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DRUG DEVELOPMENT AND CONSERVATION OF BIODIVERSITY IN WEST AND CENTRAL AFRICA: A MODEL FOR COLLABORATION WITH INDIGENOUS PEOPLE

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ABSTRACT

The main focus of the African ICBG project is the establishment of an integrated program for the discovery of biologically active plants for drug development and biodiversity conservation, and at the same time ensure that local communities and source countries derive maximum benefits for their biological resources and their intellectual contribution. Although the project has three main sub-themes (biodiversity conservation, sustainable development and drug discovery), integration was emphasized from the conception of the program and has remained a fundamental point in the execution of various projects under this program. As a result, the African ICBG program differs in many ways from similar projects elsewhere. The African ICBG is a collaboration of the Walter Reed Army Institute of Research, Washington, DC (WRAIR), Bioresources Development and Conservation Programme (BDCP), the Smithsonian Tropical Research Institute, and nine other institutions in Cameroon, Nigeria and the United States of America. Scientists from the participating developing countries are involved in all aspects of the program so that information, principles and procedures developed during this work will be internalized in Africa and extended beyond the duration of the proposed project. The drug discovery component has yielded many lead compounds with potential for the treatment of malaria, leishmaniasis, trypanosomiasis, trichomonas, opportunistic infections, AIDS and other viral infections. Activity of some of the compounds is being optimized through chemical modifications.

Keywords: Africa, ICBG, drug development, malaria, leishmaniasis, antiviral, natural products, sustainable development, biodiversity conservation, intellectual property rights.

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HISTORICAL BACKGROUND/INTRODUCTION

West-Central Africa contains the largest moist equatorial forest on the continent, indeed the second largest continuous tropical rainforest in the world (3 million square km). The species richness of the region and its importance as a center for plant endemism make it a key global center for drug discovery based on biodiversity. This forest is vital for the well being of the communities who live in its shade. It also contains an enormous store of biodiversity, with over 80% endemism in the flora, and is home to charismatic mammals such as the gorilla, chimpanzee and forest elephant. The need to conserve biological diversity is perhaps of utmost importance in Africa where the human lives are intricately linked to the environment in a symbiotic relationship in which one species cannot survive without the essential contributions from the other. Indeed, one of the greatest challenges facing the entire continent is how to facilitate economic development within the constraints of a rich but fragile environmental base. Bioprospecting using African genetic resources, if properly implemented, could provide the necessary incentive for conservation while yielding socioeconomic benefits to local

communities. Although rural forest dwellers have been stewards to the remaining tract of forest resources, people who live closest to areas with the greatest biological diversity count among the world's poorest communities.

Pharmaceutical development from botanical resources in the forested areas offers great potential for contributing to sustained economic growth if the local citizens themselves are directly involved in managing the exploitation of the resources, and are ensured a direct economic return from discoveries that are made as a result of the project. The return of benefits is an important incentive for further conservation. Therefore, there is an urgent need to conserve tropical forests as biological resources in order to ensure the future availability of the known as well as the yet undiscovered medicinal substances. There is also a critical need to conserve and maintain the genetic diversity of our varied ecosystems as a safeguard against an unpredictable future, and to ensure their availability for future generations. The present plan is to develop the International Cooperative Biodiversity Group (ICBG) on Drug Development and Conservation of Biodiversity in West and Central Africa as an embodiment of strategies for the use of forest resources in an environmentally friendly and sustainable manner.

It is equally important to address the health needs of those in developing countries. According to the World Health Organization, over 3.5 billion people in the developing world rely on plants for health care (Iwu et al., 1997). The study area in the African ICBG is currently facing an accelerated shift from a traditional setting to a modern society. The African traditional culture has a balanced relationship between nature, culture and religion that favors the judicious use of natural resources. In African ethnomedicine, the healers use medicines from local plants, minerals or animal substances; prescribe special exercises, incantations, dances or music; sacrifices and purifying rituals, all to reflect the beliefs of their community and what being healthy really means (Iwu, 1993). Man is considered part of the environment and should be content with adaptive existence rather than conquest of his habitat. The totems, taboos and other prohibitions are essential for the protection of various exotic species of plants and animals. Certain springs and waterways, forests, caves and burial grounds are deemed sacred and protected from human activities. While it is correct that most of the taboos and restrictions have religious significance, most of them are based on collective decisions of the elders who were respected for their accumulated wisdom and knowledge. There is a strong sense of communal responsibility which demands the subjugation of the individual's needs to that of the larger group (Iwu, 1993).

In 1992, the Rio Earth Summit provided a framework for the recognition of the special role played by local communities in the conservation of biodiversity and the sustainable utilization of biological resources for economic growth. Agenda 21, which was signed by over 150 heads of states and governments, stresses the need for fundamental change in political, social, economic and industrial systems in order to integrate social equity in development projects (Iwu, 1996). One of the most important outcomes of the Earth Summit is the Convention on Biological Diversity (CBD), which addressed the issues of identification, conservation and sustainable use of biodiversity. The fundamental frameworks outlined in the Convention were already reflected in an existing collaboration between the Bioresources Development and Conservation Programme and the Division of Experimental Therapeutics of Walter Reed Army Institute of Research. The main investigators in this project were Drs. Brian Schuster, Joan Jackson and Maurice Iwu. The collaboration sought to link institutions in Africa with WRAIR in Washington, DC with the twin objectives of developing drugs for parasitic diseases and building capacity in Nigeria for future joint projects. In 1994, the objectives of this collaboration were expanded to include some of the issues raised by the CBD and Agenda 21, and to fulfil the conditions of the Request for Applications issued by the National Institutes of Health (NIH), National Science Foundation (NSF) and U.S. Agency for International Development (USAID) for the ICBGs. The collaboration was expanded to include the Smithsonian Institution and other institutions in the United States and later to include institutions in Cameroon.

The expanded consortium retained the values established and defined by the earlier collaboration and made an ambitious long-term commitment to shift from a project-by-project research management scheme to a programmatic approach in which the goal is an integrated resources management program that will include drug discovery, economic development and biodiversity conservation. A key element of the strategy is the integration of scientific research, product development and socioeconomic development as a single, coherent endeavor that ensures equitable distribution of the benefits derived from the exploitation of biological resources. This approach presented enormous challenges in that there was often not a practical endpoint

that could be achieved within the relatively short periods of a research award. Our ever-expanding program goals and approach did not fit well into the usual agreements for bioprospecting and the expanded consortium was unable to interest a major corporate partner to join its application to the Fogarty International Center for the ICBG. One of the unique features of this ICBG is that the emphasis is on discovery and development of compounds for tropical diseases such as malaria, leishmaniasis and other parasitic infections rather than only for the treatment of diseases of global importance such as cancer, AIDS and metabolic disorders. The program is committed to the development of low-cost phytomedicines, in addition to the isolation of lead compounds for drug discovery.

Finally, the ICBG-Drug Development and Conservation of Biodiversity in West and Central Africa aims to demonstrate that sustainable drug development is a viable alternative to the common destructive activities such as timber harvesting, as a source of forest income for local communities.

PROJECT DESCRIPTION

Scope and Objectives

The ICBG-Drug Development and Conservation of Biological Diversity in West and Central Africa has as its primary aim the development and implementation of an effective and constructive resource management and conservation plan based on an intimate understanding of the key factors driving medicinal plant use and loss of biodiversity. The key idea is to increase the net worth of the tropical forest as a living resource and to show the feasibility of strategically using drug development as a catalyst for biodiversity conservation. The ICBG is a highly integrated team which involves scientists from the participating developing countries in all aspects of the program so that lessons learned from this project can be internalized in Africa and continued even after the end of the proposed project.

The objectives of this ICBG are to:

- Establish and maintain an inventory of species used in traditional medicine.
- Collect, chemically analyze and perform testing of plant samples for biological activity.
- Identify lead compounds for the treatment of human diseases – parasitic, fungal, viral, opportunistic infections, AIDS.
- Establish and maintain study plots for long-term assessment of rainforest ecological dynamics.
- Conduct economic value assessment of major species in the host countries and study area.
- Train scientists and technicians from participating countries in various aspects of drug development, plant ecology and taxonomy, chemistry, biology, phytomedicine, biotechnology, informatics, intellectual property rights, economic value assessment and community development.

The main thrust of this plan was the establishment of a consortium of collaborating scientists who will actually do both the discovery of lead plants and the development of active molecules into drugs. Selected plant products will be developed to preclinical stages before negotiation with the commercial partners.

The key institutions and organizations collaborating in the current African ICBG include the Division of Experimental Therapeutics of the Walter Reed Army Institute of Research, Bioresources Development and Conservation Programme (BDCP), the Smithsonian Institution, University of Dschang (Cameroon), Pace University New York, Southern Research Institute (Alabama), University of Utah, University of Miami, University of Minnesota, Florida State University, International Center for Ethnomedicine and Drug Development (Nigeria), and University of Jos, Nigeria.

The African ICBG has the following distinguishing features:

- It is one of the largest ICBG programs. There are more than ten different institutions, contributing 30 active investigators to various aspects of the project.
- Unlike other ICBG projects, this ICBG has its drug development expertise and resources in the parent organization (WRAIR). In this way, the aim is to establish a consortium of collaborating scientists who will actually do both the discovery of lead plants and the development of active molecules into drugs.
- Selected plant products will be developed to preclinical stages, prior to negotiation with the commercial partners.
- The compensation and benefit-sharing plan is based on deriving maximum benefits from the *process* of drug discovery, rather than relying mainly on the promise of future royalties that may never materialize. In this way, benefits are delivered both immediately and over time.
- The benefit sharing plan ensures that the interests and needs of various stake-holders in the source countries are addressed. A trust fund has been established by the source country scientists, traditional healers, community leaders and the national

government to ensure an equitable distribution of the benefits.

- The main target therapeutic categories for this project are tropical diseases such as malaria, leishmaniasis and trypanosomiasis. In this way, the scientific expertise held in the involved laboratories and pharmaceutical companies can be applied to the under-researched diseases of highest concern to the indigenous people (our collaborators).
- The ICBG program is not the beginning of an international scientific research project, but represents the expansion and elaboration of an existing collaboration between U.S. and African scientists.

Organizational Structure

The organization of the African ICBG provides for six Associate Programs (AP) each with a specific scope of work (Fig. 1 and Table 1):

Associate Program 1 (AP-1): Biodiversity Conservation
This AP is responsible for the establishment of biodiversity plots, conducting detailed assessments of the biodiversity of West-Central African forests, inventory and assessment of the dynamics of these forests. AP-1 provides intensive training in plant taxonomy, collection techniques, biodiversity monitoring, data analysis, environmental management and leadership for local students and natural resource technicians. The program enhances the infrastructure of local organizations by providing herbaria, computer facilities and other support. Strategies for the sustainable harvesting or cultivation of economically important species and advice to policy makers and forest managers on conservation issues is also being pursued. Institutions involved in AP-1 are the Smithsonian Institution Center for Tropical Forest Science (CTFS); the Smithsonian Institution Man and the Biosphere Program (SI-MAB); the Bioresources Development and Conservation Programme

Table 1. ICBG institutions.

Associate Program 1
Leader: E. Losos
Smithsonian Institution Center for Tropical Forest Science (CTFS)
Smithsonian Institution Man and the Biosphere Program (SI-MAB)
Bioresources Development and Conservation Programme (BDCP)
Korup National Park, Cameroon
Cross River National Park, Okwangwo, Nigeria

Associate Program 2
Leader: J. Ayafor
University of Dschang, Cameroon
School of Pharmacy, University of Pittsburgh, PA
Division of Nuclear Medicine, University of Minnesota, MN
International Center for Drug Ethnomedicine and Drug Development, Nsukka, Nigeria
African Scientific Cooperation on Phytomedicine and Aromatic Plants (ASCOPAP)
University of Buea, Cameroon

Associate Program 3
Leader: W. Milhous
Walter Reed Army Institute of Research (WRAIR)

Associate Program 4
Leader: J. Jackson
Walter Reed Army Institute of Research (WRAIR)
Haskin Laboratories, Pace University, NY
College of Veterinary Medicine, University of Georgia, Athens, GA

Associate Program 5
Leader: M. Iwu
Bioresources Development and Conservation Programme (BDCP)
International Center for Drug Ethnomedicine and Drug Development, Nsukka, Nigeria.
School of Pharmacy, University of Jos

Associate Program 6
Leader: B. Schuster
School of Pharmacy, University of Utah
Southern Research Institute, Alabama
School of Medicine, University of Miami
MDS-Panlabs/ Theta laboratories, WA
Dept. of Biological Sciences, Florida State University
International Center for Drug Ethnomedicine and Drug Development, Nsukka Nigeria
TAACF
NIAID

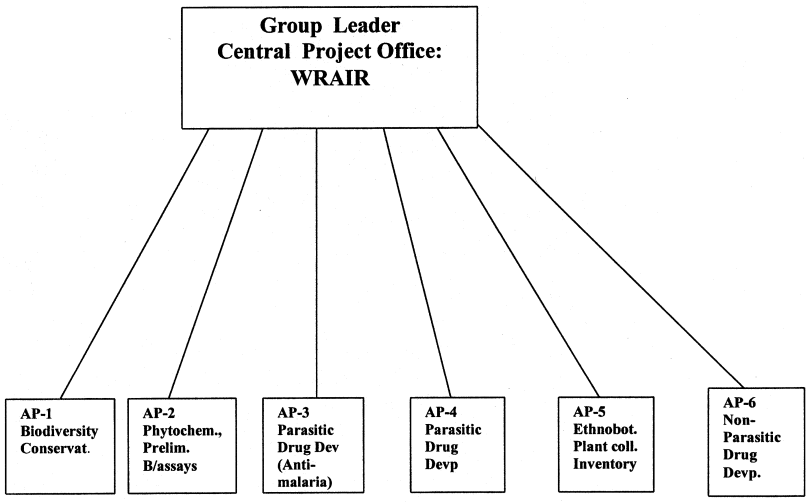

Fig. 1. Administrative structure.

(BDCP) Cameroon and Nigeria; the Korup National Park, Cameroon and the Cross River National Park Okwangwo, Nigeria.

Associate Program 2 (AP-2): Phytochemistry and Preliminary Bioassays

Activities of this AP include: identifying and characterizing the biologically active constituents of plants used as remedies in African herbal medicine; structural elucidation and optimization of selected lead compounds with potential for human health in Africa; training a cadre of young African scientists in natural products chemistry and synthetic medicinal chemistry; extraction of selected medicinal plants and initial bioassay screens of extracts; bulk extraction and bioassay-guided fractionation. AP-2 also maintains an inventory of extracts, their distribution and their status in the test systems. The development of phytomedicines for domestic marketing and of a database of phytomedical information that will be linked with the databases of ecology and ethnobotany from other APs are all part of AP-2. The key institutions in this AP are: University of Dschang, Cameroon; University of Pittsburgh; University of Minnesota and International Center for Ethnomedicine and Drug Development, Nsukka Nigeria.

Associate Program 3 (AP-3): Antiparasitic Drug Development (Antimalaria)

AP-3 is involved in *in vitro* and *in vivo* antimalaria studies, focusing on hypothesis-driven mechanism of action research and training. The institutions involved are the Walter Reed Army Institute of Research and the International Center for Ethnomedicine and Drug Development (InterCEDD), Nigeria.

Associate Program 4 (AP-4): Antiparasitic Drug Development

This AP oversees the drug discovery efforts for leishmaniasis, trypanosomiasis and trichmonas. In addition to *in vitro* and *in vivo* screens, AP-4 also provides post-doctoral training to African scientists and laboratory demonstration programs for students in the United States. The Walter Reed Army Institute of Research, Pace University and the University of Georgia are the main institutions involved.

Associate Program 5 (AP-5): Ethnobiological Inventory, Economic Botany and Plant Collection

This AP functions as the major African facilitator for the ICBG and provides logistic support to other Associate Programs. AP-5 is pivotal in developing plant selection and collection strategies for drug discovery.

AP-5 is responsible for the ethnobiological inventory of plants in the selected study areas and the Computerized Information System on African Medicinal Plants (CISAMAP) to maintain and expand the database on African medicinal plants which includes information on local names, traditional uses, floristic data, possible constituents, conservation status, agronomic data and economic value. They conduct socioeconomic value assessment (SVA) of the biological resources in the study area to highlight the non-commercial value of forest products within the cultural/religious context. AP-5's SVA program quantify the economic value of biological resources for comparison with other land use options, place in priority order the production and marketing of biological resources in local markets to provide income for local residents and provide baseline data for the for-

mulation of a sustainable management plan for the forest resources.

This AP assists with the training of West African scientists in the areas of ethnobiology, inventory, field taxonomy, research management and economic value assessment for local communities. They also train local natural resource managers and users at the national and community levels to conduct economic and market research, which will integrate the connection between conservation and development.

AP-5 was instrumental to the establishment of the Fund for Integrated Rural Development and traditional Medicine (FIRD-TM). This AP organizes rural farmers to cultivate, in fallow areas, certain plants of potential therapeutic value. The Bioresources Development and Conservation Programme (BDCP), the International Center for Ethnomedicine and Drug Development (InterCEDD), Nigeria and the University of Jos, Nigeria are the primary institutions involved in AP-5.

Associate Program 6 (AP-6): Non-parasitic Drug Development (Antiviral, Anticancer and Opportunistic Infections)

AP-6 activities include *in vitro* and *in vivo* antiviral studies; *in vitro* antineoplastic screening and biochemical assays. This AP oversees screens for: HIV, cytotoxicity, opportunistic infections, tuberculosis, cystic fibrosis and CNS activities as well as post-doctorate training. The Walter Reed Army Institute of Research, the University of Utah, Southern Research Institute, MDS-Panlabs, the International Center for Ethnomedicine and Drug Development, Florida State University, the Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF) and National Institute of Allergy and Infectious Diseases (NIAID) are the institutions involved.

PROGRAM ACTIVITIES

Drug Development

Four basic methods are generally utilized in the selection of plants to be investigated for biological activity. These are: 1) random selection of plants followed by mass screening, 2) selection based on ethnomedical uses, 3) leads from literature searches and review of databases, and 4) chemotaxonomic approaches. Most drug development programs based on natural products utilize one or two of these methods to select plants for investigation. Our ICBG team has developed a customized approach that involves a carefully designed ethnomedical survey, followed by a chemical and biological profile of plant candidates, and finally, integrating the results with information from literature and

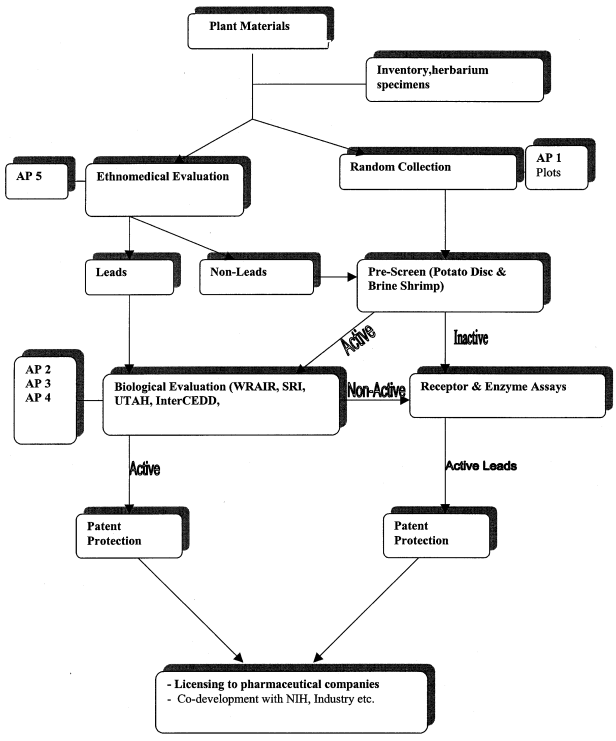

Fig. 2. Sample distribution and tracking scheme.

chemotaxonomic evaluation to generate a highly selective prioritized list. This method has been tested to a limited scale in the search for new antimalarial, antileishmanial and antiviral drugs. In each case the correlation factor was more than 85%.

In the drug development component of the program, the emphasis is on the identification of new therapeutic leads over the broadest possible variety of plant sources as can be possible with the available resources. Compounds (not crude extracts) with remarkable biological activity would be co-developed with assistance from related drug development programs at the NIH or through the collaboration arrangement with pharmaceutical companies (Fig. 2). By this approach, value is added to the plant material before being offered to the commercial partners.

Development of Plant Selection Strategy

The selection of the plants to be investigated has been a point of emphasis in our program. We have relied on a method based on ethnomedicine, since it gave us a very high percentage of active leads after chemical analysis. It has been established that a high correlation does indeed exist between the pharmacological activity/clinical use of plant isolates and their established traditional use as herbal medicines (Iwu, 1995).

A working group is convened prior to any ethnographic field work to evaluate available information and to prepare a regional study on the epidemiology, traditional medicine, culture and ecology of the people and their environment. This pre-collection study also includes a thorough review of information on plants known to be used in the area as remedies. This involves using existing databases and information gathered from the consultant herbalists and local health officials.

An advisory team, consisting of botanists, medical doctors (western trained) and a pharmacognosist, then briefs the working group using case presentations of diseases identified in the epidemiology report. These case descriptions of specific diseases are presented to traditional healers or shaman. Photographs of diseases with readily visible symptoms are also utilized. The working group interviews the informants in a carefully pre-determined manner. In seeking information, emphasis is on the identifiable symptoms rather than diseases. The approach relies upon recognition of common signs and symptoms. Terms such as “malaria” or “cancer” are not utilized even when the informant is educated or familiar with the terms. As much as possible, only individuals with good knowledge of the area and who speak the local language are used.

Prescreens and Preliminary Bioassays

About 1000 plant samples are subjected to preliminary bioassays each year. About 200 of the most active extracts (or fractions/isolates) are tested against each disease category. Out of this number, the 25 most active extracts are selected for *in vivo* studies, tertiary screens and further development. Strict selectivity is required to ensure that only extracts with the greatest promise of containing therapeutically useful compounds are investigated. Three pre-screens are used for the initial selection. They are rapid, reliable and inexpensive and can screen a relatively large number of plant extracts at field laboratories. Automated and specific receptor binding assays then augment these screens and enzyme-based assays in the U.S. laboratories.

The pre-screens are:

Brine shrimp lethality bioassay (*Artemia salina*): a simple general bioassay to predict possible activity of crude extracts and isolates.

Potato disc bioassay: a test for detecting compounds with possible anticancer activity. It is based on the inhibition of crown gall, a neoplasm of plants induced by the bacterium *Agrobacterium tumefaciens*, in suitably prepared potato discs.

Antifungal bioautographic assay and microbial evaluation: Tests extracts against two fungi, two Gram-positive and two Gram-negative bacteria. Active extracts are selected for bioassay directed fractionation and active constituents can be identified rapidly in two steps.

The results of the pre-screen are evaluated and extracts directed to the appropriate secondary biological evaluations. The results from the primary and secondary screens direct the fractionation of active extracts. The active fractions are fractionated further to a highly active fraction that is separated chromatographically to obtain the active compound(s). Isolates with biological activity are subjected to spectral analysis (UV, IR, proton NMR, carbon-13 NMR and mass spectroscopy) and the determination of melting points, optical rotation, etc. Spectroscopic equipment is also used in the U.S laboratories.

Antimalaria

A total of 500 samples from plant materials used in traditional medicine for the treatment of malaria were extracted and submitted for *in vitro* activity against *Plasmodium falciparum* at the Division of Experimental Therapeutics, Walter Reed Army Institute of Research. About 70% showed remarkable activity. Twenty of these have been selected for further studies

by bioassay-guided fractionation. Twenty-three antimalarial compounds comprising 12 different chemotypes have already been isolated and characterized. Two plant families, Annonaceae and Apocynaceae, appear to be common ingredients in the preparation of traditional malaria remedies in West and Central Africa. As part of the plan for future work, other members of these plant families will be collected from the biodiversity plots and evaluated for antimalarial activity. One of the active compounds from *Cryptolepis sanguinolenta* showed a strong spectrum of activity against drug-resistant *Plasmodium falciparum* parasites. Chemical optimization of the above mentioned lead yielded sanguinoletine, which when compared to chloroquine, is only 10-fold less potent against the chloroquine-sensitive D6 strain but seven-fold more potent against the chloroquine-resistant W2 strain of *P. falciparum* in culture.

Twenty plant samples are undergoing *in vivo* antimalarial screening. From the evaluation of the bioassay data, we are focusing on five chemotypes. These isolates are currently being optimized by comparing their activity with that of related analogues in order to establish a structure-activity relationship.

Antileishmania

We have evaluated the antileishmanial activity of 130 extracts representing 52 plant species used in traditional medicine. About 39% of the extracts possess significant *in vitro* antileishmanial activity when compared to pentavalent antimonials. Ten chemically novel antileishmanial compounds were selected for future work based on their chemical class and lack of any obvious toxicity. These include *Dorstenia multiradiata*, *Olax viride*, pregnane glycosides found in *Dracaena manii*, β-carboline indole alkaloids isolated from *Picralima nitida*, and compounds derived from bioassay-guided fractionation of *Chasmathera dependens*, *Calliandra portoricensis* and *Cassyntha filiformis*. The compounds are currently being isolated in large quantities for *in vivo* bioassay.

Antitrypanosomiasis

Ten of the extracts tested for *Trypanosoma brucei* consistently gave *in vitro* IC_{50} values at or below 10 μg/ml and were considered sufficiently active to warrant testing of more purified extracts. Three extracts from *Picralima nitida* and two from *Aframomum meleguatta* showed strong *in vitro* activity on four strains of *Trypanosoma b. brucei* and three *T.b. rhodesiense* clinical isolates. Bioassay guided fractionation of *Afromomum aulocacarpus*, led to the isolation of an antitrypanosomal compound with a 10–15-fold increase in the activity of the parent extract. *Glossocalyx brevipes* similarly gave highly active alkaloid compounds with *in vitro* IC_{50} values < 1 μg/ml.

Antitrichomonas

Seven extracts showed activity against Trichomonas. These include three fractions from *Picralima nitida* and two extracts from *Aframomum meleguatta*. These extracts showed remarkable activity against two strains of *Trichomonas vaginalis* (both susceptible and resistant strains to metronidazole) and *Tritrichomonas foetus*. In the trichomonad screen, an extract of *Glossocalyx brevipes* was most active and had a MIC value of 0.0125 μg/ml.

Antiviral

Extracts were screened for activities against HIV, herpes, influenza and yellow fever viruses. Two plant extracts showed high potential activity against HIV. The most active constituent of one extract has been isolated and characterized. One of the plant isolates showed *in vitro* activity against Ebola virus. The active constituent has been identified as a non-toxic lactone.

Opportunistic Infections

Twenty-two extracts were tested against *Cryptosporidium* and *Toxoplasmosis* sp., two samples were found active for each organism. One of the active compounds from *Cryptolepis sanguinolenta* which showed activity against *Plasmodium falciparum* malaria was also active against *toxoplasmosis and cryptosporidium*. Further testing is being performed. We are also investigating for activities against tuberculosis.

A summary of our drug development leads is shown in Table 2.

Table 2. Summary of ICBG drug development leads.

Disease	Extracts tested	Activity (%)	Leads[+]
Malaria	500	343 (69%)	20
Leishmania	130	52 (40%)	6
Cytotoxicity	20	16 (80%)	5
Viral	30	16 (53%)	2
Trypanosomiasis	27	13 (48%)	3
Trichomonas	25	10 (40%)	7
Opportunistic infection:			
Cryptosporidium	22	7 (31%)	2
Toxoplasmosis	22	6 (27%)	2

[+]Isolated and characterized molecular leads.

Biodiversity Conservation

Training and One Hectare Biodiversity Plots

The biodiversity conservation project has established the first set of ten permanent (1 ha each) biodiversity monitoring plots in Cameroon and Nigeria. All plots show high species density and diversity that are comparable with plots in other tropical areas. The species density and diversity will be compared to the results from the 50-ha plot established in the Korup National Park, Cameroon. These 1 ha plots will enable the ICBG to determine the availability and hence the sustainability of the sourcing methods used for some of the medicinal plants used in the project area. The establishment of the plots is linked to on site training, which helps local communities to set-up similar plots in environmentally sensitive areas as Community Forest Areas (CFA).

Korup Forest Dynamic Plot

Korup National Park occupies 1259 km^2 in the southwest corner of Cameroon. The park is about 50 km inland in the Bight of Biafra and shares about 25 km of its western borders with the Cross River National Park in Nigeria. Elevation ranges from sea level along the Atlantic coastal region to 1079 m on Mount Yuhan near the center of the park. The 50-ha plot is located in tropical evergreen forest 1 km south of the Chimpanzee camp and 552 m above sea level. The terrain around the area is rugged with huge gneiss boulders and steep cliffs. KFDP is fairly flat in the middle and rises at both ends of the North-South axis. The central part of the plot lies in a valley and is traversed by a big stream through the middle flowing in an east-west direction. The variation in elevation and presence of the stream satisfied our goal to select an area heterogeneous both in terms of soil type, aspect, topography and vegetation type. The site was also considered to be typical of the forest found in the area.

In accordance with the Smithsonian Institution Center for Tropical Forest Science (CTFS) methodology, every stem $\geqslant$1 cm dbh is being mapped, measured, tagged and identified. The mid-line starting point for enumeration is located near a westward flowing river that runs through the center of the plot. Initial results offer an interesting representation of flora from the low-lying swampy areas to the rockier terrain. Generally, the forest in which the plot is located has an unbroken canopy at ~15–25 m with scattered taller emergents and the understory is dense with lianas and small stems. With 20.84 ha enumerated as of the end of 1998, the total number of stems censused was 138,875.

The botanical team classifies each individual flora to species, including juvenile and non-flowering adults. To ensure accuracy of the identifications, less than half are identified in the field. Voucher specimens of unidentified species within the plots and fertile specimens at the plot are collected and dried in the locally constructed drier at Chimpanzee camp and an electric dryer at KFDP headquarters. After the specimen are sorted to morphospecies, they are taken to our project herbarium for comparison with growing collections or if necessary to Herbier National du Cameroon, Limbe Botanic Garden, Missouri Botanical Garden or Royal Botanic Gardens, Kew.

Based on preliminary results of the KFDP census data, the ICBG will be monitoring over 300,000 individual trees and an estimated 500–600 species when the full 50 ha are completed this year. In addition to an extensive taxonomic inventory, the KFDP database will represent the most intensive resource on tree demography and distribution patterns for a single forest community in all of Africa. One of the most striking original findings is that Korup plot has quite a dense and diverse forest, largely due to the smaller-sized trees (1–10 cm dbh). Within the first hectare, there are 7502 trees $>$1 cm dbh. The density is very high compared to identical Forest Dynamics Plots in Panama (4880 trees/ha), Penninsular Malaysia (6700 trees/ha) and Ecuador (6000 trees/ha). With 283 species in the first hectare, species diversity in Korup probably falls near the middle in comparison with other Forest Dynamic plots. For example, the average hectare in Thailand has 97 species, in Panama 172, in Penninsular Malaysia 495, in Sarawak 581 and in Ecuador 603.

A trait of particular importance for our ICBG drug screening program is speciosity (or number of species) of genera and families within a community. A successful 'hit' from one plant species often leads our scientists to search for closely related species for screening. Speciosity within the KFDP compares favorably with other forest sites. In the first hectare, early results indicate that, of 7502 individuals, there are at least 48 plant families and at least 132 genera. The most speciose genera in 1 ha of the KFDP are *Cola* [Sterculiaceae] (11 species), Rinorea [Violaceae] (11), Beilschmiedia [Lauraceae] (10), Diospyros [Ebenaceae] (9), Memecylon [Melastomataceae] (6) and Drypetes [Euphorbiaceae] (5). The Anacardiaceae family is also speciose.

This ICBG and the Smithsonian Man and Biosphere Program have conducted two training courses on biodiversity measuring and monitoring. Ten plots have

been set up in Nigeria and Cameroon. The data from these plots have also been analyzed.

Sustainable Development

Socioeconomic Value Assessment (SVA)

To enable the countries to plan for sustainable management, a thorough economic assessment is needed of the ecosystem from which the botanical resources will be harvested. The ICBG SVA projects include: valuation of the resources related to pharmaceutical development as well as non-timber products presently being used by the community; the potential for increased commercialization of some of these products; the environmental services rendered by this intact natural system (i.e., watershed management); potential timber and non-timber resources; potential for tourism development, etc. It is important that the governments of the nations involved clearly understand all potential uses of these areas, economic as well as cultural. The SVA assess local cultural values in an attempt to obtain the best use of the resource for all, i.e., to properly understand value of the resources and comprehend all potential uses economic and cultural.

Phytomedicines Development

The research performed under the ICBG has the benefit of providing information that would lead to the development of local herbal medicines, which could then provide a more affordable, and in some cases more effective, form of local health care. The importance of data generated through the pharmaceutical R&D process for the study of traditional medicines for standardization, toxicity and active constituents is often under-estimated (Iwu, 1994). A major part of the arrangement under this ICBG is to pass on information concerning acute toxicity of traditional remedies back to the healers so that they can use such remedies more appropriately.

The cornerstone of establishing economic incentives for biodiversity conservation will be the provision of a mechanism which will adequately localize the external benefits and costs associated with using genetic resources (Iwu, 1995; Gollin, 1992). The development of phytomedicines could provide such a link. They are relatively low cost to produce and would allow the developing country to keep a greater share of the drug discovery benefit. The return on investment for phytomedicines compares favorably with that from pharmaceutical development. The international market for processed herbal products such as phytomedicines, nutraceuticals and personal care preparations is huge and has been estimated at $27 billion per annum (Iwu et al., 1997). The development of traditional medicinal agents as credible phytomedicines is undoubtedly a more direct way to give value to forest resources.

Capacity and Infrastructure Building

This project provides for various training programs both in country and in the United States for ecologists, biologists, chemists, pharmacologists, ethnobiologists and field taxonomists. This non-monetary benefit strengthens the ability of the scientists of the two countries to conduct similar projects in the future.

We have set up comprehensive phytochemical laboratory services in Nigeria and Cameroon. Our research has shown great promise in the development of new, unique chemicals with therapeutic potential, particularly for malaria and leishmaniasis. These laboratories also provide phytomedicine standardization services to local healers. Good working relationships have been established with local industries so that products developed by the ICBG can be manufactured.

In Africa, NGOs have always been actively involved in nature conservation. There are over 200 NGOs in Nigeria alone (Iwu & Laird, 1997). Many of them are regional in both their membership and operation. One of the objectives of the ICBG is the strengthening of the capacity of BDCP, a local network created by University researchers to address the problems of conservation.

BDCP, which has now established autonomous branches in both Nigeria and Cameroon (as well as Guinea and South Africa) is an international umbrella organization that is a critical administrator, monitor, and arbiter of the various interests involved in this ICBG.

The ICBG provides some basic infrastructure support for existing BDCP programs, such as: cultivation trials in the Calabar region for the valuable medicinal species *Physostigma venenosum* (once used as an ordeal poison); assistance to local forest communities in acquisition of legal rights to communal lands; and farm inventories in both Northeastern and Southeastern Nigeria. The ICBG also provided BDCP with basic funds which were used to purchase herbarium equipment, four-wheel drive vehicles (one each for Nigeria and Cameroon), computers, laboratory equipment and basic office costs.

The ICBG is supporting various branches of the Nigerian Union of Herbal Medical Practitioners. Pilot projects have been initiated with the Enugu State

Branch (9th Mile Corner) and the Niger State Branch (Bida). Efforts are being made to identify suitable partners in Cameroon for similar collaboration. ICBG has provided immediate reciprocity funds and access fees to the association. The funds will also be used in the following on-going projects by the Union: a) A Medical Complex: whereby healers and western trained physicians jointly attend to patients; b) plant nursery facilities for the ex-situ conservation of plants used by the healers in their practice; c) cultivation of selected medicinal plants as hedges for the demarcation of the herbal garden; and d) preparation and storage of samples in the community based herbal pharmacy.

Local communities are important collaborators for the ICBG, particularly in the Nigerian research component, but increasingly in Cameroon as well. It would be useful to define "local community" in the context of this discussion, since the dilemma often arises that, while wonderful plans and policies can be made on behalf of "local communities," no one knows what is really meant by the term (Iwu & Laird, 1997). Rather than become embroiled in debates about relative "indigenousness", the ICBG approaches the issue on a practical footing, working with existing local authorities (for example, chiefs, traditional healers, village councils, development associations) in communities in which ownership and authority are generally clearly defined. These communities usually share cultural and tribal ties, have well-structured systems of leadership (chief, which is more a colonial implant, but has some political power, councils, etc.), relative areas of specialty and are self-defining entities. It is not our place to go in search of a "community" beyond what local people have defined for themselves, nor to "appraise" the situation in order to decide on their behalf the "truly representative" bodies (Iwu & Laird, 1997; Iwu, 1995; Laird, 1995).

In West-Central Africa, the cultural and socioeconomic split between urban and rural communities is not as severe as elsewhere, and the exchange of experiences and knowledge more fluid. The African members of the ICBG do not perceive themselves as detached intermediaries between foreign donors and the rural communities. Almost every member of the ICBG team has a village home in the project area of eastern Nigeria and western Cameroon. The working arrangements adopted for the ICBG are the outcome of several months of village meetings, discussion with influential members of the community and negotiation with the appropriate government agencies.

Training

The ICBG has organized and co-sponsored many training courses and workshops on such subjects as: measuring and monitoring biodiversity; plant taxonomy; collection techniques; forest management; cell and tissue culture; enzyme production; DNA manipulation; phytomedicine and pharmaceutical development and the integration of western and traditional medicine (Table 3). These training programs have brought government experts, academia, private sector, regulatory authorities, herbalists and pharmaceutical companies together to find practical solutions to utilizing Africa's immense biodiversity in a sustainable manner.

Trust Fund

A major accomplishment was the establishment in Nigeria of the Fund for Integrated Rural Development and Traditional Medicine (FIRD-TM). The management of this trust fund is completely independent of the ICBG but administers funds only for the purposes outlined in its charter, viz., conservation, drug development and socioeconomic well-being of rural communities. The FIRD-TM has an independent board composed of leaders of traditional healers' associations, government officials, representatives of the village council and technical experts from scientific institutions. The predominance of traditional solidarity systems supplies a social structure, which ensures community participation in FIRD-TM projects.

Fifty percent of the royalty generated from the licensing of the drugs developed during this project will be distributed through a legal Trust Fund – the Global Fund for Health (GFH), which has been established for this purpose. The Board of Management consists of representatives from the U.S.A., Cameroon and Nigeria. The GFH is completely independent but administers the funds only for the purposes outlined in its Charter. Most of the work under this ICBG is carried out in Community Forest Areas (CFAs) and the royalty sharing will be restricted to these local government council areas. Each community has established a consultative committee drawn from the executive of the village union or town association, village heads and the professional guild of healers. It is this village committee which will make decisions and select priorities regarding compensation and projects to be funded. BDCP has used this approach in the past with considerable success.

It is our position that when determining compensation for access to genetic resources that emphasis should be placed on capacity building rather than

Table 3. ICBG workshops/training programs.

Title of training activity	Description	Sponsoring organization/Location
Ethnobiology and Field Taxonomy Course	Fundamental concepts in ethnobiology, Differential approaches to ethnobiological studies, Community participation in ethnobiological studies, ethnobiology and economic devpt, Ethnobiological collections, Preparing ethnobiological and plant collection data sheets.	ICBG, BDCP (Nsukka, Nigeria, Enugu, Nigeria, Douala, Cameroon, Limbe, Cameroon)
Symposium on Traditional Medicine and National Development	Provided opportunity for traditional healers and western-trained scientists to discuss best methods to integrate both systems into primary health care.	ICBG, BDCP, Nigerian Union of Herbalists (Enugu, Nigeria)
Congress on Utilization of Tropical Plants and Biodiversity Conservation	A forum for an interdisciplinary discussion of strategies for the sustainable utilization of tropical plants as economic resources and the development of practical conservation systems.	ICBG, BDCP, BSP, WWF, Shaman Pharm., (Douala, Cameroon)
SI-MAB Biodiversity Measuring & Monitoring Course	Interactive workshop which explored SI-MAB permanent plot methodology for measuring and monitoring biodiversity and its use as a foundation for a regional network of plots. Includes surveying and use of GIS.	ICBG, Smithsonian Institution (Limbe, Cameroon; Nsukka, Nigeria)
Commercial Production of Indigenous Plants as Phytomedicines	Discussions on formulation of strategies for the production and standardization of herbal remedies.	ICBG, BDCP (Lagos, Nigeria)
Sub-regional Workshop on Biotechnology – Cell and Tissue Culture	Techniques of plant cell and tissue culture with application to agriculture and related industries.	ICBG, BDCP, National Agency for Science and Engineering (Nsukka, Nigeria)
Bioprospecting and Strategies for Industrial Exploitation of Medicinal and Aromatic Plants	Strategies and technologies for establishing bioprospecting programs.	ICBG, BDCP, ICS-Trieste, UNIDO, OAU-STRC, West African Pharm. Federation (Enugu, Nigeria)
Standardization and Regulation of Herbal Medicine	Criteria for evaluating the quality, safety and efficacy of herbal medicines.	ICBG, BDCP, National Agency for Food and Drug Admin. & Control (Abuja, Nigeria)
Economic Valuation Course	Protocol for socioeconomic evaluation studies, questionnaires, household and market surveys.	ICBG, BDCP (Enugu, Nigeria, Nsukka, Nigeria)

• African ICBG collaborators also participated in various conferences in the areas of drug development, biodiversity conservation, informatics, intellectual property rights and sustainable development.
• The African ICBG is currently supporting two students in phytochemistry, one student in *in vivo* cancer screening and
• One student in Agronomy at M.Sc and Ph. D. levels. Several post-doctorate fellows are engaged in research activities at the ICBG laboratories in Nsukka, Nigeria and Dschang, Cameroon.

short-term cash payments. Nigeria and Cameroon should endeavor to add value to their resources before trading the samples. The objective is to build a lasting relationship between the parties rather than negotiating for immediate compensation. If properly planned, biological resources should be a viable vehicle for sustainable development (Bouillet-Cordonnier & Laird, 1995).

Information Management

This ICBG has developed databases of African medicinal plants (AfricMed) and ecological information (BioMon), and are incorporating these with additional information from economic value assessments and ethnobotanical surveys into a relational database called the Computerized Information System on African Medicinal and Aromatic Plants (CISAMAP). The CISAMAP will link information on African medicinal plants throughout sub-Saharan Africa.

CISAMAP is an off-line database network on African medicinal plants. This database is based at the International Center for Ethnomedicine and Drug Development (InterCEDD) in Nsukka, Nigeria. CISAMAP is a network of four ICBG databases:

- AFRICMED: An inventory of plants used in traditional medicine in West and Central Africa and epidemiological surveys of the use of these plants. AFRICMED contains information on medicinal plants (nomenclature, medicinal uses, other uses, plant attributes, chemical constituents, pharmacology, plant/chemical trails, side effects and literature). It also contains information on floristic plants (nomenclature, morphology, ecology, distribution, threatened status, endemic status and literature) and horticultural plants (propagation, cultivation, and literature).
- ICBG-WRAIR Drug Development Inventory: A database of plant material, extractions, chemistry and biology.
- Biodiversity Measuring and Monitoring (BioMon) database: A database of plants found in the network of ICBG small biodiversity plots in Nigeria and Cameroon. It has the capability to plot sample collection locations on maps as well as digital overlays of roads, rivers, railways and topography of West and Central Africa.
- Korup Forest Dynamic Project (KFDP) Tree Demographic database: A database of plants found in the ICBG 50 hectare biodiversity plot near Nigeria-Cameroon border. Both BioMon and KFDP databases are linked to the Smithsonian network of similar plots all over the world. Efforts are being made to integrate these databases in an online format.

All ICBG databases are being integrated into the Computerized Information System on African Medicinal and Aromatic Plants (CISAMAP). The data generated will be made available to federal and state herbaria to promote access to necessary research information in Nigeria and Cameroon. This has an important impact on the improvement of health and resource development in both countries.

BENEFIT SHARING PLAN

The ICBG has been designed to deliver a range of benefits to a variety of partners over a number of years. Delivering benefits to reach the intended target group was found to be a very difficult undertaking. It became necessary first to address the following questions in the benefit- sharing plan: Who should benefit? How should they benefit? When should they benefit?

Contrary to the views expressed in contemporary literature and among advocacy groups, it is not possible to implement a fair and equitable benefit sharing plan without addressing these issues. While a process of discussion and negotiation is inevitably required to determine the detailed accounting of the nature and distribution of benefits, broad parameters can be sketched out from the start, and this is what we have tried to do in the following discussion. It is important to note, however, that many of the most significant benefits provided by this type of multi-disciplinary and multi-institutional program are the least obvious, the most mundane-seeming, and certainly those that have attracted the least attention. We cite, for example, the difficult to quantify role of human and institutional relationships in developing capacity and expertise through informal exchanges. This might be manifested through access to funds, publications and literature, potential corporate collaborators, and the ideas of an expanded network of colleagues (Iwu & Laird, 1997). Although the compensation plan remained loyal to the aims and objectives of the funding agencies, a strategy was developed which will ensure benefits to the host country both immediately and in a sustainable manner over a long time. Our compensation plan was based on deriving maximum benefits from the process of drug discovery rather than the promise of huge royalties that may never materialize or at best would materialize eight to ten years after discovery.

Benefits are broken down into two categories: *Immediate* ones arise from the process benefits of doing the research and development phase of the project. Examples are infrastructure-building, equipment, paid samples, training, etc. *Long-term* ones arise from the post development or product license phase of the project, e.g., royalties.

Types of Compensation

Short Term and Immediate Compensation – Collection Fees to Individuals and Communities

Plants are collected directly from local communities and payment and compensation is effected in three modes. First, a “small” cash payment is made to the informant/collector. Secondly, the community is assisted in their development projects, and thirdly, the medical member(s) of the ethnobotanical team consults with the local healers and provides volunteer medical assistance if requested.

Long Term Benefits – Royalty Payments

The royalty derived from licensing drugs developed from any of the leads provided under this ICBG will be distributed between the informant/herbalist, the com-

munity and the scientific inventors. The role of the source country scientists in this arrangement is essentially that of facilitating the contact between the ICBG and the healers, not as middlemen or brokers. They will be considered in the same category as their colleagues in the developed countries who contributed intellectually to the development of the drug. The traditional healer or informant is expected to benefit under this category (depending on the extent of his contribution) as well as benefit as a member of the community from where the product is derived. The individual informant will also benefit from bulk recollections.

The royalties will be distributed as follows:

- 20% of all royalties and other considerations generated from licenses of inventions will be distributed equitably among those parties contributing intellectually to the invention, taking into account their relative contribution and ensuring that inventors in each case receive not less than 15%.
- 50% of all royalty income and other considerations to BDCP to be used solely for programs and projects designed to promote sustainable economic development relating to biodiversity conservation in Nigeria and Cameroon. In order to distribute these benefits, an independent Trust Fund has been established as outlined in the Compensation and Benefit Sharing Plan.
- 30% of all royalty income and other considerations will be donated to a Tropical Disease Drug Development Program based at Walter Reed in order to further research efforts on under-studied diseases of the developing countries.

The following general principles were arrived at after several discussions of the benefits that would accrue to the ICBG partners within Nigeria and Cameroon. The result is that benefits are selected from a matrix identified by the partners themselves rather than perceived by outsiders and dictated from outside. This discussion is by no means complete, and "benefit-sharing" will be a constantly evolving area.

GENERAL PRINCIPLES OF THE BENEFIT SHARING PLAN

The provision of compensation to institutions in source countries and distribution of royalties have been formulated to ensure that the following principles are adhered to:

1. The distribution of the benefits will ensure that economic benefits are channeled back to the area in which the source plant was found with provision made to compensate individuals, rural communities and local institutions. Modalities will be selected to address each individual circumstance, taking into consideration the fact that cash may not be the most appropriate benefit.
2. Revenues generated from this project will be used solely for projects that will promote conservation of biological diversity and drug development, as well as economic well being of rural communities.
3. Local communities, through town associations, village heads and the professional guild of healers, should be empowered to make decisions regarding compensations and projects in their localities.
4. The African members of this ICBG will be involved at all stages and in all aspects of the drug development process and this experience will enhance their capacity to undertake similar ventures in the future on their own. It is our hope that our work will generate not only pure chemical isolates as pharmaceutical leads but will help the source countries in standardizing their phytomedicines and return such information as benefits to traditional healers. In all cases, compensation will be on a case-by-case basis.
5. While the development of drugs may be the most visible activity under this ICBG, equal importance is accorded to the conservation and economic development aspects of this project. The ICBG has established viable scientific partnerships between United States scientists and their colleagues in Nigeria and Cameroon. The aim is to assist the source countries' scientists to strengthen their capacity to protect the biodiversity in their area now and in the future.
6. All the scientists and individuals who contributed intellectually in the selection, identification and processing of the medicinal plants and their subsequent isolation and development as medicinal agents will be compensated as appropriate. Traditional healers who assisted in identifying the plant materials and/or contributed in the plant selection process will also be compensated.
7. Appropriate recognition must be given to the contribution of all parties to the development of a therapeutic agent. Individuals who provided information leading to the discovery of an active molecule from a plant must be acknowledged in all publications and patents arising from the work. The community from which the plant was sourced will also be cited in publications and patent appli-

cations. The methodology adopted for this project will rely more on information from specialist medicine men and acquisition from lay people will be minimal.

8. We recognize that necessary tasks in ensuring equitable distribution of benefits include attribution and labeling of ideas, access to instruments of protection and monitoring for infringement, and assistance of technical and legal experts. The customary and universal applicable methods of protecting and perfecting intellectual property rights (patents, copyrights, trademarks, trade secrets, and appellation of origin) may not be adequate for the purposes of this ICBG.
9. While the right of individuals to their land and the resources derived from it will be respected in the allocation of benefits, the group is cognizant of the fact that information concerning the specific use of a plant drug is often not the exclusive property of an individual informant or healer but belongs to the realm of Cultural Resources (CRs) that belongs to an entire community or village. This raises the question of ethics as to the competence of any one person to reveal information that has been entrusted to him as a custodian. This concern has to be balanced with the fundamental human rights of the professional herbalist to be treated as individuals with rights to their private property and knowledge.

Ethical Issues and Socioeconomic Considerations

Since a significant part of the approach outlined in this project involves the use of knowledge collected from indigenous medical practitioners and native populations living in the project area, serious thought has been given to resolving the enormous ethical and economic issues that are inherent in this approach. This includes the complex, culture-specific ownership patterns in different parts of the world and especially in attempting to separate individual material and intellectual property rights from what have been perceived as communal resource in traditional societies. The requirement for prior informed consent has to be undertaken within a cultural setting where most biodiversity belongs to what could be appropriately classified as public domain.

The above concerns have been considered both in the design of the projects outlined here and also in the selection of the diseases to be studied. Steps have been taken to ensure that royalties derived from this project will be channeled to the benefit of host countries and the local communities near the project sites.

In the absence of a universally applicable model that addresses these concerns, the Group has adopted a framework for reciprocity and equitable distribution of benefits from biodiversity that addresses participatory development, environmental sustainability and poverty alleviation.

Documentation of agreement or informed consent is required before confidential information is provided by a source in-country, particularly a traditional healer unless the source is a member of the ICBG. All licenses require ("to the extent it is commercially feasible") that the licensee seek to obtain future supplies of raw materials for research and development, as well as manufacturing, from the source country of original sample collection (Boom, 1990). Payment for the samples is determined on a case-by-case basis. In situations where large samples of plant material are required for follow-up studies, the licensee provides a written statement that the material has been collected in a sustainable manner and when appropriate an environmental impact assessment and/or a census of the species is commissioned or has been conducted to ensure that the plant is not threatened by over-harvesting.

CONCLUSION

The African ICBG Program serves as a national and international model of interdisciplinary collaboration among multiple funding agencies and multiple collaborating partners in the United States and developing countries. This ICBG is generating important lessons on financial, administrative, and legal aspects of such collaborations. The orchestration of agreements between mutually benefiting partners and with local groups, protection of IPR and equitable benefit sharing between scientists and institutions in industrialized and developing countries are being defined. The integration of modern drug discovery methods with traditional and contemporary local botanical and medicinal approaches, cost-effective strategies for studying and conserving biodiversity, political and socioeconomic aspects of conservation, and sociological aspects of international research are being advanced.

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