Neurex, Eisai

Adapted from: NCI Questions and Answers About NCI's Natural Products Branch at http://www.cancer.gov/cancertopics/factsheet/Therapy/natural-products

Marine Biotech **Drugs from the sea index** at http://www.marinebiotech.org/dfsindex.html

section 2

Problems with Marine Bioprospecting

Private-public partnerships

"There is an undeniable reality that commercial activity is qualitatively different than scientific and educational activity of a similar nature, due to the very different forces and motivations that drive them."[57] United States District Judge Royce C. Lamberth

High costs of Marine Bioprospecting

The cutting edge nature of the technology used in marine bioprospecting and the vast capital investment it demands, puts marine bioprospecting out of reach of most public institutions, particularly those from developing countries. For instance, a public institution will struggle to cover the costs of ocean expeditions, estimated to be around $30 000 per day and $1 million for 30 days.[58] Marine bioprospecting is a science which is restricted to a privileged few wealthy nations and institutions.[59] However, in order to overcome this impediment, public-private partnerships are on the increase. This allows well-off nations and public institutions to participate in marine bioprospecting and for the corporate sector to lay their hands on the marine wealth of developing countries. Developing countries are keen to enter into partnership arrangements which allow them opportunities to reap some benefits from marine bioprospecting.

Sharing the costs: need for public-private partnerships

These partnerships are typically brokered between cancer or national health research institutions, universities and corporations actively engaged in marine bioprospecting. The United States National Cancer Institute (NCI) was the first to conduct large scale sample collections of invertebrates, and is the leader in marine bioprospecting.[60] The NCI heads the National Cooperative Drug Discovery

Program, and plays a lead role in various public-private marine bioprospecting programmes.[61] Their specific interest in marine resources as part of their arsenal to fight against cancer and HIV, makes the NCI one of the world's most active marine bioprospectors. **Other leading and active players in the field include PharmaMar, Johnson and Johnson, Bristol-Meyer Squibb, Novartis, Diversa (now Verenium), SCRIPPS Institution of Oceanography and Harbor Branch Oceanographic Institution.** It is not unusual for leading experts from public institutions to also be the founders of private institutions. For example, an expert on extremophilic archaebacteria, Karl Stetter, is a co-founder of Diversa; and Craig Venter, a former member of the National Institute of Health, is a founder of Celera Genomics.[62]

Cooperation between rich and poor

Developing countries often negotiate from a position of weakness: an astute bioprospector could easily take its business elsewhere, to neighbouring states for instance, where marine biodiversity may be similar and where regulations are comparatively more lax and restrictions minimal.[63] Further, it is difficult for developing nations with little resources to monitor their territorial waters since collecting samples such as mud from the bottom of the sea could be done inconspicuously from any boat.

Nevertheless, developing countries are beginning to distinguish between private bioprospecting for commercial gain and public research conducted in the public interest. In this way, R&D by public institutions are not restricted and at the same time, bioprospecting conducted by private institutions is regulated, albeit only at the private law level.

Distinguishing between research and commercialisation: problem or a solution?

Since public-private partnerships have become commonplace, it is becoming increasingly difficult to distinguish between commercialisation and pure research. This is further compounded by the fact that public institutions apply for and hold patent rights vis-à-vis novel marine natural compounds and therefore commercially benefit from licensing agreements. In these circumstances, the distinction between private commercialisation of natural products and public research becomes superfluous, since public research institutions benefit from patents and its licensing rights. Because these agreements are governed by private law – as they are private commercial contracts, they are not in the public domain. This

means that information about the project, the bioprospecting itself and all other relevant information are privy only to the parties to the contract. Neither the public or government for that matter, will have a way of knowing or monitoring current projects that are underway, or will be able to scrutinise what is being collected, the quantities being collected and where collections are being made.[64, 65] Research findings and other relevant information stemming from the joint marine exploration ventures are kept secret until patent protection is obtained.[66]

Interestingly, research institutions are finding themselves on the backfoot as they too, battle for access to information, particularly with regard to the non-disclosure of findings by private institutions after marine samples are shared. A biologist at Woods Hole Oceanographic Institution is quoted as saying the following to underline this point:

"We are wary of companies taking the samples and not communicating results ... As a result, some academics do not provide samples to industry."[67]

Problems associated with patents

Because patent law requires the subject matter of a patent application to be previously undisclosed and unpublished before a patent can be granted, research findings from marine bioprospecting are usually kept out of the public domain. In the event of a potentially useful and novel compound being discovered, the private institution will typically require the public institution to sign a confidentiality agreement, undertaking not to publish its findings until after a patent application has been filed. Thus, it will become increasingly common for research findings stemming from marine bioprospecting to be published several years after the conclusion of the research, thereby precluding any public benefits that could have been derived from the earlier sharing of knowledge and information.

A further problem arises when the orientation of the research is driven by corporate interests. Public-private partnerships entail sharing of costs, resources and expertise, and this will mean that inevitably, research and resources will be oriented towards marine organisms most likely to yield a commerical product. Furthermore, research institutions themselves are encouraged to seek patent protection over novel compounds so that they may cash in on profits from licensing rights. Thus, research institutions (backed by public funds) are focusing on R & D which bring in profits through licensing of intellectual property rights, rather than research in the public interest. For instance, the University of California prides itself as being the top university in the United States for having acquired intellectual property rights, and in turn, receives revenue from licensing of such

rights. [68] Indeed, its income from licensing rights of 5 patents alone amounted to $48 million in 2007.[69]

Environmental Concerns

It is argued that because small and indiscriminate amounts of initial samples are collected, and the prohibitively high costs involved, there are little or no resultant adverse environmental impacts from marine bioprospecting.[70] However, this is not accurate.

It is conceded that initially, small samples are collected. However, if commercially viable products are discovered, then larger marine samples are harvested.[71] Even where only minute samples are collected, if these are extracted from fragile environments or are themselves rare and vulnerable species, the collection can still have detrimental environmental impacts.

Typically, primary marine samples are initially collected randomly in small quantities of marine organisms and screened for possible 'hits' to determine bioactivity. These initial collections are relatively small, usually not exceeding one kilogram. If bioactivity is detected, then it becomes a 'lead', which will require collection in greater numbers of between 1-5kg. By the time it reaches the clinical trial stage, large scale collection of hundreds – even thousands of kilograms are required, depending on the organism being collected.[72]

Private industries most commonly hire collectors and this may cause damage to the environment. Even the initial, small-scale collection phase can be detrimental, especially where the collectors are inexperienced,[73] or samples are collected in extreme environments and where inappropriate methods of collection are used.[74] The life forms found in the deep oceans are often slow growing, due to the lack of light and nutrients. The Orange Roughby is a good example, as it is a fish that lives in the deep seas and attains maturity for reproduction at 25 years of age and can live up to 125 years.[75] Even a small disturbance can be detrimental, as the species may not be able to reproduce quickly enough to regain the numbers that it had lost. This is especially so in environmentally sensitive tropical and deep sea coral reefs as well as hydrothermal vents.

A major drawback with the commercialisation of marine based products is the large amount of organisms required to produce a small quantity of commercially viable products. For instance, the production of Halichondrin B requires one tonne of sponges to produce a mere 300mg.[76, 77] Other examples include the production of just 1mg of cephalostatin requiring 450 kilograms of acorn worms; 1mg of

dolastatin requiring 1,600 kilograms of sea hares; and under 1mg of spongistatin requiring 2,400 kilograms of sponge.[78]

Even the most promising chemical compound will have no commercial, patent or licensing value if its continued supply is inadequate or insecure. Currently, most chemical compounds are harvested from the wild, or through aquaculture or by synthesis (i.e. synthetically producing the chemical compound). However, both synthesis and aquaculture have major disadvantages. Industrial, bulk, low cost synthesis is extremely rare, since the procedures may be complex or costly. Aquaculture on the other hand, requires the host to have a high reproduction rate and grow rapidly in accessible environments.[79] Thus with wild harvesting being the most accessible method of collection, this method can be very detrimental to the environment. For instance, the unsustainable wild harvesting of a rare cone snail *Conus magus* for its active ingredients has put tremendous pressure on the species.[80] This is unfortunate and unnecessary, since its properties can easily be synthesised.[81]

Free-for-all

The United Nations Convention on the Law of the Sea (UNCLOS) states that areas and their resources outside the national jurisdiction are the common heritage of mankind, and thus cannot be subject to laws of a state, or ownership by anyone.[82] Currently, there is no binding, legally enforceable and comprehensive international treaty governing bioprospecting in the high seas. Since technological development now makes previously inaccesible bioprospecting in the high seas possible, and since national laws only regulate coastal waters, the high seas are currently a free for all.

The prevention of loss of marine biodiversity within territorial waters depends on the effective bioprospecting laws of a country as well as effective enforcement. Limited resources, technology and expertise often associated with developing nations makes effective implementation and enforcement of legislation difficult if not nigh impossible. This concern is discussed further in Section III.

section 3

Policy and legal issues

Marine bioprospecting in South Africa

South Africa is endowed with rich marine biodiversity consisting of around 11000 species, of which, over 25% are endemic.[83] Despite this biological wealth, South Africa's research in natural marine chemistry has been stymied by lack of technological and financial resources. Thus South Africa has made a late advent into the field. It was only in the 1990's that South Africa began its marine bioprospecting, when the then University of Natal collaborated with the Oceanographic Research Institute and PharmaMar; and Rhodes University collaborated with the Scripps Institution of Oceanography (SCRIPPS) and National Cancer Institute (NCI).[84]

Currently, natural marine product chemistry research is mainly conducted at Rhodes University in the Eastern Cape, and by smaller groups such as the University of KwaZulu-Natal.[85] Some of the other active researchers involved in marine biodiversity studies include the Council of Scientific and Industrial Research (CSIR), University of Cape Town, University of Western Cape, University of Port Elizabeth; and various other institutions in the Eastern Cape and KwaZulu-Natal.[86]

However, these public research institutions currently lack the technology and/or financial resources to conduct marine research and expeditions on their own, let alone bring a commercial product to the market.[87] This makes South Africa an ideal candidate for partnership arrangements with wealthier and better resourced foreign research institutions, pharmaceutical and agrochemical companies.

Below, are some recent examples of marine bioprospecting arrangements between Rhodes University, Grahamstown, South Africa and various foreign institutions.

Public-private partnerships involving Rhodes University

The following two case studies were made possible through the early research contributions made by Dr Marcel Tonye Mahop.

Case study 1

While we discuss the policy and regulatory system in South Africa pertaining to marine bioprospecting in detail below, in this case study, we describe the self regulatory nature of marine bioprospecting in South Africa through public-private partnerships and some of the key issues arising from this.

In the 1990's, Rhodes University (Chemistry Department) based in Grahamstown in the Eastern Cape, signed an Access and Benefit Sharing (ABS) agreement with SmithKline Beecham (now GlaxoSmithKline) for the use of South African marine invertebrates in drug development.[97] In this partnership, numerous marine resources were found to have moderate anti-inflammatory, anti-cancer and anti-HIV characteristics, although no patents have yet been filed. [98,99]

The partnership yielded some benefits to Rhodes University, such as increased capacity in the field of marine and invertebrate taxonomy and natural products chemistry, and the acquisition of useful research equipment.[91] More specifically, GlaxoSmithKline provided up-front benefits such as equipment; training in research; certification in advanced technical diving; and scholarships for students conducting research in marine resources. Further, it has promised to pay royalties should any commercial production result from the partnership.[92] The collection is carried out by both GlaxoSmithKline Staff as well as Rhodes University. The samples are then sent for extraction by GlaxoSmithKline, and 100mg of each sample are kept by them and the rest returned to Rhodes University.[93]

Between 1998 – 2000, Rhodes University Chemistry Department collaborated with the National Cancer Institute (NCI) and Coral Reef Research Foundation, to research the use of South African marine invertebrates for the development of anti-cancer drugs.[88]

The NCI has crafted its own standardised MoU. The NCI's standardised letter of collection (LoC)[89] and a memorandum of understanding (MoU) are used routinely in all their joint ventures.[90]

The features of NCI's standardised MoU/LoC include the following:

- that patents must be applied for and be held either held jointly or independently by the NCI;

- that the NCI is obliged to share technology, expertise and knowledge used during the bioprospecting agreement with the partner;
- that the LoC has the same patent provisions as the MoU. However, in addition, LoC demands the sharing of any traditional knowledge relating to the bioprospecting from the contracting country, and requires the contracting country to obtain written permission of the holders of such knowledge; and
- should a third party require samples collected or kept by those who are party to this MoU, they are obliged to approach the source country from which the resource was collected, with the object of entering into a Material Transfer Agreement with the country of origin.

The partnerships were seen as being ahead of its time, since it was concluded in the absence of bioprospecting legislation. Despite this fact, a collection permit was obtained from the Department of Environmental Affairs and Tourism (DEAT) in terms of other legislation.[94]

Standard LoCs and MoUs in the absence of adequate national legislation are becoming commonplace. However, as with any private contracts, the basis of negotiation can be on an unequal footing. It can expecially be worrying if bioprospecting is unmonitored in certain countries, such as South Africa. Bearing this in mind, it is recommended that government keep track of all terrestrial and marine based bioprospecting, and scrutinise MoUs and LoCs, to inform the drafting of appropriate legislation for marine bioprospecting.

Case study 2

Established in 1904, the Department of Chemistry of Rhodes University is renowned as a quality research centre. The Department of Chemistry employs highly skilled research staff[95] for its various areas of research interests, which include amongst others, marine natural product chemistry.[96]

Rhodes University's Department of Chemistry entered into a bioprospecting partnership with the SCRIPPS Institution of Oceanography, for the period 2001-2005. This was in regard to the bioprospecting of marine invertebrates for their use in the development of anti-cancer drugs. The research was funded by the National Institutes of Health (NIH) who concluded a MoU with Bristol-Myers Squibb Pharmaceutical Research Institute specifically for pharmaceutical drug research and development with respect to the samples gathered by Rhodes University.[100]

The SCRIPPS Institution of Oceanography is a graduate school of the University of California, San Diego. Its research interest spans across various areas pertaining

to marine resources, including marine biotechnology and biomedicine, marine biodiversity and conservation, and coastal resources.[101] Further, the SCRIPPS' Centre for Marine Biotechnology and Biomedicine is researching the development of a drug in the treatment of cancer, derived from the marine organisms.[102] There are indications of scientific breakthroughs as a result of the isolation of a chemical from a rare species of coral to fight breast and ovarian cancers,[103] including a compound Diazonamide A, which is used in preclinical trials (see Table 1). SCRIPPS' Centre collaborates with the University of San Diego Cancer Centre, as well as with other academic institutions and the pharmaceutical industry and has recently entered into a $100million contract with Pfizer to undertake projects of mutual interest including research in novel ways to treat uncured diseases.[104]

The Marine and Coastal Management of the Department of Environmental Affairs and Tourism (DEAT) approved the partnership between Rhodes University and SCRIPPS based on the MoU between the parties, and granted a collection permit to the parties in June 2001. The purpose of the partnership under the MoU, is to evaluate potential uses, principally in the therapy of cancer and HIV disease, of the chemicals extracted from South African marine organisms.

With regard to intellectual property rights issues, the MoU gives SCRIPPS the right to file, prosecute and maintain patent applications on inventions, including foreign patent applications. SCRIPPS is, however, obliged to inform Rhodes University of any foreign applications, and provide Rhodes University with the details of such applications. The MoU also deals with the distribution of the proceeds arising from the licensing of any patented invention to third parties interested in further commercial development. In this event, Rhodes University would reap 50% of the proceeds deriving from any licensing of the patented invention, after deduction by SCRIPPS of the costs for the maintenance of the patent rights.

Pursuant to the MoU, some collections of marine resources took place both within and outside of South Africa's jurisdiction. Most of the large-scale collections of samples (c. 500-1000 g wet mass each of 100-150 samples per collection) of marine resources took place within SA's jurisdiction as defined by the Maritime Zones Act.[105] A variety of species of South Africa's marine fauna and flora were collected including invertebrates, notably the ascidians, soft corals, molluscs and sponges, and some algae and microorganisms.[106] Approximately 150 samples of the marine resources of interest were collected each year and extraction of the active ingredients was done at Rhodes University.[107] For the period 2003-2004, over 5100 marine extracts were prepared for testing.[108] Toxicity and biological tests were carried out to determine the biological activity of the ingredients in order to assess their potential use in the development of anti-cancer drugs.

Niehaus, P. 2005. Leminda millecra. http://www.surg.co.za/home/html/qanda/qanda_2005/leminda_millecra.htm (accessed 29 September 2008). See Table 2.

Hypselodoris capensis from Port Elizabeth. 2003. By Rowe, C. Sea Slug Forum. http://www.seaslugforum.net/display.cfm?id=11170 (accessed 29 September 2008). See Table 2.

The MoU governed only the relationship between Rhodes University and SCRIPPS and not the other actors, namely the NIH and the Oncology Drug Discovery department of Bristol-Myers Squibb Pharmaceutical Research Institute. The NIH was a major financial contributor to the marine bioprospecting project between SCRIPPS and Rhodes University, and NIH was awarded a grant through its National Cooperative Drug Discovery Group (NCDDG) funding scheme. The NCI also plays a central role in the NCDDG. The aim of the scheme is to '*discover and develop new natural product anticancer therapeutic agents from chemically-prolific groups of marine invertebrates and unexplored marine microorganisms*'.[109]

Bristol-Meyers Squibb entered into a separate agreement with SCRIPPS concerning the samples to be made available. This was intended to enable

Rhodes University to collect the resources and undertake the initial extraction and screening, and Bristol-Meyers Squibb would conduct the in-depth pharmaceutical tests. The relationship between Rhodes University and Bristol-Meyers Squibb was therefore to ensure that the collected marine resources and initial screening would be distributed by them to Bristol-Myers Squibb for further studies.[110]

Over a period of time, Rhodes University has been able to amass a rich collection of marine biodiversity.[111] Today, these materials are kept in freezers at the Rhodes' Department of Chemistry, and provide a rich store of information for research and education purposes. Indeed, some of this information is used in NRF funded projects in the search of malaria resistant compounds.[112] In addition, the financial injection by the NIH has been useful in supporting graduate students and post-doctoral research at Rhodes University and has gone a long way towards establishing the Chemistry Department as a leader in marine natural product research on the African continent.[113]

The various collaborations between Rhodes University and SCRIPPS however, did not yield any patentable invention. The literature indicates very low biological activity of the ingredients isolated and characterised from South Africa's marine resources.[114] It is repeatedly stressed that the very low biological activity observed is not sufficient to proceed to the stage of drug development. For example, some specimens of the endemic red soft coral *Alcyonium fauri* were collected near Port Alfred in South Africa yielded three related sesquiterpenes including the major metabolite rietone.[115] After some relevant biological tests, it was noted that rietone exhibited very moderate anti-inflammatory activity that precluded any consideration for further pharmaceutical development.[116]

In summary, the collaboration between SCRIPPS and Rhodes was beneficial to Rhodes in a sense that they were able to accumulate samples of the bioprospected materials, and accumulate knowledge from the endeavour. However, it is up to the parties involved to regulate themselves. It is highly recommended that the South African government keep track of bioprospecting activities not only on land, but in the oceans as well. A consolidated manual is needed on the applicable laws pertaining to terrestrial bioprospecting as well as marine bioprospecting. This should include but not limited to applicable laws of the sea, legislation on enforcement and compliance, applicable international treaties, jurisdictional issues and so forth.

Table 2: Marine samples collected by Rhodes University

Species	Collection site	Ingredients of interest	Further development
Marine ascidian, *Pseudodistoma* sp. (order of Ascidiacea)	Tsitsikamma Marine Reserve and Algoa Bay	Active ingredient in the group of acyclic amino alcohols with anti-microbial properties	No further development in a pharmaceutical product
Soft corals *Capnella thyrsoidea*, order of Alcyonacea	Tsitsikamma Marine Reserve	Xenicanes diterpenes (anti-inflammatory)	No further development
Pieterfaurea unilobata, soft corals in the order of Alcyonacea	Port Alfred	Pregnadiene sterols (anti-inflammatory)	No further development
Alcyonium fauri, endemic soft corals of order Alcyonacea	Port Alfred	Sesquiterpenes (anti-inflammatory)	No further development although NCI was involved in further assays
Cladiella kashmani, soft corals of order Alcyonacea	Ponto-do-Ouro (Southern Mozambique)	Diterpene flaccidoxide (anti inflammatory)	No further development
Siphonaria capensis, Molluscs	Bushman's river near Port Alfred	Polypropionate (no special activity indicated)	No further development, although University of Queensland in Australia was involved in further assays
Siphonaria serrata, molluscs	Cape Recife near Port Elizabeth	Polypropionate (no special activity indicated)	No further development, although University of Queensland in Australia was involved in further assays
Trimusculus costatus, molluscs	Cintsa West near East London, Eastern Cape	Labdane diterpenes (chemical defence against predatory fish)	No further development
Hypselodoris capensis, molluscs	Endemic to Tsitsikamma Marine Reserve	Sesterpenes (anti microbial)	No further development
Chromodoris hamiltoni, molluscs	Aliwal Shoal	Latrunculins A and B and a series of diterpenes	No further development
Leminda millecra, molluscs	Algoa Bay	Sesquiterpenes	No further development
Tsitsikamma pedunculata, sponge	Algoa Bay	Pyroloinminoquinones in the family of alkaloids (chemotaxonomic marker)	No further development
Tsitsikamma favus, sponge	Algoa Bay	Bis-Pyroloiminoquinones (chemotaxonomic marker)	No further development in anti cancer drugs
Plocamium corallorhiza, red algae	Kalk Bay, near Cape Town; and Kenton-on-sea on the Eastern Cape coast	Halogenated nanoterpenes	No further development of anti cancer drugs
Lyngbya majuscule, cyanobacteria	Collected from Kenyan coast	Depsipeptide (antanapeptin A)	Very modest activity and no further development of anti cancer drugs

*Adapted from Davies-Coleman, M & Beukes. 2004. **Ten Years of Marine Natural Products Research at Rhodes University**. South African Journal of Science. 100: 540-544.

International environmental agreements

Marine bioprospecting occurs most frequently in international waters, and hence, the associated issues of cross border conservation, resource management and regulation naturally arise.

South Africa has signed numerous international environmental treaties (binding and non-binding) pertaining to the conservation and sustainable use of the Oceans, including the following:

- Abidjan Convention: Convention for Cooperation in the Protection and Development of the Marine and Coastal Environment of the West and Central African Region
- Agenda 21
- Agreement relating to the implementation of Part XI of the United Nations Convention on the Law of the Sea of 10 December 1982
- Agreement on Straddling Fish Stocks and Highly Migratory Fish Stocks
- Antarctic Treaty
- Bonn Convention on Conservation of Migratory Species
- Bonn Guidelines
- Code of Conduct for Responsible Fisheries
- Convention Concerning the Protection of the World Cultural and Natural Heritage
- Convention on the Conservation of Antarctic Marine Living Resources
- Convention on International Trade in Endangered Species
- Compliance Agreement and Code of Conduct for Responsible Fisheries
- Nairobi Convention: Convention on the Protection, Management and Development of the Marine and Coastal Environment of the Eastern African Region
- South African Development Community Protocol on Fisheries
- South East Atlantic Fisheries Organisation Convention
- United Nations Convention on the Law of the Sea
- United Nations Convention on Biological Diversity
- United Nations Framework Convention on Climate Change

Detailed discussion follows on the United Nations Convention on the Law of the Sea and the United Nations Convention on Biological Diversity, the two agreements that are most pertinent to marine bioprospecting.

The United Nations Convention on the Law of the Sea (UNCLOS)

The United Nations Convention on the Law of the Sea (UNCLOS) is a legally binding international treaty which came into effect on 16 November 1994.[117] It has, to date, 157 Parties including South Africa, who ratified the treaty on 23 December 1997. UNCLOS regulates the use of the seas and oceans so that it promotes peace between nations, allows for efficient use of the resources, whilst at the same time, protecting, preserving and conserving the marine environment.[118]

UNCLOS considers a seabed area that occurs outside of a national jurisdiction as being part of common heritage. This means that this type of seabed and the minerals and other resources beneath it cannot be subject to private ownership.[119] Mining specifically is governed by the International Seabed Authority. Whilst areas within 12 nautical miles from land is subject exclusively to state laws and control, the resources that lie in areas within territorial waters of the 200 nautical mile or Exclusive Economic Zone (EEZ), are governed by international treaties as well as national laws. The right to exploit, develop, manage and conserve such resources vests with the national states, bearing in mind international laws.[120] Marine scientific research (excluding commercialisation or bioprospecting for commercialisation) is also encouraged for the benefit and good of humankind.[121] It provides further that research should be made available to the public.

However, a serious shortcoming of UNCLOS is that it fails to deal with key bioprospecting issues, such as ownership of marine life forms through intellectual property rights. Furthermore, it separates Marine Scientific Research from commercialisation, a distinction that is increasingly becoming blurred within the context of public-private partnerships, as already discussed. There is also recognition that the treaty should deal with the protection for biodiversity beyond national jurisdictional areas.[122,123]

The Convention on Biological Diversity

The international agreement on the Convention on Biological Diversity (CBD), was the first international environmental agreement to deal with bioprospecting, the conservation of biodiversity, and access and benefit sharing (ABS).

ABS pertains to a specific regulatory system governing accessing genetic resources from the country of origin in a fair and equitable manner. It requires that proper formal consent is obtained from the provider country, and any benefits and technology is transferred in exchange for such resources, once proper consent is obtained.

The CBD was signed at the United Nations Conference on Environment and Development in Rio de Janeiro, Brazil, in 1993.[124] There are 168 signatories and 191 parties to the Convention, including South Africa, who ratified the Convention on 2 November 1995.[125]

The CBD is accompanied by legally non-binding Guidelines dealing with bioprospecting, commonly called the 'Bonn Guidelines.' The Bonn Guidelines were finalised at the 6th meeting of the Conference of parties of the CBD, and has been ratified by South Africa.

The Bonn Guidelines provide practical examples of key bioprospecting requirements of the CBD, such as prior informed consent (PIC), mutually agreed terms (MAT), dispute settlement mechanisms, and benefit sharing agreements (BSA). [126]

The CBD recognises the sovereignty of States over their own resources, but imposes an obligation on Parties to the CBD to minimise negative impacts beyond its jurisdiction.[127] Parties are also required to cooperate with each other in relation to activities beyond national jurisdiction.[128] The CBD envisages transfer of biological resources, and promotes technology transfer and encourages Parties to implement legislation to facilitate access to the technologies of private institutions.[129]

The CBD applies to all bioprospecting activities; however, a significant problem arises when bioprospecting activities occur in remote parts of the oceans, beyond national jurisdictions. This is so because the CBD only applies to areas within the State's national jurisdiction,[130] and specifically does not apply to bioprospecting beyond national borders.

Specifically relating to marine and coastal conservation and management, the Conference of Parties (COP) of the CBD in 1995, adopted the "Jakarta Mandate on Marine and Coastal Biological Diversity". This mandate outlined five key areas identified by the Subsidiary Body on Scientific, Technical and Technological Advice (SBSTTA) regarding the conservation and sustainable use of marine and coastal biological diversity, which should be discussed by the COP for implementation.[131,132] These included integrated management of marine and coastal areas; sustainable use of marine and coastal living resources; establishment of marine and coastal protected areas; mariculture; and alien species.[133] In order to take this work forward, a Group of Experts on Marine and Coastal Biological Diversity was established.[134] Over the years, each area of work was addressed by the COP, and further ad hoc working groups were established to deal with the issues thematically, including the Ad Hoc Technical Expert Group on Marine and Coastal Protected Areas and the Ad Hoc Technical Expert Group on Mariculture.

Several years down the line, and at COP 8 in 2006, issues of marine and coastal management were discussed, as well as concerns relating to genetic resources beyond the limits of national jurisdiction, and the need for the establishment for protected areas in such areas.[135,136,137] These discussions identified the gaping hole regarding the protection and management of areas outside national jurisdiction and as such, there was an endeavour to work together with the United Nations General Assembly to close this gap. As can be seen from the report of the subsidiary groups submitted to the General Assembly (see below), there is an attempt by the groups to take into consideration the progress reached, but thus far, there is no full integration.

United Nations General Assembly

In 1999, the United Nations General Assembly established the United Nations Open-Ended Informal Consultative Process on Oceans and the Law of the Sea (Consultative Process) to monitor and facilitate its work on various issues concerning the oceans, from security and safety, fishery to sustainable development.[138] From its first meeting in 2001, to its most recent work relating to marine resources in 2007, it addressed amongst others, its concerns related to the inadequate management, conservation and sustainable use of marine resources.[139] As a result of the concern expressed by the Consultative Process, the General Assembly established the *Ad Hoc* Open-ended Informal Working Group of the General Assembly to study issues relating to the conservation and sustainable use of marine biological diversity beyond areas of national jurisdiction (the Working Group) in 2004.[140]

At the eighth meeting of the Consultative Process on the 30 July 2007,[141] delegates discussed the possibility that a standardised code of conduct be developed for scientists who conduct bioprospecting activities in order to protect the environment, especially little known and highly sensitive systems such as deep sea hydrothermal vents. However, concerns were also expressed that such a code would not be legally binding and thus making compliance and enforcement problematic. Concerns were also raised about the inequity in technological capacity between the developing and the developed nations, and the inequities arising from this.

The most recent meeting held by the second meeting of the Working Group relating to marine biological diversity beyond areas of national jurisdiction was on 28 April to 2 May 2008.[142] In this decision it highlighted the need for deeper scientific understanding of the vulnerable deep sea as well as the need to narrow the gap between the scientific understanding and policy. It looked at the progress made

by various international bodies such as the CBD, ISA and Food and Agriculture Organization of the United Nations (FAO). Some delegations also noted the need for Environmental Impact Assessments for existing and /or new activities relating to the oceans outside areas of national jurisdictions, as a possible management tool. All in all, it expressed the view that better co-operation was needed on all levels to develop sustainable conservation and management tools.

Summary of international agreements

To summarise, there are currently significant gaps pertaining to marine bioprospecting in the two most relevant international treaties, especially with regard to bioprospecting that takes place in the areas outside national jurisdictions. At the same time, there is international recognition of this problem and attempts are underway to attend to these at the international level.

With regard to the regulation of bioprospecting within national jurisdictions, the CBD provides important regulatory guidance and minimum standards. However, comprehensive and holistic legislation to regulate bioprospecting within national borders are left up to Parties to the Convention. South Africa, along with many other developing nations is in the process of harmonising and implementing its laws in order to regulate bioprospecting, However, most of the attention has been diverted to regulating terrestrial bioprospecting, with marine bioprospecting having fallen by the way side.

National policy and law

South Africa's policy on Marine Bioprospecting

In South Africa, the applicable national and provincial policies pertaining to marine biodiversity protection, conservation and management are disjointed, dealing largely with fishing rights and species-specific protection.[143] The most relevant policy relating to marine bioprospecting is the White Paper on the Conservation and Sustainable Use of South Africa's Biological Diversity.[144]

The White Paper serves as the main policy and broad framework on Biodiversity and Conservation, thus is treated currently as the leading document on this subject. The implementation of the White Paper resulted in the enactment of the National Environmental Management: Biodiversity Act 10 of 2004, as well as the National Biodiversity Strategy and Action Plan, which are both discussed in detail below.

Further implementation will be outlined in the medium term National Biodiversity Framework, which will be published in the coming months.[145]

The White Paper largely deals with conservation of biological diversity of South Africa and the importance thereof in establishing protected areas, and providing incentives for such protection. Specifically relating to bioprospecting, it recognises it's genetic wealth and previous exploitation of South Africa's biological resources by foreign private institutions. Further, it recognises that although there are bioprospecting activities occurring within South Africa, the benefits and the technologies are harnessed by foreign bioprospectors, with very little returning to South Africa. The White Paper therefore aims to remedy the situation through implementation of appropriate legislation to regulate bioprospecting activities.

This policy, however, contains a gap which is mirrored in the current legislative framework, in that it fails to recognise the increasing bioprospecting activities occurring in the oceans. As a result, the policy does not envision a uniform strategy to deal with marine bioprospecting, nor does it display the foresight in recognising the need to consolidate existing legislation and plug loopholes. At best, it touches on the marine bioprospecting in a fragmented manner. For instance, such as through establishment of separate legislative frameworks for protected areas including marine protected areas, conservation of fisheries, and on accessing biological resources. This fragmented approach is reflected in the current legislative framework in existence today. Thus, South Africa currently lacks discreet policy dealing with marine bioprospecting. Although there are several initiatives underway towards closing this significant policy lucuna, these appear to be inadequate as discussed below.

The national Department of Environmental Affairs and Tourism (DEAT) released South Africa's National Biodiversity Strategy and Action Plan (NBSAP)[146] in 2005. The NBSAP recognises that the coastline is poorly protected and has committed the state to protecting 20% of its coast by 2010. However, marine coastal and biodiversity protection mainly focuses on fishing for the purposes of consumption. The NBSAP also highlights that the conservation of terrestrial and marine organisms is dealt with by a plethora of overlapping national, provincial and local government legislation and competencies. The NBSAP aims to rectify this situation through harmonisation and clarification of laws.

It is worth noting that the NBSAP on the whole does not deal specifically with marine bioprospecting activities at all.

The DEAT also released its three year Strategic Plan: 1 April 2008 to 31 March 2011.[147] With respect to marine resources, the aim is to draft legislative measures for fully functioning Marine Protected Areas, and aquaculture projects in order to aid

conservation and sustainable development. In relation to marine bioprospecting, the Strategy only makes mention of the fact that it is the government's intention to regulate bioprospecting and access and benefit sharing through the development of a bioprospecting register / database by 2009.

The South African National Biodiversity Institute (SANBI), in charge of promoting the sustainable use and conservation of biological diversity in South Africa, was established under the National Environmental Management: Biodiversity Act (NEMBA), No. 10 of 2004. SANBI has outlined its three year goals and objectives in its Strategic Plan for 2008-2011.[148] The aim is to implement the NBSAP and its obligations in terms of NEMBA within the context of DEAT's Strategic Plan. SANBI hopes to develop a threatened Red Species List for marine species, as well as to establish a monitoring system for marine protected areas. It however, hardly acknowledges the need for marine bioprospecting regulation and enforcement.

In the course of research for this paper, we have attempted to obtain information from the MCM division of DEAT on several occasions and it quickly became apparent to us that there is a palpable lack of information on current bioprospecting activities and applicable policies and laws. The current Director of the International Marine and Fisheries Cooperation division of DEAT, Mr Mongesi Ngoro (former Directorate of Compliance) acknowledged this fact, and commented as follows: "to put it bluntly, there are no policies or laws governing marine bioprospecting in South Africa".[149] He added that marine bioprospecting currently was a free for all in South Africa and that it was up to the bioprospectors to find the applicable laws to ensure compliance. He further acknowledges that there is a need for public consultation that involves experts in the field, in order to enhance better understanding of the subject matter within government.

We have been unable to find any information from DEAT on previous, current or future marine bioprospecting activities.

Mr Ngoro further elucidated that although South Africa is a Party to many international conventions and treaties such as UNCLOS, there is little capacity within government to attend and participate in international negotiations. Many international discussions and negotiations such as those taking place under the auspices of the United Nations Open-Ended Informal Consultative Process on Oceans and the Law of the Sea, the *Ad Hoc* Open-ended Informal Working Group to Study Issues Relating to the Conservation and Sustainable Use of Marine Biological Diversity Beyond Areas of National Jurisdiction, etc. go unattended by the South African government.[150] This means that South Africa is not part of the international discourse and discussions pertaining to marine bioprospecting and associated problems. There is, however, an attempt to remedy this situation.

Recently, the positions within International Marine and Biodiversity Cooperation were filled in order for South Africa to attend meetings associated with the treaties it has ratified, and to foster an understanding of the relationship between the different international treaties, in order also to facilitate implementation and enforcement through national laws.[151]

Inter-departmental communication/co-ordination within the various branches of DEAT on the subject of marine bioprospecting, appears to be limited. Many departmental officials at the MCM did not seem to be aware of any bioprospecting activities, nor the laws that applied to such activities.

Gaps in South African National Laws on Marine Bioprospecting

Although there are laws regulating bioprospecting in South Africa, these do not deal with marine bioprospecting and indeed, may not in any event, be the appropriate tools to do so. These laws are highly fragmented, and present a confusing regulatory labyrinth. Some of the primary applicable legal instruments include the National Environmental Management: Biodiversity Act 10 of 2004, National Environmental Management: Biodiversity Act, 2004: Regulations on Bioprospecting, Access and Benefit Sharing (Regulation No R138 of Government Gazette 30739 of 8 February 2008), and Marine Living Resources Act 18 of 1998.

Due to the lack of a single cohesive legal instrument, the South African government relies on bioprospectors to pick and choose the applicable laws whose obligations they may wish to comply with.

National Environmental Management: Biodiversity Act 10 of 2004

The primary legislation dealing with bioprospecting activities is the National Environmental Management: Biodiversity Act (NEMBA).[152] It is also the primary piece of national legislation that implements South Africa's international obligations under the CBD.

NEMBA defines bioprospecting as "any research on, or development or application of, indigenous biological resource for commercial or industrial exploitation".[153] It includes activities such as systematic search, collection and extraction of biological resources, and thus covers marine bioprospecting as well.

Chapter 6 of the Act deals specifically with bioprospecting activities as well as ABS. This Chapter makes it illegal for anyone to conduct bioprospecting activities involving indigenous biological resources or to export such products, without first obtaining a permit from the Minister of Environmental Affairs.[154] Before a permit may be obtained, the applicant has to obtain Prior Informed Consent (PIC) by disclosing

to the person providing access to the resources where the bioprospecting is to occur, and all the relevant information regarding the bioprospecting. In addition, a Material Transfer Agreement (MTA) and a Benefit Sharing Agreement must be entered into between the bioprospector and the person giving access. These must be approved by the Minister of Environmental Affairs and Tourism.

The NEMBA Act is complex. Although enacted in 2004, some of the provisions and chapters of the Act only come into effect when a notice is published to this effect in the Government Gazette. While most of the provisions of NEMBA came into force on 1 September 2004, Chapter 6, which deals with bioprospecting only came into effect on 1 January 2006.[155] The Bill for the regulation of bioprospecting was finally published on 8 February 2008, and came into force on the 1 April 2008.

National Environmental Management: Biodiversity Act, 2004: Regulations on Bioprospecting, Access and Benefit Sharing (Regulation No R138 of Government Gazette 30739 of 8 February 2008)

The purpose of these Regulations is to implement the procedural requirements for permit applications of NEMBA. It also sets out the requirements of PIC, MAT, BSA, and MTA, through permit application forms.[156]

NEMBA and its Regulations only apply to those bioprospecting activities undertaken within South African's borders or its national jurisdiction. Where such activities take place within the Exclusive Economic Zone (EEZ), the bioprospecting activities have to considered within the context of the applicable international laws governing the EEZ. Due to the complex nature of NEMBA, it has not to date, been used to regulate marine bioprospecting.

A further problem associated with NEMBA and its Regulations, is the emphasis on encouraging public research and development with minimal government oversight. This is done by exempting pure research (as opposed to research for commercial purposes) from compliance with the central permitting provisions of NEMBA.[157] In essence NEMBA and its Regulations attempt to distinguish between the commercialisation, development and research phases of bioprospecting.[158] As was discussed earlier, marine bioprospecting is characterised by public-private partnerships, which makes the distinction between the various phases difficult, if not impossible. This exemption would create a loophole in the law, as it relies on the intention and *bona fides* of the bioprospectors to determine the phases of bioprospecting. Marine bioprospectors can so easily argue that their explorations are only for purely scientific and research purposes and in so doing, evade compliance with the Act.

Intellectual Property Rights from Publicly Financed Research and Development Bill

Attempts to separate pure research from commercialisation in bioprospecting will be further hampered by impending legislation called the *Intellectual Property Rights from Publicly Financed Research and Development Bill [B46B-2008.]* [159] This Bill was debated and adopted with amendments on 3 September 2008, and is awaiting proclamation by the President.[160] The IPR Bill encourages public institutions to seek intellectual property protection over their research and in so doing, ensure monetary gains through licensing rights and so forth. This implies that research and development may not readily be put in the public domain since the research findings will not be published until after the intellectual property right is sought. Furthermore, it may entice public institutions away from pure scientific research for the benefit of the public, in favour of research driven by commercial interests. Interestingly, the Bill may have the effect of undermining the exemption of NEMBA discussed above. The IPR Bill encourages research institutions to seek intellectual property protection from the outset. This mean that once research institutions are set to seek IPR protection, it will not be able to claim the exemption provide for by NEMBA and its Regulations, since seeking IPR will be considered as being part of the commercialisation phase of bioprospecting.

As was outlined earlier, due to the complex nature of the Biodiversity Act, those that control access to the oceans, namely the Marine and Coastal Management (MCM), do not use NEMBA to regulate marine bioprospecting. Instead, they rely on the loose interpretation of the Marine Living Resources Act.

Marine Living Resources Act 18 of 1998

The most applicable legislation regarding protection of marine resources is the Marine Living Resources Act (MLRA).[161] The MLRA mainly covers issues relating to the conservation and sustainable use of marine resources, but it concentrates specifically on fishing activities. The MLRA requires persons to seek permits and authorisations from the MCM (under the auspices of DEAT) to conduct certain fishing activities. Although the MLRA does not specifically mention bioprospecting, it covers recreational fishing, and it can therefore be argued that bioprospecting activities are included. In terms of section 43 of the Act, it also allows the Minister to create marine protected areas by way of Government Gazette Notice. The accompanying Regulations[162] regulate fishing activities, with the emphasis placed on the regulation of specific marine resources, fishing activities, methods of fishing and so forth.

The MLRA has to be read together with legislation that outlines the national boundaries of its territorial waters, such as the Maritime Zones Act[163] and Prince Edward Islands Act.[164] In terms of enforcement, the Living Marine Resources Fund was established in terms of the Marine Living Resources Act[165] to enable monitoring and regulating of various areas of fishing, including management and administration, research, compliance and enforcement. However, the Fund is experiencing severe shortages and has inadequate resources to sustain effective monitoring functions.[166]

National Environmental Management: Protected Areas Act 57 of 2003[167]

The National Environmental Management: Protected Areas Act[168] also has relevance in terms of marine bioprospecting. It contains provisions that enable certain areas to be declared as marine protected areas, in order to conserve biodiversity, protect rare or threatened species and promote sustainable use of the environment.

Compliance and enforcement

South Africa is currently experiencing difficulty in controlling the poaching of marine life especially abalone and crayfish.[169, 170] Due to the lack of control, the Minister of the Department of Environmental Affairs and Tourism on the 26 October 2007, declared a ban on the fishing of abalone off South Africa's coastal waters.[171,172] Abalone is currently protected under Convention on International Trade in Endangered Species (CITES), and banned for export, however, due to lack of monitoring at exit points, poached abalone continue to be exported out of the country.[173]

The reason that South Africa experiences such difficulty is because of the prohibitively expensive nature of the monitoring costs. With fuel costs rising from $310 per ton in July 2003 to $680 in 2006; a single vessel costs up to R220 000 [$ 24 336] per day to be in port and R690 000 [$ 76 327] per day to be at sea.[174]

As discussed, the Marine Living Resource Fund,[175] is experiencing severe shortages in order to conduct patrol and research activities effectively.[176] This includes monitoring and regulating various fishing activities, management and administration, research, compliance and enforcement. Thus it is nearly impossible for South Africa to monitor illegal poaching, let alone illegal bioprospecting of marine resources.

In summary, South Africa currently lacks comprehensive legislation to monitor and regulate marine bioprospecting activities. There is a lacuna in international law as well, which leaves South Africa wide open to marine biopiracy and exploitation. The highly fragmented laws, together with severe lack of resources for monitoring and enforcement makes the regulation of marine bioprospecting a herculean challenge.

Conclusion

Commercial product development based on marine organisms is an extremely lucrative field. Despite the costs associated with such activity, exploring for genetic and chemical goldmines in the depths of the oceans has been on the increase. This marine bioprospecting activity is largely unregulated, and the developing world is struggling to address the multifaceted nature of the challenges associated with regulation and enforcement. As illustrated through the two South African case studies, the absence of regulation, and resources for monitoring and enforcement means that developing countries will have to rely on the good grace, conduct and bona fides of bioprospectors.

This situation is exacerbated by the inherent problems associated with public-private partnerships. Marine bioprospecting is promoted as an activity which advances humankind; encompassing research which deepens scientific knowledge, and which holds the promise of saving lives and easing human suffering through novel drug development. In light of this, it is easy to obfuscate the profit driven private interests involved in marine bioprospecting, the unequal and unregulated nature of the public-private partnerships, and the huge cost to the environment.

Thus owing to the relatively new field of marine bioprospecting, the world is wading in waters at its own and nature's peril. In the high seas where there are international regulations to mitigate some of the potential damage, reliance is placed on the good conscience of scientists and industry that they will do the right thing.

It seems that for now, ownership is being claimed even in the deepest oceans and the most sensitive environmental locations as researchers and industry claim their stake over novel compounds and genetic treasures found. Nevertheless, it is extremely urgent that public awareness of the issues be raised, so that ordinary citizens hold government, the public and private sectors accountable.

References

1. Feist, P. **A tale from the sea to Ara-C**. http://www.pfeist.net/ALL/arac/ (accessed 2 June 2008).
2. UNU. 2007. **An update on marine genetic resources: scientific research. Commercial uses and database on marine bioprospecting**. http://www.ias.unu.edu/resource_centre/Marine%20Genetic%20Resources%20UNU (accessed 23 June 2008).
3. Ruth, L. 2006. **Gambling in the deep sea**. European molecular biology organisation report 7(1): 18.
4. Hunt, B and Vincent, A. 2006. **Scale and sustainability of marine bioprospecting for pharmaceuticals**. Ambio 35(6); 57 at 59-63; FAO Corporate Workshop on Marine Bioprospecting Synopsis. http://www.fao.org/docrep/009/a0337e/A0337E15.htm (accessed 9 November 2007).
5. UNU. 2007. **An update on marine genetic resources: scientific research. Commercial uses and database on marine bioprospecting**. http://www.ias.unu.edu/resource_centre/Marine%20Genetic%20Resources%20UNU (accessed 23 June 2008)
6. Scheepers, A. 2006. **Synthesis of triprenylated toluquinone and toluhydroquinone metabolites from a marine-derived *Penicillium fungus***. Rhodes Masters thesis. 6
7. UNU. 2007. **An update on marine genetic resources: scientific research. Commercial uses and database on marine bioprospecting**. http://www.ias.unu.edu/resource_centre/Marine%20Genetic%20Resources%20UNU (accessed 23 June 2008).
8. Feist, P. **A tale from the sea to Ara-C**. http://www.pfeist.net/ALL/arac/ (accessed 2 June 2008).
9. Munro, H.G et al. 1999. **The discovery and development of marine compounds with pharmaceutical potential**. Journal of Biotechnology 70: 15-16.
10. Newman, D.J and Cragg, G.M. 2004. **Marine natural products and related compounds in clinical and advanced preclinical trials**. Journal of Natural Products 67:1216.
11. Narsinh, L. 2004. **Biotechnological potential for marine sponges**. Current Science 86 (11): 1507-1508.
12. UNU. 2007. **An update on marine genetic resources: scientific research. Commercial uses and database on marine bioprospecting**. http://www.ias.unu.edu/resource_centre/Marine%20Genetic%20Resources%20UNU (accessed 23 June 2008).
13. Da Rocha, A.B et al. 2001. **Natural products in anticancer therapy**. Current Opinion in Pharmacology 1:366-367.
14. IUCN **Bioprospecting marine resources: conservation, concerns and management implications** at www.iucn.org/themes/marine/Word/BIOPROSPECTING%20MARINE%20RESOURCES-CBD-Info.doc (accessed 6 November 2007).
15. Zhang, L. 2005. **Exploring novel bioactive compounds from marine microbes**. Current Opinion in Microbiology 6: 276.
16. Simmons, T.L. *et al*. February 2005. **Marine natural products as anticancer drugs**. Molecular Cancer therapeutics 4(2): 333.
17. Centre for Marine Biodiversity. **Biodiversity in the marine environment**. http://www.marinebiodiversity.ca/cmb/what-is-marine-biodiversity/biodiversity-in-the-marine-environment (accessed 20 October 2008).
18. UN Atlas of the Ocean. **Marine biodiversity. http://www.oceansatlas.org/servlet/CDSServlet?status=ND-0xNzg4NSZjdG5faW5mb192aWV3X3NpemU9Y3RuX2luZm9fdmlld19mdWxsJjY9ZW4mMzM9KiYzNz1rb3M**~ (accessed 23 June 2008).
19. Fenical, W. 1983. **Marine plants: a unique and unexplored resource** in "Plants: the potential for extracting protein, medicines, and other useful chemicals". p.147.
20. Green, J. 2005. **Bioprospecting in the high seas**. FAO workshop on Marine Bioprospecting Synopsis. http://www.fao.org/docrep/009/a0337e/A0337E15.htm (accessed 9 November 2007).
21. Bull, A.T. and Stach, J.E.M. 2007. **Marine actinobacteria: new opportunities for natural product search and discovery**. Trends in Microbiology 15(11): 491.

22. Haefner, B. 12 June 2003. **Drugs from the deep: marine natural products as drug candidates**. Drug Discovery Today 8: 536.
23. Ruth, L. 2006. **Gambling in the deep sea**. European molecular biology organisation report 7(1): 17.
24. Synnes, M. 2007. **Bioprospecting of organisms from the deep sea: scientific and environmental aspects**. Clean Technology and Environmental Policy 9: 53.
25. Sydney Morning Herald. 24 October 2003. **Ocean census finds 200 000 – plus marine lifeforms**. http://www.smh.com.au/articles/2003/10/24/1066631610205.html?from=storyrhs (accessed 8 November 2007).
26. Ruth, L. 2006. **Gambling in the deep sea**. European Molecular Biology Organisation Report, 7(1): 17.
27. Synnes, M. 2007. **Bioprospecting of organisms from the deep sea: scientific and environmental aspects**. Clean Technology and Environmental Policy 9: 53-56.
28. Donia, M. and Hamann, M.T. 2003. **Marine natural products and their potential applications as anti-infective agents**. The Lancet: Infectious Diseases 3: 338.
29. Haefner, B. 12 June 2003. **Drugs from the deep: marine natural products as drug candidates**. Drug Discovery Today 8: 536.
30. Newman, D.J and Cragg, G.M. 2004. **Marine natural products and related compounds in clinical and advanced preclinical trials**. Journal of Natural Products 67: 1216.
31. Hay, M.E and Fenical, W. 1996. **Chemical ecology and marine biodiversity: insights and products from the sea**. Oceanography 9:1. p10. http://www.tos.org/oceanography/issues/issue_archive/issue_pdfs/9_1/9.1_hay_fenical.pdf (accessed 16 October 2008).
32. Haefner, B. 12 June 2003. **Drugs from the deep: marine natural products as drug candidates**. Drug Discovery Today, 8: 536; Newman, D.J and Cragg, G.M. 2004. **Marine natural products and related compounds in clinical and advanced preclinical trials**. Journal of Natural Products 67: 1218.
33. BBC news. 10 July 2006. **Snail venom painkillers launched**. http://news.bbc.co.uk/2/low/health/5165124.stm (accessed 19 Nov 07).
34. Biotech Pharmacon. **Marine bioprospecting**. http://www.biotec.no/category.php?themeID=20&categoryID=99 (accessed 9 November 2007); Casas, E *et al*. 2007. **Marine natural product bioprospecting: screening and production of bioprocess development of novel bioactive compounds**. Journal of Biotechnology S235.
35. Zhang, L. et al. 2005. **Exploring novel bioactive compounds from marine microbes**. Current Opinion in Microbiology 6: 276.
36. Mayer, A.M.S. et al. 2007. **Marine pharmacology in 2003-4: marine compounds with anthelmintic, antibacterial, anticoagulant, antifungal, anti-inflammatory, antimalarial, antiplatelet, antiprotozoal, antituberculosis and antiviral activities; affecting the cardiovascular, immune and nervous systems, and other miscellaneous mechanisms of action**. Comparative biochemistry and physiology 145: 557.
37. Dunlap, W.C. et al. 2007. **Biomedicals from the phytosymbionts of marine invertebrates: a molecular approach**. Methods 42: 359; Munro, H.G *et al*. 1999. **The discovery and development of marine compounds with pharmaceutical potential**. Journal of Biotechnology 70: 17-18.
38. Haefner, B. 12 June 2003. **Drugs from the deep: marine natural products as drug candidates**. Drug Discovery Today, 8: 536.
39. SciDev.net. **Time for new deal on marine bioprospecting**. http://www.scidev.net/Opinions/index.cfm?fuseaction-readOpinions&itemid=37&language=1 (accessed 6 November 2007).
40. Krajick, K. 1 May 2004. **Medicines from the sea**. http://www.smithsonianmag.com/specialsections/ecocenter/medicine.html?c=y&page=2 (accessed 24 June 2008).
41. UNU. 2007. **An update on marine genetic resources: scientific research. Commercial uses and database on marine bioprospecting**. http://www.ias.unu.edu/resource_centre/Marine%20Genetic%20Resources%20UNU (accessed 23 June 2008).
42. Newman, D.J. and Cragg, G.M. 2005. **Political, legal, scientific and financial aspects of marine discovery programmes**. FAO workshop on Marine Bioprospecting Synopsis. http://www.fao.org/docrep/009/a0337e/A0337E15.htm (accessed 9 November 2007).
43. Green, J. 2005. **Bioprospecting in the high seas** in FAO workshop on Marine Bioprospecting Synopsis. http://www.fao.org/docrep/009/a0337e/A0337E15.htm (accessed 9 November 2007).

44. Wikipedia. **Drug Development**. http://en.wikipedia.org/wiki/Drug_development (accessed 23 June 2008).
45. United States mission to the United Nations. 25 June 2007. **Press release number 163 (07)**. http://www.usunnewyork.usmission.gov/press_releases/20070625_163.html (accessed 29 September 2008).
46. UNU. 2007. **An update on marine genetic resources: scientific research. Commercial uses and database on marine bioprospecting**. http://www.ias.unu.edu/resource_centre/Marine%20Genetic%20Resources%20UNU (accessed 23 June 2008).
47. Bio Bridge Ltd. January 2005. **Prospects for Marine Biotechnology in the UK**. Volume 2:47.
48. UNESCO. 2005. **Deep Sea Genetic Resources: what is their potential?** Fifth Trondheim Conference on Biological Diversity. www.trondheimconference.org/attachment.ap?id=4417 (accessed 23 June 2008).
49. Marine Biotech. **The pipeline and the finish line**. http://www.marinebiotech.org/pipeline.html (accessed 20 November 2007); Kijjoa, A. and Sawangwong, P. 2004. Drugs and cosmetics from the sea. Marine Drugs 2: 74.
50. UNESCO. 2005. **Deep Sea Genetic Resources: What is their potential?** Fifth Trondheim Conference on Biological Diversity. www.trondheimconference.org/attachment.ap?id=4417 (accessed 23 June 2008).
51. Leary, D. 2005. **Bioprospecting and the genetic resources of hydrothermal vents on the high seas: What is the existing legal position? Where are we heading and what are our options?** In Shotton, R. (Ed.) 2005. Deep Sea 2003: Conference on the Governance and Management of Deep-sea Fisheries, Conference Poster Papers (1–5 December 2003, Queenstown) and Workshop Papers (27–29 November 2003, Dunedin), New Zealand. FAO Fish. Proc. 3/2. FAO, Rome. pp. 455–487.
52. Leary, D. 2005. **Bioprospecting and the genetic resources of hydrothermal vents on the high seas: What is the existing legal position? Where are we heading and what are our options?** In Shotton, R. (Ed.) 2005. Deep Sea 2003: Conference on the Governance and Management of Deep-sea Fisheries, Conference Poster Papers (1–5 December 2003, Queenstown) and Workshop Papers (27–29 November 2003, Dunedin), New Zealand. FAO Fish. Proc. 3/2. FAO, Rome. pp. 455–487.
53. Sederma. **Venuceane**. http://www.sederma.fr/Actives/Venuceane.htm (accessed 7 July 2008).
54. Marine Biotech. **Marine bioprospecting: mining the untapped potential of living marine resources**. http://www.marinebiotech.org/biopro.html (accessed 6 November 2007); UN Atlas of the Ocean. **Bioprospecting**. http://www.oceansatlas.org/servlet/CDSServlet?status=ND0xODQ1Ny4xODQ3MCY2PWVuJjMzPWRvY3VtZW50cyYzNz1pbmZv (accessed 7 October 2008).
55. Marinebiotech.org. **The pipeline and the finish line**. http://www.marinebiotech.org/pipeline.html (accessed 20 November 2007).
56. Marinebiotech.org. **The pipeline and the finish line**. http://www.marinebiotech.org/pipeline.html (accessed 20 November 2007).
57. United States District Court for the District of Columbia. *Edmonds Institute v Babbitt* 'Memorandum Opinion', Civil Action 98-561. http://www.edmonds-institute.org/yellowstone98561.pdf (accessed 29 September 2008).
58. Ruth, L. 2006. **Gambling in the deep sea**. European molecular biology organisation report 7(1): 18.
59. UNESCO. 2005. **Deep Sea Genetic Resources: What is their potential?** Fifth Trondheim Conference on Biological Diversity. www.trondheimconference.org/attachment.ap?id=4417 (accessed 23 June 2008).
60. FAO. **Workshop on marine bioprospecting synopsis**. http://www.fao.org/docrep/009/a0337e/A0337E15.htm (accessed 9 November 2007).
61. Hallock, Y.F. and Cragg, G.M. 2003. **National Cooperative Drug Discovery Groups (NCDDGs): a successful model for public private partnerships in cancer drug discovery** 41: 71-91.
62. Ruth, L. 2006. **Gambling in the deep sea**. European molecular biology organisation report, 7(1): 18.
63. SciDev.net. **Time for new deal on marine bioprospecting**. http://www.scidev.net/Opinions/index.cfm?fuseaction-readOpinions&itemid=37&language=1 (accessed 6 November 2007).
64. Hunt, B. and Vincent, A. 2006. **Scale and sustainability of marine bioprospecting for pharmaceuticals**. Ambio 35(6): 57.
65. UNESCO. 2005. **Deep Sea Genetic Resources: What is their potential?** Fifth Trondheim Conference on Biological Diversity. www.trondheimconference.org/attachment.ap?id=4417 (accessed 23 June 2008).
66. UNU. 2007. **An update on marine genetic resources: scientific research. Commercial uses and database on marine bioprospecting**. http://www.ias.unu.edu/resource_centre/Marine%20Genetic%20Resources%20UNU (accessed 23 June 2008).

67. Shank, T. in Ruth, L. 2006. **Gambling in the deep sea**. http://www.nature.com/embor/journal/v7/n1/full/7400609.html (accessed 29 September 2008).
68. University of California. **UC means business: the economic impact of University of California**. http://www.ucop.edu/pres/ucmeans.pdf (accessed 7 October 2008).
69. Farrell, M. 12 September 2008. **Universities that turn research into revenue**. Forbes. http://www.forbes.com/2008/09/12/google-general-electric-ent-tech-cx_mf_0912universitypatent.html (accessed 7 October 2008).
70. Moore, B. in Ruth, L. 2006. **Gambling in the deep sea**. European molecular biology organisation report 7(1): 18.
71. Bioone. **Scale and Sustainability of Marine Bioprospecting for Pharmaceuticals**. http://www.bioone.org/perlserv/?request=get-document&doi=10.1579%2F0044-7447(2006)35%5B57%3ASASOMB%5D2.0.CO%3B2&ct=1 (accessed 9 November 2007).
72. Hunt, B. and Vincent, A. 2006. **Scale and sustainability of marine bioprospecting for pharmaceuticals**. Ambio 35(6): 57.
73. IUCN **Bioprospecting marine resources: conservation, concerns and management implications** at www.iucn.org/themes/marine/Word/BIOPROSPECTING%20MARINE%20RESOURCES-CBD-Info.doc (accessed 6 November 2007).
74. Hunt, B. and Vincent, A. 2006. **Scale and sustainability of marine bioprospecting for pharmaceuticals**. Ambio 35(6): 58-60.
75. Synnes, M. 2007. **Bioprospecting of organisms from the deep sea: scientific and environmental aspects**. Clean Technology and Environmental Policy 9: 57.
76. Munro H.G. et al. 1999. **The discovery and development of marine compounds with pharmaceutical potential**. Journal of Biotechnology 70: 19.
77. C.E et al. 2004. **Merging the potential of microbial genetics with biological and chemical diversity: an even brighter future for marine natural product drug discovery**. Natural Product Reports 21: 106.
78. United Nations. 12 March 2007. **Report of the Secretary General on the oceans and the law of the sea**, A/62/66, 47.
79. Munro H.G. et al. 1999. **The discovery and development of marine compounds with pharmaceutical potential**. Journal of Biotechnology 70: 19.
80. BBC news. 20 October 2003. **Drug-hope snails imperilled**. http://news.bbc.co.uk/2/low/science/nature/3207632.stm (accessed 19 Nov 07).
81. Hunt, B. and Vincent, A. 2006. **Scale and sustainability of marine bioprospecting for pharmaceuticals**. Ambio 35(6); 57 at 61.
82. UNCLOS Article 136, 137, 140 and 141.
83. MBSAP. 2005. http://www.cbd.int/doc/world/za/za-nbsap-01-en.pdf (accessed 30 September 2008).
84. Scheepers, B.A. 2006. **Synthesis of triprenylated toluquinone and toluhydroquinone metabolites from a marine-derived Penicillium fungus**. Rhodes University Masters thesis. 6-7.
85. Davis-Coleman, M. *et al.* March 2000. **The status of genetic and biochemical analysis of marine organisms in South Africa**. http://www.nrf.ac.za/publications/marinerep/genetic.htm (accessed 6 November 2007).
86. Atwood, C.L. *et al.* March 2000. **Conservation of marine biodiversity in South Africa**. http://www.nrf.ac.za/publications/marinerep/conserve.htm (accessed 12 November 2007).
87. Cragg, G.M. *et al.* 1995. **Natural product discovery and development: new perspectives on international collaboration**. Journal of Natural Products 58: 1325-1357.
88. Wynberg, R. 2006. **South African legislative case study**. In Lettington, R.J.L & Mwanyiki, S. (eds), Case Studies on Access and Benefit Sharing (International Plant Genetic Resources Institute), p. 129.
89. WIPO. http://www.wipo.int/tk/en/databases/contracts/texts/html/nciloc.html (accessed 8 September 2007).
90. WIPO. http://www.wipo.int/tk/en/databases/contracts/texts/html/ncimou.html#patent (accessed 8 September 2007).
91. International Plant and Genetic Resources Institute. 2006. **Case studies on access and benefit sharing**. http://www.bioversityinternational.org/Publications/Pdf/1149.pdf (accessed 29 August 2007).
92. Tangley, L. 1996. **Ground rules emerge for marine bioprospectors**. BioScience 46(4): 247.

93. Biowatch. **Biodiversity prospecting within South Africa: A profile of some of the involved sectors**. http://www.biowatch.org.za/main.asp?include=docs/reports/1996/bioprospects/chapt3.html (accessed 30 September 2008).
94. Wynberg, R. 2005. **Benefit-sharing in South Africa: fact or fiction?** http://www.biowatch.org.za/docs/benefit_sharing.pdf (accessed 29 August 2007).
95. http://www.chem.ru.ac.za/staff.html (accessed 15 May 2007).
96. http://www.chem.ru.ac.za/research.html (accessed 15 May 2007).
97. Wynberg, R. 2002. **Institutional responses to benefit sharing in South Africa**. In Laird, S.A (ed.) Access and Benefit Sharing legislation in South Africa. (IUCN): 56.
98. Davis-Coleman, M. *et al*. **The status of genetic and biochemical analysis of marine organisms in South Africa**. http://www.nrf.ac.za/publications/marinerep/genetic.htm (accessed 8 September 2007).
99. Davis-Coleman, M. and Beukes, D.R. 2004. **Ten years of marine natural products research at Rhodes University**. South African Journal of Science 100: 540-543.
100. Personal communication, Professor Davies-Coleman (11 September 2007).
101. SCRIPPS. **Research overview**. http://sio.ucsd.edu/About/Research_Overview/ (accessed 11 June 2007).
102. SCRIPPS. **Centre for marine biotechnology and biomedicine**. http://cmbb.ucsd.edu/ (accessed 11 June 2007).
103. SCRIPPS. **Marine biotechnology and biomedicine**. http://sio.ucsd.edu/About/Research_Overview/Marine_Biotechnology_and_Biomedicine/ (accessed 16 May 2007).
104. News RX: Drug Law Weekly. 2 January 2007. **Scripps research institute enters 5-year $100 million collaboration with Pfizer.** http://www.newsrx.com/newsletters/Drug-Law-Weekly/2007-01-02/2201022007233DL.html (accessed 9 September 2007).
105. Maritime Zones Act 15 of 1994.
106. Davies-Coleman, M. and Beukes, B.R. 2004. **Ten years of marine natural products research at Rhodes University**. South African Journal of Science 100: 540.
107. Fenical, W. *et al*. 2003. **New anticancer drugs from cultured and collected marine organisms**. Pharmaceutical Biology 41: 6.
108. Fenical, W. *et al*. 2003. **New anticancer drugs from cultured and collected marine organisms**. Pharmaceutical Biology 41: 6.
109. Fenical, W. *et al*. 2003. **New anticancer drugs from cultured and collected marine organisms**. Pharmaceutical Biology 41: 6.
110. Fenical, W. *et al*. 2003. **New anticancer drugs from cultured and collected marine organisms**. Pharmaceutical Biology 41: 6.
111. Davies-Coleman, M. and Beukes, D.R. 2004. **Ten years of marine natural products research at Rhodes University**. South African Journal of Science 100: 539.
112. Personal Communication, Professor Davis-Coleman (11 September 2007).
113. Email communication from Professor Davies-Coleman dated 16 May 2007.
114. See publications listed by Professor Davis-Coleman at Rhodes University. **Professor Michael T. Davies-Coleman: research publications (2003-2008)**, http://people.ru.ac.za/chdc/Papers.htm (accessed 22 October 2008).
115. Davis-Coleman, M. and Beukes, D.R. 2004. **Ten years of marine natural products research at Rhodes University**. South African Journal of Science 100: 539 at 540-543.
116. Davis-Coleman, M. and Beukes, D.R. 2004. **Ten years of marine natural products research at Rhodes University**. South African Journal of Science 100: 539 at 540-543.
117. UN. **Status of the United Nations Convention on the Law of the Sea, of the Agreement relating to the implementation of Part XI of the Convention and of the Agreement for the implementation of the provisions of the Convention relating to the conservation and management of straddling fish stocks and highly migratory fish stocks**. http://www.un.org/Depts/los/reference_files/status2008.pdf (accessed 7 October 2008).
118. Preamble of the UN Convention on the Law of the Sea.
119. Article 136 and 137. UN Convention on the Law of the Sea.

120. Article 55 and Article 56. UN Convention on the Law of the Sea.
121. Article 238 – Article 241. UN Convention on the Law of the Sea.
122. Spott, P. 16 June 2005. **Who will own deep sea life?** http://www.csmonitor.com/2005/0616/p13s01-sten.html (accessed 2 July 2008).
123. Speer, L. *et al.* **WCPA – marine plan of action, building representative networks of High Seas MPAs**. http://groups.google.com/group/wcpamarine-summit/web/iucn-wcpa---marine-high-seas-work (accessed 2 July 2007).
124. CBD. **Sustaining life on earth**. http://www.cbd.int/convention/guide.shtml?id=action (accessed 15 September 2007).
125. CBD. **List of Parties**. http://www.cbd.int/convention/parties/list/ (accessed 7 October 2008).
126. See Article 26, articles contained in section C, Articles 41 and 44 of Section D, Article 59 and Annexure II.
127. Article 3 of CBD.
128. Article 5 of CBD.
129. Article 16 of CBD.
130. Article 4 of the CBD.
131. CBD. **COP 2 Decision**. http://www.cbd.int/decisions/?lg=0&m=cop-02&d=10 (accessed 8 October 2008).
132. See further UN. **Implementation of the Jakarta Mandate on Marine and Coastal Biological Diversity**. www.un.org/Depts/los/general_assembly/contributions2004/CBD2004.pdf (accessed 8 October 2008).
133. CBD. **Programme of Work**. http://www.cbd.int/marine/resources.shtml (accessed 20 October 2008).
134. CBD. **Background**. http://www.cbd.int/marine/pow.shtml (accessed 20 October 2008).
135. CBD. **COP 8 Decision VIII/21**. http://www.cbd.int/decisions/?m=COP-08&id=11035&lg=0 (accessed 8 October 2008).
136. CBD. **COP 8 Decision VIII/22**. http://www.cbd.int/decisions/?m=COP-08&id=11036&lg=0 (accessed 8 October 2008).
137. CBD. **COP 8 Decision VIII/24**. http://www.cbd.int/decisions/?m=COP-08&id=11038&lg=0 (accessed 8 October 2008).
138. General Assembly Resolution 54/33, 24 November 1999.
139. UN Division of Ocean Affairs and the Law of the Sea. **United Nations Open-ended Informal Consultative Process on Oceans and the Law of the Sea**. (accessed 20 October 2008).
140. General Assembly resolution 59/24 of 17 November 2004.
141. United Nations General Assembly. **Sixty-second session report on the work of the United Nations Open-ended Informal Consultative Process on Oceans and the Law of the Sea at its eighth meeting** A62/169. http://daccessdds.un.org/doc/UNDOC/GEN/N07/443/75/PDF/N0744375.pdf?OpenElement
142. General Assembly **A/63/79**.
143. DEAT. **Policies and Legislation**. http://www.environment.gov.za/ (accessed 8 October 2008).
144. DEAT. **White Paper on the Conservation and Sustainable Use of South Africa's Biological Diversity, General Notice 1095 of 1997**. http://www.environment.gov.za/PolLeg/WhitePapers/Biodiversity/Contents.htm (accessed 7 October 2008).
145. Personal communication with Ms Lutch, Director of Biodiversity and Conservation, DEAT. 21 October 2008.
146. NBSAP. http://www.cbd.int/doc/world/za/za-nbsap-01-en.pdf (accessed 30 September 2008).
147. DEAT. 2008. **Strategic plan 01 April 2008 to 31 March 2011**. http://www.environment.gov.za/AboutUs/StratDoc/StratPlan/DEAT_Strat%20PlanApr2008-2011.pdf (accessed 30 September 2008).
148. SANBI. Strategic Plan 2008 - 2011. http://www.sanbi.org/csp&bp/SANBI%20CSP%202008-2011.pdf (accessed 30 September 2008).
149. Personal communication with Mr Mongesi Ngoro, Director of the International Marine and Fisheries Cooperation Division, DEAT. 1 October 2008.
150. Personal communication with Mr Mongesi Ngoro of DEAT, Director of the International Marine and Fisheries Cooperation Division. 1 October 2008.
151. Personal communication with Mr Mongesi Ngoro of DEAT, Director of the International Marine and Fisheries Cooperation Division. 1 October 2008.
152. National Environmental Management: Biodiversity Act 10 of 2004.

153. Section 1 of NEMBA, Act 10 of 2004.
154. Section 81(1) and Section 81(2), NEMBA, Act 10 of 2004.
155. Proclamation 47 in Government Gazette No. 26887 of 8 October 2004.
156. Regulation 2 of the Bioprospecting Regulation No 138 of Government Gazette 30739.
157. Regulation number R149 of the Government Gazette 30379.
158. Regulation 1 of the Bioprospecting Regulation No 138 of Government Gazette 30739.
159. Department of Science and Technology. http://www.dst.gov.za/publications-policies/legislation/bills/Tag_C_IPR_from_PFR_Bill.DOC
160. Parliamentary Monitoring Group. 3 September 2008. **Intellectual Property Rights from Publicly Financed Research & Development Bill: deliberations & adoption**. http://www.pmg.org.za/report/20080903-intellectual-property-rights-publicly-financed-research-development-b (accessed 29 September 2008).
161. Marine Living Resources Act 18 of 1998.
162. Government Notice R1111 of 2 September 1999.
163. Maritime Zones Act 15 of 1994.
164. Prince Edward Islands Act 43 of 1948.
165. Marine Living Resources Act 18 of 1998.
166. Parliamentary Monitoring Group. 3 November 2006. **Problems and solutions related to Marine and Coastal Management and the Living Resources Fund: briefing by Minister**. http://www.pmg.org.za/viewminute.php?id=8466 (accessed 14 November 2007).
167. National Environmental Management: Protected Areas Act 57 of 2003.
168. National Environmental Management: Protected Areas Act 57 of 2003.
169. MCM. **Abalone in Crisis**. http://sacoast.uwc.ac.za/education/resources/abalone.htm (accessed 6 October 2008).
170. Jordan, B. 25 August 2008. **Big fish fight state's crayfish plans**. The Times. http://www.thetimes.co.za/Business/BusinessTimes/Article1.aspx?id=828413 (accessed 6 October 2008).
171. Legalbrief. 30 October 2007. **Abalone Fishing Banned**. http://www.legalbrief.co.za/article.php?story=20071030083927990 (accessed 25 June 2008).
172. Benton, S. 26 October 2007. **South Africa bans abalone fishing**. http://www.southafrica.info/about/sustainable/abalone-261007.htm (accessed 25 June 2008).
173. Gosling, M. 3 October 2008. **A blank cheque for abalone poachers**. http://www.iol.co.za/index.php?set_id=1&click_id=14&art_id=vn20081003053330167C483451 (accessed 16 October 2008).
174. Parliamentary Monitoring Group. 3 November 2006. **Problems and solutions related to Marine and Coastal Management and the Living Resources Fund: briefing by Minister**. http://www.pmg.org.za/viewminute.php?id=8466 (accessed 14 November 2007).
175. Marine Living Resources Act 18 of 1998.
176. Parliamentary Monitoring Group. 3 November 2006. **Problems and solutions related to Marine and Coastal Management and the Living Resources Fund: briefing by Minister**. http://www.pmg.org.za/viewminute.php?id=8466 (accessed 14 November 2007).