United Nations Panel Discussion – World Oceans Day

John J. Stegeman remarks

Honorable Director, Professor Freestone, fellow panelists, ladies and gentlemen: Thank you very much for the opportunity to be here, and to participate in these events to mark the first UN observance of World Oceans Day. It is indeed a pleasure and an honor for me to participate in this important panel discussion. I think that the comments you heard from the last speaker concerning ocean acidification and the potential impact of increased levels of carbon dioxide on ocean pH, and the consequences for organisms, may be among the more important comments made here today.

I would like to applaud the United Nations for this recognition of World of Oceans Day, which should foster greater recognition of the oceans' vital role in life on earth. A number of years ago, there was a cartoon in The New Yorker magazine, which depicted several women sitting, talking. One said: "I don't know why I don't care about the bottom of the ocean, but I don't". Hopefully, events such as those associated with World Oceans Day will increase the global awareness of just how critical the oceans are to all life on earth.

As I grow older, I find that I am given more to thoughts of just what an amazing planet this is. And it is amazing in large part for the astonishing diversity of life that exists here. Consider if you will, that you were able to travel to some newly discovered extrasolar planet, and were to discover oceans of water, green plants, colored flowers, and animals in the air, on land and in the water. Such an astounding discovery would capture the interest of the whole world. And yet here it is; it is *our* planet that has these oceans and this stunning diversity of life! This diversity is leading to a greater knowledge of the potential for the use of biological systems in meaningful and appropriate ways that help humankind. There is a growing knowledge of this diversity, which is greater in the oceans than on land; greater numbers of species live in the oceans than on land and we know far less about them. This diversity is fuel for the growth of marine biotechnology.

The topic I was to address is the industrial application of marine biotechnology, in the context of managing ocean resources; "Our Oceans, Our Responsibility". So what is marine biotechnology? In simple terms it is the technological use of marine organisms, biological processes, materials or genes, in some way that benefits humankind. Experience to date indicates that biotechnology has enormous potential to impact areas that are important to humankind; in aquaculture, agriculture and processing of foods, in medicine and health, in industry, in research, and in maintaining a healthy environment. Potential areas also include generation of energy. There are a number of impressive, and often repeated, examples of marine biotechnology successes that can be found by searching the web. Not all can be mentioned here, and so only a few are highlighted.

There are hundreds of marine natural products identified that have properties indicating potential utility in industrial processes, health or research. The discovery of enzymes in sponges that catalyze the synthesis of silicon-based polymers of defined structure at nanoscale levels has great potential for use in biotechnological generation of silicon nanomaterials, with applications in many areas. Adhesive proteins synthesized in vitro by genes from mussels are able to form strong bonds underwater, to substrates difficult for other adhesives to adhere to. Pharmaceutical agents have long been sought from marine species. Candidates include compounds that are potential antibiotics, antivirals, anticancer agents, anti-inflammatory agents and so forth. However, there still are relatively few such products that have been approved for clinical use. However, there appears to be a resurgence of interest in expending the effort to bring such compounds to the market. There are growing numbers of other interesting processes of marine microbes that are being considered for development, including the use of biological processes for mediating environmental cleanup of spills of chemicals or petroleum or such.

The impact of marine natural products on health is of long standing. In the 1950's analysis of natural products from sponges led to the isolation of novel nucleosides, spongothymidine and spongouridine, that have arabinose rather than ribose as the sugar component. These nucleosides, with a different sugar moiety, prompted a synthetic modification of nucleosides for potential interference with DNA synthesis. This led to the development of arabinose-cytosine, or Ara-C, that is widely used clinically against lymphomas and leukemias, particularly Hodgkin's lymphoma and acute myelogenous leukemia. Members of my own family have been treated for leukemia, quite successfully, with this clinically important drug derived from the hint in spongouridine. While there are other drugs in development from marine sources, it is important that these come principally from marine natural products chemistry. The pace of discovery has been good for years, but moving along the path to a clinically useful drug has at times been agonizingly slow.

The impact of marine biotechnology on health does not need to be direct to be important. Enzymes from deep-sea vent organisms, for example “vent DNA polymerase” are used in polymerase chain reactions or PCR, a technological advance that has touched virtually every aspect of biology for cloning genes and for measuring their levels of expression. Limulus amoebocyte lysate, derived fro horseshoe crab blood, is used to detect bacterial endotoxin to ensure the safety of intravenous fluids. A very important discovery of the fluorescent proteins from coelenterates has had a major impact in our understanding of conditions in health and disease. This green fluorescent protein is thus not directly used in treatment or as a therapeutic agent but in research to understand how gene expression is involved in health and disease. The gene for green fluorescent protein can be attached to the promotor regions of various other genes, and when in a transgenic organism the gene of interest is turned on that causes the expression of GFP, which lights up green so that you can see very easily the location and timing of when the gene if interest is expressed. This is substantially important, evident in the awarding of the 2008 Nobel Prize in Chemistry for green fluorescent protein discovery and development.

So this is the present. There are more than a few successes, and the value estimated for biotechnological exploitation of resources in the sea is in the hundreds of millions and indeed billions of dollars worldwide. What about the future? Where does the future come from? Where will the new discoveries come from? And how will we exploit further the diversity that exists in the oceans for biotechnologically useful materials?

I can offer my own view of how this future will be achieved, how we will be able to efficiently and wisely exploit diversity in the seas to identify new chemicals, processes and genes. I consider five important features of how to achieve this. These are wise searching, biological knowledge, a prepared mind, genome studies, and data handling, and these features are interwoven as well.

An example of wise searching is how we go about seeking microbes that may generate chemicals that will affect the growth of other microbes, involving biological understanding. Such growth-inhibiting chemicals would be potential antibiotics.

A recent Danish expedition, Galathea 3, scientist sampled from around the world in part searching for bacteria that may influence the growth of bacteria, that is bacteria that may generate antibiotics. What is now known is that the bacteria that live in the water column are less likely to produce chemicals that interfere with the growth of other microbes than are those bacteria that live on surfaces. This makes sense as it is on the surface of a copepod or the surface of a fish or the surface of a rock or a small particle, that growth of one species may be effected by the growth of another species competition for resources, etcetera. So it is reasonable to expect that antimicrobials may be elaborated by species growing on surfaces. Searching for these interactions can be done quite simply using the growth plate technique that led Alexander Fleming to the serendipitous discovery of penicillin. This kind of approach is something that could be done simply, to explore coastal waters around the world for raw materials potentially of biotechnological interest, including in areas and in coastal states where the cost of doing the elaborate natural products chemistry and gene searching may be cost prohibitive. We should seek out opportunities to employ simpler technologies to take advantage of and perhaps exploit diversity that exists in coastal states all over the world.

The second feature is biological knowledge, and an example would be improved understanding of methods for culturing organisms. At present, the vast majority of microbes that are being discovered have yet to be cultured, as the conditions for obtaining these organisms in culture are simply not known, haven't been identified. As understanding of requirements of organisms improves, then culturing of organisms may increase and as that happens then the opportunities to identify organisms that produce useful products, whether antivirals or antibacterials or anticancer agents becomes more feasible.

A third feature may increase the exploitation of diversity is a prepared mind in ecological studies. As an example of this, a group at the Oceanographic Institution in Woods Hole have been studying interactions between phytoplankton and a viral control of phytoplankton populations. Viruses that infect phytoplankton may act to determine or influence the abundance of viable phytoplankton cells. In examining the basis for the viral interaction they stumbled upon two chemicals that influenced the infection process and the survival of phytoplankton cells. These two chemicals are now being examined carefully for their potential, one as an anticancer agent and the other as an antiviral agent. The prepared mind of the investigators allowed them to think that the action of these chemicals in phytoplankton had possible biomedical implications.

A fourth feature that will lead to growth of future exploitation of marine resources is genomic studies. The current approaches for DNA sequencing have expanded the amount of information that may be gained from a single sample, and that information is revealing a greater abundance of microbial species than had been thought even a few years ago. There may be as much as tenfold or a hundredfold greater abundance of species than thought, and the rare species may possess unusual metabolism or genes that could provide raw material for all sorts of uses. Genome studies are also showing that there may be greater numbers of genes in gene families that have importance in biological processes involving chemicals. For example, in sea urchin there are twice as many genes in a gene family known as cytochrome P450, that code for enzymes that degrade pollutants, than there are in humans. The suggestion is that there may be unusual properties of these genes in sea urchin that are largely involved in defense against or in metabolizing toxic chemicals, which may find use, for example, in dealing with contaminated environments. A gene from one species that is able to metabolize chemicals could be put into a species of bacteria or phytoplankton that may be used to metabolize and remediate contaminated environments. There would be questions about the release of such transgenic organisms yet the potential may be there.

The fifth feature is one that may not be thought of commonly, but that would be of data handling. There are massive amounts of data being acquired on genetic and other properties of marine organisms and handling this amount of data understanding the implications for a particular genomic feature requires an ability to deal with this.

An additional area to these five is technological development that will allow exploration and sample retrieval from sites not previously available or available only with great difficulty. For example, within the past weeks there has been a successful re-visitation of the Challenger deep in the Mariana trench by scientists at the Woods Hole Oceanographic Institution and other places. They have constructed a remotely operated vehicle that was able to successfully visit the very deepest part of the ocean. With this deep diving remote vehicle the entire world ocean is now accessible and samples of these areas may be obtained offering new raw material for discovery of biotechnologically interesting properties.

So what are the limitations in being able to exploit the marine biodiversity for biotechnological purposes? Three come to mind, which I lable discovery, development and distribution of benefits. By discovery, I mean investment in research, which as a principle limiting factor. As an example, the identification of potential drugs is mostly by academic natural products chemists, and funding of research in that area is key to identification of new compounds. Likely, this will require cooperation, among agencies, partnerships with commercial interests, and cooperation among governments.   There is progress in such partnering. An example partnership between the National Institutes of Health and the National Science Foundation in the U.S., which resulted in a competitively funded program of Centers for Oceans and Human Health. The subtitle of the COHH program is *"Risks and remedies from the sea"*. The program deals with risks from pathogens, risks from harmful algal blooms (which are increasing worldwide) but also supports efforts to discover and for identify new pharmaceutical agents or other agents of direct relevance to human health. While this example is cooperation between agencies within a government, I think that cooperation between governments as are equally feasible. Examples of such cooperation, I think, should be highlighted, recognizing that cooperation is a way to enhance the rate of discovery.

Secondly, the development of biotechnological resources that are known is a big impediment. For example, the effort and cost required or bringing a potential drug, identified from any source, can be enormous. The time to bring a potential drug to and through phase II or phase III trials can be years, often a decade. The financial support for this is difficult to obtain and without a strong indication that there would be a financial recovery for investments, public or private, then it is questionable whether there would be a development even with signs there would substantial benefit to society. Generally, there needs to be a champion, someone who is interested in this for the sake of the science but who can see the potential and will do what it takes in order to bring that potential to a reality. Many examples of drugs in the pipeline are there because of the dedication of an individual to the science and subsequently to seeing the potential is actually used.

Lastly, an impediment to successful development is the consideration of distribution of benefits and materials to the global community. With discovery of raw material in coastal state jurisdictional waters, it is important that there be a reasonable financial benefit to those who have undertaken the effort and financial risk. It is equally important that financial and material benefits accrue to those coastal states and worldwide. Material benefits may for example, be antiviral drugs important for the health of the populations worldwide, and thus distribution globally, in particular, in regions of developing countries, where financial possibilities for purchase are limited, is very important. Secondly, plans for distribution of financial benefits of biotechnological materials discovered in the open ocean or in the commons beyond any jurisdictional waters, need to be examined carefully, for benefit to all states including landlocked states that do not have their own marine biotechnological resources.

In closing, I think that all coastal states have potential biotechnical resources, and countries the world over have centers or institutes of marine biotechnology. In preparing remarks for this meeting, I happened upon an article in the Jakarta Post, of April 7th, 2009, considering marine biotechnology, and I quote: "Eventually marine biotechnology will influence, in one way or another, virtually all of mankind's productive activities, whether they be agriculture, health services, industry, energy production, or environmental remediation. Marine biotechnology will fuel this exciting new frontier and provide enormous economic potential for future generations to take advantage of. Although industrialized nations have benefited greatly from this new frontier, developing nations have as much or more to gain from advances in marine biotechnology."

I agree with this sentiment, that all coastal states have potential biotechnological resources. To develop these requires investment but identification of those resources, for example bacteria with the potential to influence the growth of other bacteria, could be done even with limited resources. I think that the coming years will see increased attention to the biotechnological potential and also increased attention to maintaining the diversity and ensuring that those species on this planet which may benefit us, will be safely, and successfully exploited.

Again, I thank you very much and am grateful to the United Nations for World Oceans Day, for this panel discussion, and for the opportunity to be here.