

# Early Lessons for the International Cooperative Biodiversity Groups

## BIODIVERSITY AND HUMAN HEALTH

*Edited by*

**Francesca Grifo and Joshua Rosenthal**

*Foreword by*

**Thomas E. Lovejoy**

The implications of biodiversity loss for the global environment have been widely discussed, but only recently has attention been paid to its direct and serious effects on human health. Biodiversity loss affects the spread of human diseases, causes a loss of medical models, diminishes the supplies of raw materials for drug discovery and biotechnology, and threatens food production and water quality.

■ ***Biodiversity and Human Health*** brings together leading thinkers on the global environment and biomedicine to explore the human health consequences of the loss of biological diversity. Based on a two-day conference sponsored by the National Institutes of Health, the National Science Foundation, and the Smithsonian Institution, the book opens a dialogue among experts from the fields of public health, biology, epidemiology, botany, ecology, demography, and pharmacology on this vital but often neglected concern.

Contributors discuss the uses and significance of biodiversity to the practice of medicine today, and develop strategies for conservation of these critical resources. Topics examined include:

- the causes and consequences of biodiversity loss
- emerging infectious diseases and the loss of biodiversity
- the significance and use of both prescription and herbal biodiversity-derived remedies
- indigenous and local peoples and their health care systems
- sustainable use of biodiversity for medicine
- an agenda for the future

The book provides a common framework for physicians and biomedical researchers who wish to learn more about environmental concerns, and for members of the environmental community who desire a greater understanding of biomedical issues.

If you would like to order the entire book, please contact the publisher: Island Press, Inc.

## ■ CHAPTER 13

### **Integrating Drug Discovery, Biodiversity Conservation, and Economic Development: Early Lessons from the International Cooperative Biodiversity Groups**

#### ■ JOSHUA ROSENTHAL

Biodiversity prospecting offers a valuable opportunity to directly address one of the most important relationships between biodiversity and human health - our dependence on nature for medicine. Drug discovery from natural products, if appropriately designed and carried out, can provide economic incentives for the conservation of the diversity of plants, animals, and microorganisms on earth. While natural products drug discovery has a long history (see Laughlin and Fairfield, Chapter 7; Grifo et al., Chapter 6), the idea that this process could yield conservation and development benefits is relatively new. This integrated approach, commonly known as "bioprospecting," has received a great deal of attention in recent years as a potential tool for conservation (for examples see Reid et al. 1993; Eisner and Beiring 1994; Endangered Species Coalition 1995; Goering 1995). Statements regarding the importance and potential of bioprospecting have become common in the conservation organizations and many governments. Bioprospecting is also a major concern of the United Nations Convention on Biological Diversity. However, despite widespread interest in the concept, significant attempts to carry out fully integrated bioprospecting projects have been very few.

The International Cooperative Biodiversity Groups represents a novel experimental program that is one of the first large-scale attempts to design and execute such a multidisciplinary approach to drug discovery. The program was designed to stimulate the field of bioprospecting, to gather evidence on the feasibility of bioprospecting as a tool for conservation and economic development, and to provide models for its future development. In addition to these ambitious goals, it is hoped that the program will provide insight into important scientific questions regarding the relative efficiency of different scientific modes of drug discovery from natural products. Finally, in the spirit of the United Nations Convention on Biodiversity, the program aims to promote equitable sharing of benefits that flow from both the research process and its potential commercial products. This final goal also represents an important experimental effort for which there are few models in existence.

In the first two and a half years of work the International Cooperative Biodiversity Groups (ICBG) have made significant progress toward several of these long-term goals, and some valuable lessons have been learned regarding benefit-sharing and the requirements of international partnerships. Here I provide a brief overview of the program and the groups that are carrying out this pioneering work, followed by a summary of their progress to date in several areas. I will also describe some of the lessons that have been learned during the establishment and early work of the groups.

#### ■ International Cooperative Biodiversity Groups

##### ■ *History, Goals, and Program Structure*

In 1992 three agencies of the U.S. Government - the National Institutes of Health (NIH), the National Science Foundation (NSF), and the U.S. Agency for International Development (USAID) - launched the International Cooperative Biodiversity Groups program. The goals and design of the program were based on recommendations that emerged from a jointly sponsored and widely attended conference held the year before in Washington, D.C. (Schweitzer et al. 1991).

The ICBG program is based on the premise that appropriately designed natural products research and development can bring both short- and long-term benefits to the countries and communities that are the stewards of genetic resources [Schweitzer et al. 1991; Grifo 1996]. Sharing benefits from both the

research process and from any drug discoveries that are made down the road creates incentives for conservation and provides alternatives to destructive use.

The program has three principal goals that reflect the mandates of its three government agency sponsors. The first is to improve human health through the discovery of new therapeutic agents to treat diseases of importance to both developed and developing countries. This includes the preparation of crude materials, bioassay testing, chemical isolation, and preclinical evaluation of agents from natural sources to treat or prevent cancer, infectious disease including AIDS, cardiovascular diseases, malaria, mental disorders, parasitic infections, and other diseases.

The second goal is to conserve biodiversity through valuation of diverse biological organisms and the development of local capacity to manage these natural resources. This goal encompasses creating incentives at all levels for the preservation of intact habitat; increasing the knowledge base upon which conservation activities are based; and developing long-term ecological and economic strategies to ensure more sustainable harvesting of targeted organisms.

The third goal of the program is to promote sustainable economic activity in less developed countries by sharing the benefits of the drug discovery and conservation research processes. This is accomplished in part through benefit-sharing agreements that use novel contractual arrangements to ensure an equitable financial return to the host country, group, or organization that facilitates the drug discovery process. In addition, support for research and capacity-building targeted toward the needs of the source country or countries represented within the group fulfill this goal.

Each of the International Cooperative Biodiversity Groups is a consortium of academic institutions, local and international private voluntary organizations, and in most cases a private pharmaceutical company. One or more of the partner organizations of each ICBG is based in the source country. The Groups are run by an academic principal investigator, who directs his or her own program in natural products chemistry, drug development, or ethnobiology and coordinates the activities of several associate programs. Each associate program is charged with one or more of the basic missions of the ICBG - biodiversity inventory, collection and conservation, screening and chemistry, drug development, and economic development. Training and other local capacity-building efforts are usually part of each of the associate programs. The awards that fund the groups are in the form of cooperative agreements, rather than grants. This means that the U.S. Government has continued involvement in the projects through scientific advisory committees that include representatives from each funding agency. The Fogarty International Center of the NIH manages the program and provides policy advice to the groups.

Equitable research and benefit-sharing agreements are key to the conservation and development goals of bioprospecting. Because patent law is unable to reward stewardship of biodiversity and traditional knowledge (Greaves 1994; Mays and Mazan 1996), contractual agreements that guarantee that benefits will flow from the research process and its potential products provide a crucial incentive mechanism to stimulate conservation of these endangered resources [Grifo and Downes 1996; Iwu 1996; Rosenthal (in press)].

Applicants for the ICBG awards were given a description of program goals and intellectual property principles to use in the design of their research proposals and contractual agreements. Formal written agreements that govern treatment of intellectual property and benefit-sharing were required of all applicants prior to making an award. The funding agencies are generally not party to the ICBG research and benefit-sharing agreements. As a result, the U.S. Government representatives are prohibited by federal statute from stipulating terms or structures of those agreements. Rather, the funded parties were asked to develop workable agreements to fit the nature of the organizations, countries, communities, and resources involved, within the general framework of the program's principles.

The ICBG Request for Applications (RFA TW-92-01) and other background papers (Schweitzer et al. 1991; Grifo and Downes 1996; Grifo 1996) describe these principles in detail. In general, they require that

full disclosure and informed consent are carried out, that both near- and long-term benefits are shared with appropriate source country communities and organizations, that pertinent international and local laws are followed, that local customs are respected, and that credit is given to local indigenous or other intellectual contributors whenever possible. This approach to intellectual property and contractual agreements is also an experiment from which valuable lessons may be learned.

### ■ **ICBG Awards**

In September of 1993 and 1994, following a multidisciplinary peer review of 34 competitive proposals, five groups were selected for funding at an annual level of \$400,000 to \$500,000 per group, with an expected duration of five years.

*Dr. David Kingston* of Virginia Polytechnic Institute and State University (VPISU) is studying rainforest plants in Suriname, in collaboration with the Forest People of Suriname, Conservation International - Suriname, the National Herbarium of Suriname, the Missouri Botanical Garden, Bedrijf Geneesmiddelen Voorziening Suriname, and Bristol-Myers Squibb Pharmaceutical Research Institute.

*Dr. Jerrold Meinwald* of Cornell University is the group leader for the study of insects and related organisms from the dry tropical forests of the Guanacaste Conservation Area in Costa Rica, in conjunction with the Instituto Nacional de Biodiversidad (INBio) of Costa Rica, the Universidad de Costa Rica, and Bristol-Myers Squibb Pharmaceutical Research Institute.

*Dr. Barbara Timmermann* and colleagues of the University of Arizona are studying arid land plants in Latin America (Argentina, Chile, Mexico), in collaboration with the Instituto de Recursos Biológicos de Argentina, Universidad Nacional de la Patagonia, Pontificia Universidad Católica de Chile, the Universidad Nacional Autónoma de México, Purdue University, G.W.L. Hansen's Disease Center, and the Medical and Agricultural Divisions of Wyeth-Ayerst/American Cyanamid Co.

*Dr. Walter Lewis* of Washington University is group leader for ICBG research on plants that have been used medicinally for generations in Andean tropical rainforests of Perú. He is collaborating with several organizations of Aguaruna people under the leadership of the Confederacion de Nacionalidades Amazonas del Peru, the Universidad San Marcos, the Universidad Peruana Cayetano-Heredia, and Monsanto-Searle Co.

*Dr. Brian G. Schuster* leads a group from Walter Reed Army Institute of Research that is focusing on cures for parasitic diseases from rainforest plants of Africa (Cameroon and Nigeria). Their collaborators are the Smithsonian Institution, the Bioresources Development and Conservation Programme, the University of Yaounde in Cameroon, the Biodiversity Support Program, and Shaman Pharmaceuticals.

For more information on the initiation of the program and the review process that led to these awards, as well as details of the group members and their objectives, see Grifo (1996).

### ■ **ICBG Summary Progress and Development**

The first three ICBGs (Suriname, Latin America, Costa Rica) have now completed three years of research and development work. The last two ICBGs (Africa and Perú) are completing their second year of funding, but because of various delays in getting started both have completed little more than a year of research and development activity. All together they are working in 8 countries in Latin America and Africa: Costa Rica, Perú, Suriname, Chile, Argentina, Mexico, Cameroon, and Nigeria. I will summarize here some preliminary scientific and development activities of the groups, including biodiversity collections and screening, research methods, and local capacity-building efforts.

## ■ ***Biodiversity Collections and Screening Activities***

The initial steps in natural products drug discovery research involve the description, bulk collection, and biological screening of samples for activity (see Grifo et al., Chapter 6). In some projects plant collections are made in close coordination with shamans or other local informants. Following drying and extraction, the samples are run through a battery of bioassays, or screens, for potential activity in the therapeutic areas of interest.

Following initial screens, "positive samples" or "hits" undergo a very lengthy process of re-testing, re-collection, and biochemical analysis to ensure that a find is novel, sufficiently active, and biochemically manageable before it is pursued further. At each step most of the samples are eliminated, leaving fewer and fewer samples to study (see Artuso, Chapter 8). The decision to continue with a given sample involves numerous variables beyond those just mentioned. The strategic interests of the partners and the instincts of the investigators are two such variables that can be very important to the process. As a result, many samples that are eliminated continue to be valuable resources for future use by the source country partners as new partnerships form and advances in screening technology take place.

In their first two years, the five ICBGs collected over 3,000 bulk samples representing approximately 2,500 species of plants, insects, and mollusks. These samples produced approximately 7,500 extract samples, most of which have undergone initial testing. Collected samples have been examined in over 120 different bioassays reflecting a dozen disease areas, including cancer, AIDS, fungal, bacterial and viral infections, tuberculosis, malaria, leishmaniasis, heart disease, central nervous system and reproductive disorders, as well as several agricultural uses. All together, this represents over 100,000 separate screening events. These numbers represent primarily the activities of the first three ICBGs - Suriname, Costa Rica, and Latin America - which began more than a year before the Africa and Peru ICBGs.

When biological activity is detected and confirmed for a sample in at least one screen it is considered a positive hit. The hit rates among screening institutions vary widely depending upon the number and types of screens the group is running and their methods. To date, hit rates among the ICBGs range from 5 to 25% of the samples analyzed. Currently, approximately 350 samples are of continuing interest and approximately 35 are considered to be high priority leads for treatment of malaria, leishmaniasis, tuberculosis, drug-resistant bacterial infections, and central nervous system disorders. While a number of these leads currently look very promising, it is quite possible that none will lead to a new drug (see Artuso, Chapter 8; Grifo et al., Chapter 6).

## ■ ***Random, Biorational, and Ethnomedical Approaches to Drug Discovery***

The ICBGs use various combinations of three general methods of sample collection and drug discovery research - random, biorational, and ethnomedical. Traditional approaches to natural products drug discovery by chemists and commercial researchers generally begin with collection of samples of plants, fungi, insects, and other biological specimens. Collection is guided principally by the desire to sample the greatest diversity possible. This sampling method is frequently referred to as a "random" approach. Collectors tend to take most identifiable specimens that they encounter, in some cases with a modest bias toward taxonomic groups that are known to be chemically interesting. Biorational approaches to discovery utilize more detailed knowledge of the biology of the specimens. For example, a relatively undamaged plant in a forest in which most plants show considerable damage from insects may be more likely to contain potent chemicals. This approach may increase our efficiency in finding useful chemicals compared with methods that depend on random techniques alone (Eisner 1989). Similarly, many researchers have championed the use of ethnomedical knowledge from traditional societies as a more direct means of finding specimens of utility in developing modern therapies for important human diseases (Cox and Balick 1994; Lewis and Elvin-Lewis 1995; Conte 1996). Many traditional societies have highly evolved systems of herbal medicine that represent valuable, yet rapidly disappearing intellectual resources (see Cox, Chapter 9).

One eventual product of the ICBG program will be information regarding the comparative efficiencies of these approaches. While data to assess these issues are, at present, insufficient, several developments are worth noting.

The Costa Rica ICBG uses a biorational approach in focusing part of their collection and screening efforts on insects that display notable chemical ecology in their interactions with plants and predators. Recently, this group further extended this approach by recognizing the biological differences in the different parts of a given species and physically subdividing specimens of a given species into finer units prior to extraction and screening. This move was based on the knowledge that biologically distinct structures on one individual insect or plant frequently differ chemically as well. One insect species can be divided developmentally into egg, larva, pupa, adult, and it can be divided structurally into head, body, fecal product, etc. Products of the interaction of plants and insects, such as galls, may conceivably also differ chemically from either of their parent organisms.

Similarly, one plant can logically be divided into units such as leaves, flowers, fruits, twigs, stem bark, stem wood, root bark, and root wood. Separation of some of these parts is a component of the research approach of several of the ICBGs. The relative age of the structure as well as the degree and type of microorganisms infection it exhibits may also be potentially important variables for the initial screenings.

Sustainable use of these organisms requires that sampling practices make judicious use of structures and developmental stages that might injure the viability of the organism or its population (see Peters, Chapter 15).

Ethnomedical knowledge is utilized in different ways in four of the ICBGs. For at least some of the collections in the Africa, Suriname, and Perú ICBGs this knowledge is used explicitly to help guide the sample collection process, and in more limited ways during screening and subsequent chemical analyses as well. In the Latin America ICBG, ethnomedical knowledge is gathered primarily to help ensure preservation of that knowledge and maximize the potential of rewarding it with financial benefits, even if the link to the product is made after a discovery.

The Suriname and Perú ICBGs have explicit research designs that will attempt to provide data on the relative efficiency of ethnomedically based searches versus more random searches, although data are not yet available to assess this. The answers may depend, in part, on the measures of efficiency used. Number of species examined, collection time, and financial investment per hit, for example, are all reasonable measures depending upon one's interest.

While there have been a number of 'meta-studies' comparing ethnomedical to random and other approaches (Lewis and Elvin-Lewis 1995), it has been difficult to produce truly comparable samples. A precise study should control for geographical, seasonal, and other potential effects on the chemistry of the organisms being studied. One also needs to utilize the same or comparable bioassays. One organizational challenge to the ICBGs attempting this comparison is posed by the fact that large commercial partners continually modify and replace their assays. Because sample collection using ethnomedical techniques tends to be much more time consuming than random collections and does not necessarily involve reproductive specimens, coordinating the collection, identification, and testing of the two sample types is difficult.

Use of biological and ethnomedical information on the species being studied also poses some complex issues for control of the potential intellectual property it represents. Early disclosure of the identities and uses of the species being studied could weaken the control that source country partners have over that information (Laird 1994). Each of the ICBGs has chosen to deal with these issues in slightly different ways. Some of the ICBGs provide some of this information to their drug development partners with the samples, under strict confidentiality and limited use agreements. Others provide only numbered samples initially. In these arrangements, when a sample appears to be of interest, its species name is generally

released to research partners, with consent of all source country parties, to help ascertain if the active sample represents a novel compound.

### ■ ***The Numbers Game***

Irrespective of the collection approach, drug discovery from natural products is, in part, a number game (see Artuso, Chapter 8). Once a lead sample has been identified, skill and insight in natural products chemistry become important. But until that point, screening larger numbers of samples for a greater number of therapeutic possibilities and other uses generally increases the likelihood of finding a valuable lead.

Each of the ICBGs involves more than one institution in the screening process. The collaborating institutions within each group frequently arrange to use different bioassays and generally work in different therapeutic areas to maximize efficiency and avoid potential conflicts of interest. For example, the Latin American Arid Lands ICBG has four different institutions doing bioassays. The industrial partner has two divisions: Wyeth-Ayerst screens for a variety of medical uses and American Cyanamid is searching for agricultural and veterinary end uses. Simultaneously with that search, Purdue University is looking for generally bioactive compounds, the G.W.L. Hansen Center is looking for antituberculosis compounds, and the Universidad Autonoma de México is running cytotoxicity assays.

All of the ICBGs are facilitating the development of additional screening programs in the source countries with which they are collaborating. Where possible, the source country programs and those of other academic partners further enable work on diseases such as tuberculosis, malaria, and leishmaniasis that are rarely within the standard early screening portfolio of major pharmaceutical companies.

### ■ ***Biodiversity Information Resources***

A prerequisite for conservation and sustainable use of biodiversity is having information on the identity and distribution of the organisms within a habitat. The plants and insects collected for drug discovery research form only a part of that information gathering process for the ICBGs. Almost all fieldwork activities include collection and documentation of plants and animals throughout the region. Each ICBG is compiling preserved specimens in at least one institution in the source country and one in the U.S. for the development of resources for biodiversity research and management. This information is being recorded in geographic information systems and other computer databases in each country. In several of the ICBGs these databases complement other existing resources in the source countries (Costa Rica, Perú, Suriname ICBGs), and in others (Latin America and Africa ICBGs) entirely new systems have been created to manage ICBG data and make them available to managers. It is hoped that these databases will become more and more integral components of land use decisions within the country in the coming years.

### ■ ***Capacity-Building in the Source Country***

Long-term development of the scientific, commercial, and management capacity of source countries may be the single most valuable benefit of bioprospecting research and development work (Juma 1993; Baker et al. 1995; Ten Kate 1995). Capacity-building is a central component of all three goals of the program - drug discovery, conservation, and economic development. For the ICBGs, capacity-building means training, equipment transfers, and infrastructure development in collaborating institutions and communities.

ICBG trainees include source country technicians, graduate, postgraduate and postdoctoral students, and faculty. Training includes long-term and degree program work as well as short technical courses and workshops in biodiversity description and management and biomedical science. To date, over 135 students and technicians from at least 15 developing country institutions have received or are receiving

training in association with the ICBGs. These include numerous exchanges between the United States and host-country universities.

A few examples will illustrate the types of training involved. Two graduate students from Argentina are being trained at GWL Hansen's Disease Center in antituberculosis screening. A postdoctoral researcher from Cameroon is receiving long-term training at Walter Reed Army Institute of Research in natural products chemistry and anti-leishmania screening, as are several students and faculty in Perú. Several technicians in Suriname are being trained in the use of geographic information systems (GIS) to record biodiversity inventories and ethnobotanical information from the Amazon rainforest and its peoples. Parataxonomists are being trained in Costa Rica to identify and raise numerous species of insects in field conditions, interested community members in the Peruvian rainforest are being trained in ethnobotanical collection methods, and more than a dozen African biologists have completed a short course in ethnobotanical methods in Cameroon.

Equipment transfers to source country collaborators come both through government funding and directly from commercial partners. Laboratory equipment related to the preparation, extraction, storage, and microbiological screening of specimens is commonly transferred to the source country. Other equipment purchases include herbarium storage cases, computers, software, and field equipment to aid with biodiversity description and management. Infrastructure development efforts include vehicle purchases, renovation of laboratories, herbaria and a medical clinic, and improvements to a community-managed ecotourism lodge.

## ■ **Early Lessons from the ICBGs**

While the program is still too young to permit an evaluation of the effectiveness of bioprospecting for integrated drug discovery, conservation, and economic development, some valuable lessons can be learned from the experience that the ICBGs have gained in establishing their partnerships.

### ■ ***Benefits-Sharing***

Sharing the benefits of the process and product of drug discovery research with source country partners and communities is one of the central elements of the ICBG program. The types of benefits, the identities of the beneficiaries, and the development of benefit-sharing agreements are complex issues that the ICBGs are attempting to address. I will provide a short summary of some early lessons in this important area. More in-depth analyses can be found in Rubin and Fish (1994), Iwu (1996), Grifo and Downes (1996), and Rosenthal (in press).

The types of benefits that flow to source countries and communities from ICBG research and development include monetary and non-monetary benefits. It is important both to provide benefits in the near-term to help address acute needs and provide for long-term benefits that will help source countries develop options for resource use, while improving quality of life in a lasting way. Specifically, the types of benefits include advance payments, royalty earnings in the event of a commercialized product, capacity-building efforts, research on priority diseases or regions, and the establishment of collaborative relationships with long-term potential.

Advance payments are increasingly considered critical by source countries and communities. These offer a very attractive balance to the risk and delays associated with royalty earnings from bioprospecting ventures, and in some cases may result in a trade-off with royalty rates. In several of the ICBGs, source country partners have received advance payments. To date, these payments have been used primarily to establish trust funds for the disbursement of small community grants for development projects such as medicinal plant cultivation and marketing, for tool purchases, written educational materials, shaman apprenticeship programs, and travel and workshops to build alliances among local community leaders.

Royalty earnings, usually a percentage of income from a commercialized product, are often the initial focus in a discussion of benefits. The four ICBGs that have a commercial licensing option with a pharmaceutical partner all have specified terms or ranges for royalty earnings in their research and benefit-sharing agreements. The division of that royalty among the stakeholders is stipulated either in the same agreements or in associated agreements.

Royalty negotiations should always take place in the context of other elements of the agreements. Examples of such other elements are advance payments and periods of sample use exclusivity. The timing of the negotiations may also be important. Final negotiations of a specific rate after a strong product candidate has been identified may net the source country the best earnings. Whenever possible all parties should have expert technical, commercial, and legal counsel to draw upon during the discussions.

In addition to monetary rewards, partnerships can provide opportunities for numerous non-monetary benefits that in some cases may have a greater overall impact. As discussed above, capacity-building through training, equipment transfers, and the development of infrastructure to carry on biomedical research and to manage natural resources are fundamentally important benefits to be gained from bioprospecting partnerships. The ICBGs are also focusing research on diseases or geographical regions of importance to the source country, and in so doing are providing a benefit that addresses local priorities. Another important benefit is the development of long-term collaborations among workers and organizations both within and between countries (Iwu 1996).

The identification of appropriate beneficiaries is one of the most complex and important issues that the ICBGs have encountered. Individuals and communities, nongovernmental organizations (NGOs), and governmental organizations are identified variously in the ICBGs as potential beneficiaries for their efforts. The choices are guided by conservation and development objectives, fairness, local laws, concepts of intellectual property, and degree of participation.

Identification of appropriate and representative indigenous organizations has been a major challenge for the Peru ICBG. Amazonian societies are in a continuing process of political reorganization and realignment (Brown 1993). Overlay of this fluid political process on the profoundly difficult task of defining ownership of the intangible cultural resources represented in medicinal plant knowledge (Brush 1994) results in an extraordinarily complex job in identifying appropriate community beneficiaries. One useful tool is the establishment of a trust fund to disburse near- and long-term financial proceeds to worth projects initiated by community members (see Moran, Chapter 11). The benefits-sharing plan currently being developed by the Peru ICBG involves management of and access to its trust fund initially by the participating organizations and includes a mechanism by which all linguistically and geographically related communities can achieve access over the long-term.

### ■ ***Informed Consent, Negotiation of Agreements, and Consensus-Building***

While the principle of prior disclosure and informed consent is widely considered to be of fundamental importance today (Convention on Biological Diversity; Cunningham 1993; Missouri Botanical Garden 1996; Grifo and Downes 1996), the application of this principle to use of the tangible and intangible resources involved in bioprospecting is a relatively recent development, and a consensus on its meaning is as yet unclear. The concept of informed consent was originally conceived with regard to protection of the personal safety of human subjects participating in medical research (NCPHS 1979). Until recent years, informed consent in ethnobiological research was generally interpreted to mean verbal disclosure to the individual regarding the potential uses of his or her knowledge. Today, the possibility that financial benefits may result from this research necessitates complex arrangements with source communities and a very thorough information sharing process. Beyond in-depth discussions with local resource providers, this process can include sharing related contracts and facilitating legal advice during negotiations. It frequently also requires sharing project descriptions, lists of collections, and progress reports on research for review by the individuals, participating organizations, and national government authorities.

The ICBG program principles require that disclosure to source country participants be as complete as possible (Grifo and Downes 1996). The specifics of this disclosure process vary according to the cultural and economic context as well as the type of arrangements and resources involved. The process frequently involves all the information described above. Complete disclosure is frequently complicated by the fact that indigenous partners, researchers, and industrial partners all may have relevant information that they consider proprietary. This information usually consists of plant species names, localities, and uses, specific bioassay techniques and chemical compositions, and financial terms in contracts. Such information is usually treated as confidential and is shared regularly only with negotiating and signing partners to written agreements. When outside parties, such as authorizing government officials, require such proprietary information, they are frequently asked to sign confidentiality agreements to protect the interests of the partners.

A thorough disclosure and education process leading up to negotiation of agreements not only empowers local communities in the current partnership, but also trains them to directly evaluate the future themselves and to negotiate on their own terms. To date, NGOs and source country universities have played a major role in mediating the negotiation process in most of the ICBGs. In addition, efforts have been made to facilitate representation of the interests of indigenous partners by qualified legal counsel. The Perú ICBG is currently renegotiating its agreements in a precedent-setting fashion, with more direct discussions between indigenous organizations and commercial partners than, to our knowledge, has been the case in other bioprospecting partnerships.

The principle of disclosure and informed consent, broadly interpreted, can also be a valuable tool for building consensus among stakeholders. Public workshops involving representatives from potential indigenous collaborators, government agencies, environmental NGOs, and researchers can simultaneously provide information, solicit input, and build consensus for the primary objectives of a project. Different versions of such workshops have now been held in all of the ICBGs. Ideally, workshops should take place prior to contract negotiation, allowing time for representatives to consult with their communities. Finally, consent from each and every individual that shares ethnomedical knowledge with ICBG researchers is obtained during the research phase of the projects. This last step also facilitates individual understanding and support for the project goals. Individuals realize that while much of their knowledge is communally derived, their participation and the biodiversity they depend on for their health (and in many cases their livelihood) have worldwide importance and potential financial benefits.

### ■ ***Established and Ongoing Presence in Source Communities***

An important prerequisite for effective design and implementation of integrated conservation and development projects is an established and ongoing presence of project-affiliated individuals and organizations in local communities (Brown and Wyckoff-Baird 1992). Such organizations and individuals can provide a direct link between the local and international components of the project. Conservation International-Suriname (Suriname ICBG) and the Bioresources Development and Conservation Programme (Africa ICBG) offer useful models in this regard. These are organizations with community-based approaches to conservation. They are staffed and managed by source country nationals, but have strong ties to international partners.

A previously established organization run by source country nationals is most likely to understand national and local health, biodiversity, and development priorities. Furthermore, it may have credibility among the local community members and can help them to formulate their economic, cultural, and other concerns into specific terms during the design, research, and development phases of the project. Such an organization can also communicate the objectives and concerns of the other partners to the local participants. Bioprospecting researchers, usually taxonomists, ecologists, chemists, and physician, may not adequately fulfill the community role, even when they are source country nationals. The professional interests and obligations of researchers, and often their cultural backgrounds, tend to restrict them to relatively brief, infrequent, and focused stays in the communities.

Lastly, a focus on defined areas and communities is critical to progress toward conservation and development objectives. The Latin America ICBG, working simultaneously in Chile, Argentina, and Mexico, has an outstanding drug discovery program. However, because of the broad geographical focus and the distance of the U.S.-based conservation and development team from the region, the design and implementation of adequate conservation and development activities have proceeded much more slowly. The group recently held workshops in Buenos Aires and Santiago to help focus these activities and has reorganized its conservation and development efforts under the direction of local institutions.

### ■ **Source Country Infrastructure and Legal Environment**

To take advantage of the possibilities that bioprospecting offers it will be extremely important for governments to facilitate development of institutional capacity and define access legislation. Minimally, governments should define which institution has the authority to issue collection permits and what, if any, its role is to be in the scientific and commercial aspects of research and development. This is taking place in many countries as they work to implement the Convention on Biological Diversity and define their policies with regard to international trade in genetic resources.

The Instituto Nacional de Biodiversidad (INBio) of Costa Rica has established a leading role for source country institutions in the field of bioprospecting due in large part to the outstanding scientific support and well-defined policies of the institution and the national government. These advantages make it a desirable partner to international researchers and pharmaceuticals companies, and a promising associate in competitive grant applications. India's competitive position is reflected in its association with one of the five ICBGs and two of the recent BOA small grants (discussed in the next section). INBio may not be an appropriate model for all source countries, however, because it works only in government-controlled national parks that do not have large indigenous populations. However, its early successes highlight the importance of a relatively streamlined and stable bureaucracy, as well as technical and commercial sophistication. When international partners seek to carry on bioprospecting work in Costa Rica they most often work directly with INBio, which coordinates the technical details of sample collection and identification where necessary, as well as the contracts and collection permits.

Optimum legislation reduces the uncertainty of scientific and commercial collaborations and stimulates innovative approaches to integrated research and development projects. Legislation that guarantees that adequate benefits accrue to source country partners will facilitate capture of the opportunities that biodiversity prospecting offers.

The ICBG program is currently affecting policy and legislative events in many countries. The governments of Suriname, Perú, Chile, Argentina, and Cameroon are directly utilizing their ICBG experience during the formation of their own resource management and genetic resource policy development. The program also provides a key example of efforts by the U.S. Government to comply with the principles of the United Nations Convention on Biological Diversity even before the treaty has been ratified by the U.S. Senate. In addition, the program has been a case-study for the Organization for Economic Cooperation and Development (OECD) Working Group on Economic Incentives for Conservation [Rosenthal (in press)].

### ■ **A Daughter Program - the Bioprospecting Opportunity Awards (BOA)**

Because of great demand for funding to carry out integrated bioprospecting and conservation research, the Fogarty International Center, in collaboration with the National Science Foundation (NSF), initiated a new small grants program modeled in part on the ICBGs. Following peer review of competitive application by NSF, four Bioprospecting Opportunity Awards (BOAs) were made in September 1995 to NSF grantees whose biodiversity studies could logically and efficiently be extended to include a chemical screening component. Funded projects include a study of tropical tree chemistry in Costa Rica as a source of environmentally friendly insecticides, a study of macro-fungi in Costa Rica for pharmaceutical potential; screening of tropical trees for pharmaceutical and agricultural potential in Panama; and one focused on

deep-sea thermal vent organisms as sources of novel pharmaceutical and industrial agents. It is not known at this time if funding for a second round of BOAs will be available.

### ■ **ICBG Funding**

In fiscal year 1995, total U.S. Government funding for the ICBG program from the three federal agencies (NIH, NSF, and USAID) was \$2.3 million. The NIH contribution was \$1.75 million, including contributions from the Fogarty International Center, the National Cancer Institute, the National Institute of Allergy and Infectious Diseases, and the National Institute of Mental Health. The NSF contributes one-half million dollars per year, as has USAID until this past year. Due to shifting priorities and diminishing resources USAID reduced its contribution to the ICBG program this past year, and future funding from that agency is in doubt. Groups are likely to receive smaller awards in the remaining two years of this cycle. Contributions to Groups from their private pharmaceutical partners to date exceeds \$400,000 of in kind investment in screening and chemistry, and at least \$200,000 in advance payments and equipment donations.

### ■ **Conclusion**

The International Cooperative Biodiversity Groups program was designed to catalyze and explore the widely cited potential of bioprospecting as a tool for drug discovery, conservation of biodiversity, and economic development. In its first two years of development, significant advances have been made toward scientific goals of drug discovery and basic chemistry and biodiversity inventory. Source country capacity-building has proceeded rapidly, and near-term financial benefits to communities have begun to flow.

Valuable lessons can be learned from its earliest efforts. The ICBGs have provided models for appropriate structuring of source-country benefits. The experiences have demonstrated the principled and pragmatic value of broad application of information disclosure and consent procedures. Furthermore, experiences have highlighted the importance of an established presence in source communities, as well as the competitive advantage of source countries with established research infrastructure and a clearly identified body with legal authority.

Clear guidelines by national governments and international bodies as well as additional public funds are important to the future of bioprospecting. Each of the ICBGs is challenged to develop its program in an uncertain, changing legal and political context. It is in large part the security of five years of ICBG funding that has offered the opportunity to explore scientific, programmatic, and commercial alternatives of biodiversity prospecting in its infancy. Governmental and other nonprofit sources of funding may continue to be important to obtain the full range of conservation and development benefits that bioprospecting offers. As the Convention on Biological Diversity is implemented around the world, and as working models are elaborated in this new field, the relative success of various approaches to biodiversity prospecting will emerge. In this context the ICBGs play a critical role in providing ambitious working models to help guide policy and program directions in the coming years.

### ■ **References**

Baker, J., R. Borris, B. Carte, G. G. Cordell, D. Soejarto, G. Cragg, M. Gupta, M. Iwu, D. Madulid, and V. Tyler. (1995). Natural Product Drug Discovery and Development: New Perspectives on International Collaboration. *Journal of Natural Products* 58: 1325-1357.

Brown, M., and B. Wyckoff-Baird. (1992). *Designing Integrated Conservation and Development Projects*. The Biodiversity Support Program - World Wildlife Fund, The Nature Conservancy, World Resources Institute. Landover, Maryland: Corporate Press, Inc.

- Brown, M. F. (1993). Facing the State, Facing the World: Amazonia's Native Leaders and the New Politics of Identity. *L'Homme* 126-128 XXXIII: 307-326.
- Brush, S. B. (1994). A Nonmarket Approach to Protecting Biological Resources. In: *Intellectual Property Rights for Indigenous Peoples: A Source Book* (T. Greaves, ed.), pp. 131-143. Oklahoma City: Society for Applied Anthropology.
- Conte, L. A. (1996). Shaman Pharmaceuticals' Approach to Drug Development. In: *Medicinal Resources of the Tropical Forest: Biodiversity and Its Importance to Human Health* (M. J. Balick, E. Elisabetsky, and S. A. Laird, eds.), pp. 94-100. New York: Columbia University Press.
- Cox, P. A., and M. J. Balick. (1994). The Ethnobotanical Approach to Drug Discovery. *Scientific American* June: 82-87.
- Cunningham, A. (1993). *Ethics, Ethnobiological Research and Biodiversity*. Gland, Switzerland: World Wildlife Fund for Nature.
- Eisner, T. (1989). Prospecting for Nature's Chemical Riches. *Issues in Science and Technology*, Winter: 31-34.
- Eisner, T., and E. A. Beiring. (1994). Biotic Exploration Fund - Protecting Biodiversity Through Chemical Prospecting. *BioScience* 44: 95-98.
- Endangered Species Coalition. (1995). *The Endangered Species Act: A Commitment Worth Keeping*. Washington, D.C.: The Wilderness Society.
- Goering, L. (1995). Rainforests May Offer a New Miracle. *Chicago Tribune*, September 12.
- Grifo, F. T. (1996). The Role of Chemical Prospecting in Sustainable Development. In: *Emerging Connections Among Biodiversity, Biotechnology, and Sustainable Development in Health and Agriculture* (Julie Feinsilver, ed.). Washington, D.C.: Pan American Health Organization.
- Grifo, F., and D. Downes. (1996) Agreements to Collect Biodiversity for Pharmaceutical Research: Major Issues and Proposed Principles. In: *Valuing Local Knowledge: Indigenous People and Intellectual Property Rights* (S. Brush and D. Stabinsky, eds.), pp. 281-303. Washington, D.C.: Island Press.
- Greaves, T. (1994). IPR, A Current Survey. In: *Intellectual Property Rights for Indigenous Peoples* (T. Greaves, ed.), pp. 1-17. Oklahoma City: Society for Applied Anthropology.
- Iwu, M. (1996). Implementing the Biodiversity Treat: How to Make International Cooperative Agreements Work. *Trends in Biotechnology* 14: 78-83.
- Juma, C. (1993). Policy Options for Scientific and Technological Capacity Building. In: *Biodiversity Prospecting* (W. V. Reid, S. A. Laird, C. A. Meyer, R. Gamez, A. Sittenfeld, D. H. Janzen, M. A. Golling, and C. Juma, eds.), pp. 199-222. Washington, D.C.: World Resources Institute.
- Laird, S. (1994). Natural Products and the Commercialization of Traditional Knowledge. In: *Intellectual Property Rights for Indigenous Peoples: A Source Book* (T. Greaves, ed.), pp. 145-162. Oklahoma City: Society for Applied Anthropology.
- Lewis, W. H., and M. P. Elvin-Lewis. (1995). Medicinal Plants as Sources of New Therapeutics. *Annals of the Missouri Botanical Garden* 82: 16-24.

Mays, T. D., and K. D. Mazan. (1996). Legal Issues in Sharing the Benefits of Biodiversity Prospecting. *Journal of Ethnopharmacology* 51: 93-109.

Missouri Botanical Garden. (1996). Natural Products Research Policy. Unpublished policy available upon request from MBG, St. Louis, MO.

NCPHS. (1979). The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. Research, National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research, Washington, D.C.

Reid, W. V., S. A. Laird, C. A. Meyer, R. Gamez, A. Sittenfield, D. Janzen, M. A. Gollin, and C. Juma. (1993). *Biodiversity Prospecting*. Washington, D.C.: Government Printing Office.

Rosenthal, J. P. (in press). Equitable Sharing of Biodiversity Benefits: Agreements on Genetic Resources. *OECD International Conference on Biodiversity Incentive Measures*. Cairns, Australia.

Rubin, S., and S. Fish. (1994). Biodiversity Prospecting: Using Innovative Contractual Provisions to Foster Ethnobotanical Knowledge, Technology, and Conservation. *Colorado Journal of International Environmental Law & Policy* 5: 23-58.

Schweitzer, J., G. Handley, J. Edwards, F. Harris, M. Grever, S. Schepartz, G. Cragg, K. Snader, and A. Bhat. (1991). Summary of the Workshop on Drug Development, Biological Diversity and Economic Growth. *Journal of the National Cancer Institute* 83: 1294-1298.

Ten Kate, K. (1995). *Biopiracy or Green Petroleum? Expectations & Best Practice in Bioprospecting*. Overseas Development Administration, London.