Meeting Report

Intellectual Property Rights, Naturally Derived Bioactive Compounds, and Resource Conservation. Meeting Report

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The first Interim Annual Meeting of the American Society of Pharmacognosy was held October 20−22, 1994, in San Jose, Costa Rica. In the symposium, which was the main scientific focus of the meeting, speakers from both developed and developing countries presented their perspectives on issues regarding intellectual property rights in regard to drug development from natural sources, conservation of natural habitats, and international conventions on bioprospecting. Careful evaluation of existing policies, laws, and conventions; sensitivity to the respective world views of prospective partners; equitable sharing of benefits including scientific collaboration; and a sense of fairness will be necessary to ensure that the genetic resources of all countries will be developed for the benefit of humankind.

The American Society of Pharmacognosy held an Interim Annual Meeting in San Jose, Costa Rica, on October 20−22, 1994. The major scientific event at the meeting was a symposium on "Intellectual Property Rights, Naturally Derived Bioactive Compounds and Resource Conservation". The symposium was cosponsored by the American Society of Pharmacognosy, the University of Illinois at Chicago, the Centro International de Productos Naturales (CIPRONA) at the University of Costa Rica, and the Instituto de Biodiversidad (InBio) of Costa Rica. Meeting organizers were D. D. Soejarto of the University of Illinois at Chicago, A. Sittenfeld of InBio, and G. A. Mora of CIPRONA. One hundred twenty-six participants from 25 countries attended the meeting. The meeting received major funding from the John D. and Catherine T. MacArthur Foundation, the Organization of American States, Shaman Pharmaceuticals, Conservation International, the University of Illinois at Chicago, and the Programa Ibero-Americana of Ciencias y Tecnologia de Desarollo.

The first day of the symposium was devoted to speakers from developed countries who presented their perspectives on the issues covered in the Symposium, while the second day was devoted to speakers from developing countries. A discussion session was held on the third day.

Developed Country Speakers

D. D. Soejarto (University of Illinois at Chicago, Chicago, IL) discussed plant sample collection considerations. Only 15−17% of the approximately 220 000 flowering plant species have been screened for medical potential. Plant samples may be selected for testing based on attempts to maximize taxonomic diversity, ecologically based approaches (e.g., allelopathy), traditional medicine information, or chemotaxonomic relationships. In order to develop continuing relationships with developing countries, joint collecting expeditions with taxonomists in host countries and financial support of collaborating herbaria are needed. This facilitates recollection work and may give substantial impetus to conservation efforts.

M. R. Boyd (National Cancer Institute, Frederick, MD) discussed the role of intellectual property rights in natural product drug development. Existing intellectual property, including knowledge, concepts, genetic resources, and cultural heritage, is critical in this process. Intellectual property can be protected by a variety of formal or informal agreements. New intellectual property, such as a new drug, can be protected by both patents and licenses. Licenses can be used to obligate the licensee to compensate owners of existing intellectual property that was important in product development, including genetic or cultural resources. Even with large scale efforts such as that mounted by the NCI in the past 10 years, patenting and licensing agreements may be difficult to obtain; despite screening some 70 000 samples, the NCI as yet has no patents or licenses, although it has filed patent applications on 13 new lead compounds.

R. P. Borris (Merck Research Laboratories, Rahway, NJ) discussed his company's natural products research program. Merck finds that natural products screening is less cost-effective than screening based on its corporate chemical library. However, because of the enormous chemical diversity and highly unusual structures in natural products, Merck maintains a natural products program. Higher plants, insects, marine organisms, and microbes, including protozoa and microalgae, are studied. Merck has set up collaborations with InBio in Costa Rica and with the New York Botanical Garden, which include upfront conservation payments, setup of

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laboratories, training in extraction and phytochemistry techniques, sharing of royalty payments, and coauthorship of patents by scientists in the collaborating institutions who help to isolate promising lead compounds.

D. Turner (Glaxo Research and Development, Stevenage, Hertfordshire, U.K.) discussed the history of his company's involvement with natural products. Glaxo screens soil, plants, marine microorganisms, and marine invertebrates in addition to its major programs based on cell biology, biochemistry, and combinatorial laboratories. The major screening strategy is to identify active principles that possess very specific inhibitory or antagonistic activities on well-defined biological targets. Glaxo typically obtains natural product source materials through suppliers such as universities or botanical institutes which may collaborate with developing country taxonomists. Suppliers whose products are commercialized will receive royalties on products with the condition that at least 40% of the royalty will be returned to the source country.

S. R. King (Shaman Pharmaceuticals, South San Francisco, CA) offered an overview of his company's strategies for working with and sharing benefits of drug discovery with indigenous peoples. In the long term, Shaman will provide a portion of profits of any and all products to all of the communities and countries in which they have worked, spreading out the risk of collaboration and hastening the time to return. The company's Healing Forest Conservancy also channels part of the profits into projects aimed at conserving biological diversity. In the short term, Shaman works to meet requests of local people working with their researchers. Many such requests relate to health care. Western-trained physicians accompany ethnobotanists on all expeditions, providing treatment for diseases not treated well by traditional medicines and guiding the implementation of disease prevention projects. Shaman also participates in support for laboratories and research training for scientists in developing countries.

S. L. Bertha (University of Illinois at Chicago (UIC), Chicago, IL) presented the University's policy on intellectual property rights for natural products. Screening samples for UIC projects are usually provided to UIC by a Consultant, who is assumed to be a valid agent of the owner of the samples (e.g., a country or indigenous group) and who has permission to collect and export them. UIC will file patent applications if new drugs are found and will negotiate license agreements with third parties for product development. UIC owns all work products obtained in research, including extracts, compounds, data, patents, etc. Income resulting from patented inventions will be shared appropriately with the sample owner. Percentages of royalties shared would be scaled to the nature of the intellectual input into a project. UIC will also share results of tests with countries of origin on a confidential basis, help to implement research training programs, and ask licensees to exercise their best efforts to purchase raw materials from the country of origin or provide finished products on to the country of origin on a preferential basis.

W. V. Reid (World Resources Institute, Washington, DC) discussed means by which countries that supply genetic resources to industrial firms might control the flow of such resources away from their regions. Technology for evaluation of biological samples is advancing rapidly, so that increasing numbers of samples can be screened effectively, thus lowering the price per sample firms are willing to pay. Supplier countries can become low-cost suppliers that provide large numbers of raw samples at low costs. They can also become value-added suppliers, providing samples with interesting ecological or anthropological background, or other attractive characteristics. Low-cost suppliers could join together to form cartels or cooperatives to market large numbers of samples in return for proportionate shares in returned benefits. In such cartels, an institution that contributed 25% of the samples marketed would receive 25% of the royalties that accrued to the cooperative, even if a marketable drug was not developed from its samples.

K. Duffy-Mazan (National Cancer Institute, Bethesda, MD) presented a paper summarizing means of filling in the gaps created by development of natural products in the context of U.S. patent law. Under U.S. patent law natural product source countries and indigenous groups cannot participate directly in patent rights and thus cannot receive financial benefits from use of their genetic resources or knowledge. To address this problem the NCI developed the Letter of Collection, now in force in several countries with which the NCI works. This document specifies, among other points, that licensees who develop compounds isolated by the NCI must work out compensation directly with source countries and address their concerns; that compensation is due to source countries even if eventual manufacture of a derived compound is completely synthetic; that data be shared on a confidential basis with source countries; that NCI may work with source countries on expanded collaborations to develop active agents; that patents on drugs be filed in the U.S. and, if applicable, the source country; that input of traditional knowledge not be disregarded; and that raw materials needed for additional studies will be supplied by or propagated in the source country.

Developing Country Perspectives

On October 21 representatives of biodiversity source countries presented their perspectives on the issues raised, with special attention to national genetic resources, conservation efforts, pertinent intellectual property rights laws, regulations for collection of material for scientific purposes, and acceptance of various international conventions on biodiversity prospecting.

Central and South America. E. Elisabetsky (University Federal do Rio Grande do Sul, Porto Alegre, Brazil) presented material based on surveys of Brazilian scientists and laboratories. A primary issue in work on the development of natural product drugs has been the wisdom of instituting patents on drugs not previously recognized in the country. Despite concerns that pharmaceutical patents would lead to high prices, legislation enabling patents on chemicals, pharmaceuticals, biologicals, and food products is now under consideration. The question of relationships with foreign entities has also been discussed at length. This led to a decree by the Ministry of Science and Technology that any collection of materials must receive permits from the National Council of Scientific and Technological Development. All collectors must collaborate with a recognized Brazilian institution, and intellectual property rights as guaranteed by Brazilian legislation must be reflected. While difficulties in the regulatory process were acknowledged, cooperation with international projects was generally regarded as a positive experience.

R. Calle (University of Antioquia, Medellin, Colombia) discussed Colombian concerns in the area of genetic resources exploitation. Maintenance of sovereignty over biological resources in developing countries is complicated by the economic pressures of dealing with the interests of international markets which demand participation in patenting schemes which do not correspond to the social and cultural norms of the developing country. Rights of indigenous communities for use of their traditional knowledge are as yet inadequately addressed. Ethnic communities do not regard their traditional knowledge as property to be sold but rather as a matter of collective responsibility to the environment—a system which fits poorly into industrial frameworks. In addition, different communities may possess the same knowledge and, thus, be thrust into commercial conflicts imposed on them by industrial interests.

R. Salazar and J. Cabrera (Ambio Foundation, San Jose, Costa Rica) presented a paper on intellectual property rights in their country. Costa Rican patent law provides for a period of protection of one year for drugs, medical products, food products, and agricultural chemicals; for other products the period of protection is 12 years. There is some feeling that Costa Rican law should be brought into line with that of other countries. Access to Costa Rica's biodiversity is provided through the Ministry of Natural Resource, Energy and Mines. Permits are extended for scientific, commercial, and subsistence collection of the flora. Export is handled by the same agency, with requirements for phytosanitary certificates and compliance with CITES regulations. Substantial concern was expressed over the trend for increasing patenting of life forms, including microorganisms, genes, and natural genetic mutations, especially for agriculturally important organisms.

R. Garcia (National Botanical Garden, Santo Domingo, Dominican Republic) spoke on the situation in the Dominican Republic. Sixty-three separate laws and a variety of resolutions and decrees regulate use of its natural products. Because of conflicts among institutions, inadequate enforcement capabilities, and outdated legislation, these laws have been unable to retard the destruction of nearly 90% of the country's forested areas. A technical body is now in the process of developing a new forest use code to help solve these problems. Biodiversity collection permits may be obtained from the Department of Plant Sanitation and the Dominican Centre for Promotions and Exportations; export is also regulated by the Wildlife Department. Previous collecting for pharmacognosy and phytochemistry studies has gone on without provision for compensation, although during the last decade the National Botanical Garden and other scientific institutions have attempted to exert partial control on this situation.

V. H. Villacres (Central University, Quito, Ecuador) discussed laws relevant to biodiversity collection and conservation in his country. Ecuador is a species-rich country: estimates of higher plants in its territory range from 25 000 to 80 000 species. Approximately 14.5% of the country is set aside in various types of reserves. Conservation of these areas is of critical interest as annual deforestation rate in Ecuador has approached 31.5%. The administration of this natural patrimony is under the Ministry of Agriculture and Livestock (MAG). Export of specimens of flora or fauna from the forests is permitted for purposes of scientific research, education, or international collaboration, in cooperation with scientific institutions that have been authorized by MAG and comply with all requisite regulations. Activities of collection or commercialization of forest organisms also require a license from the National Forest Program.

Africa. J. G. Jato (Faculty of Medicine and Biomedical Sciences, Yaounde, Cameroon) discussed his country's 1994 legislation pertinent to research on forest products. This legislation specifies that all genetic resources of the land belong to the state, which grants permits to Cameroonian nationals only for their use. Foreign interests desiring to conduct research must associate themselves with appropriate national counterparts. Permit holders are given notebooks to register the identity, quantity, and site of collection of all samples, which must be transmitted to proper authorities on a regular basis. The modalities and amounts of economic benefits will be determined proportionally to their value by the Minister of finance after consultation with other ministries. This law unfortunately marginalizes scientific research on forests and concentrates on timber exploitation and hunting. A new text specifying application of the 1994 law is now in preparation, which will address practical details.

F. Randimbivololona (Faculty of Sciences of Antananarivo, Madagascar) discussed research and regulations in Madagascar regarding biological resources. Regulations for collection of biological materials depend on the purposes for which collection is performed. Collection is generally free for personal samples or those covering individual research needs. To export medicinal plants, collectors must obtain permits from the Ministry of Applied Scientific Research for Development. Export of dried, sanitary plant materials is permitted, but export of extracts or more highly purified samples is encouraged. Malagasy scientists prefer as much as possible to export only semipurified extracts for extensive work (as well as botanical materials necessary for identification) and object to being excluded from the entire drug discovery research process after samples leave the country.

M. Iwu (Bioresources Development and Conservation Programme (BDCP), Owerri, Nigeria) discussed efforts of his institution to rationalize research on genetic materials. The BDCP has an innovative model for bioresources development. It includes the following features: (1) economic benefits to be channeled back into the area in which a source plant was found, (2) Nigerian scientists are to be involved in all drug development processes, (3) project objectives include not only development of pure compounds but standardization of local phytomedicines, (4) recognition that intellectual property rights as manifested in developed countries do not protect the traditional heritage of rural communities, (5) agreements emphasize capacity building rather than short-term cash benefits, and (6) priority is given to diseases that are endemic to the tropics.

R. Mahunnah (University of Dar es Salaam, Dar es Salaam, Tanzania) discussed the regulation of collection of genetic resources in his country. Typical formalities are entry visas, research permits, identification of relevant collaborating institutions, and conduct of joint field expeditions for bioprospecting. Tanzanian institutions can collaborate with institutions from developed countries under research agreements for short-term or long-term programs. Benefits of any discoveries are to

be shared among all parties and to include returns to the collaborating institution, government, and indigenous cultures. There are a variety of institutions involved in overseeing the implementation of bioprospecting policies, which are periodically reviewed.

Asian/Pacific Region. J. T. Baker (Australian Institute of Marine Science, Townsville, Queensland, Australia) presented a paper on Australia's new policy on access to genetic resources. The following basic principles guide Australian policy: (1) Australia will control access to its biological resources in accord with the Convention on Biological Diversity; (2) foreign access to Australian resources will be provided on the condition that contracting parties recognize Australia's ownership of the genetic material, involve Australian scientists in research on the material, and make fair and equitable returns on commercial products developed; and (3) the Commonwealth and State Governments retain rights to set fees or charges on the collection of genetic resources and receive data, materials and research reports concerning the commercial potential of such resources. Other aims of the new policy include provision for conservation, establishment of screening programs within Australia, and establishment of property rights related to indigenous knowledge.

B. N. Mehrotra (Central Drug Research Institute (CDRI), Lucknow, India) discussed the situation of India. There is no national policy on collection of plants for research, but CDRI has asked the Ministry of Environment and Forests to formulate uniform guidelines. Permission to collect plant samples can be obtained from authorities of the forest departments of the 23 Indian states, but there is great variability in the conditions for granting permits. Some have granted collection permits with restrictions such as return of research findings, payments of royalties, provision of detailed reports of collections, or sharing of benefits from patented products with state governments. Biological testing of plant materials outside of India is possible provided that an institutional collaborative program which safeguards the interests of both countries is set up.

J. C. Fong (State Attorney General of Sarawak, Kuching, Sarawak, Malaysia) discussed Sarawak's policies on intellectual property rights and biodiversity collection. To aid in implementing the objectives of the Biodiversity Convention, a permit system is being put in place. In this system applicants will enter agreements regarding the use of plant materials, the supply of information and data on research results, rights of the State to resulting patents, royalties and compensation, participation of local scientists in collection and development processes, and technology transfer. By including local scientists in the research process, Sarawak will be able to legitimately acquire intellectual property rights on plant-derived drugs. The State wishes to emphasize that these regulations are not intended to deny access to or hinder foreign organizations in the exploration of its natural resources, but to ensure reasonable benefits to all concerned parties.

D. A. Madulid (Philippine National Museum, Manila, Philippines) discussed guidelines for research collections in the Philippines. Various institutions have been working on a document establishing a new regulatory framework for genetic resources prospecting. Academic or commercial permits for biodiversity prospecting will be issued by an Interagency Committee on Biological and Genetic Resources based on written proposals. These agreements will set limits on the quantities of sample; require deposit of voucher specimens in Philippine institutions; require recognition of rights of indigenous communities; stipulate payments of royalties in case of commercial development; require participation of Filipino scientists in the collection of specimens; and encourage participation of Filipino scientists in the technical development process.

On October 22, the morning began with a special invited lecture by M. E. Wall (Research Triangle Institute) on taxol and camptothecin. A round-table discussion followed the lecture; the text of the discussion will be included in the full proceedings in the *Journal of Ethnopharmacology*.

Commentary

As can be noted from the summaries of presentations above, many contrasting viewpoints were expressed concerning the central theme of the conference—the fair and equitable sharing of the benefits of bioprospecting. These contrasting opinions are produced by several factors. Cultural and political diversity among the peoples of the world, especially those populations in developing countries, create differing perspectives on ownership, value, and responsibility to the wider human community. Also, the undue focus on discovery, development, and commercialization of pharmaceuticals as the exclusive product of exploitation of genetic resources clouds and confuses much of the debate and negotiation over access to resources wherever they are found. It should be noted that if commercial product discovery and development is the only gauge of value and successful outcome from bioprospecting, then academic programs and programs in research institutions would all be viewed as failures by definition. Rather, it is important to recognize that other significant outcomes are possible, especially in the areas of capacity building (education and training) and technology transfer.

The efforts to harmonize national and international laws and conventions as exemplified by the Rio Convention on Biodiversity and the GATT agreement will strongly influence the nature and terms of bioprospecting agreements. Similarly, individual company, country, institution, and scientist views of what constitutes "ethical" behaviors as well as fair and equitable sharing will influence the terms and conditions of agreements affording access to genetic resources. As is true in all relationships, the success of these agreements will depend on many factors: the flexibility and knowledge of the partners, the level of trust between the partners, current and future technologies, and certainly national and international laws, conventions, and policies. Because of all these factors, and because of the confidential nature of such agreements, it is not likely that a single model or framework will emerge as a standard. Instead, the specific needs and desires of the prospective parties to specific agreements must be recognized and accommodated if a productive partnership is to be established.

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