

International Cooperative Biodiversity Groups (ICBG)

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P.T.

Fogarty International Center
National Cancer Institute
National Institute of Allergy and Infectious Diseases
National Institute of Mental Health
National Institute of Child Health and Human Development
Office of Alternative Medicine
National Heart, Lung and Blood Institute
National Science Foundation
Foreign Agricultural Service

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■ **PURPOSE**

The National Institutes of Health, the National Science Foundation and the Foreign Agricultural Service (hereafter "the Government" or "the Participating Agencies") invite applications for the establishment or continuation of "International Cooperative Biodiversity Groups" to address the interdependent issues of biodiversity conservation, economic growth, and human health through discovery of therapeutic agents for diseases of importance to developed countries as well as those primarily important in developing countries. Particularly relevant disease areas and health needs include cancer, HIV-AIDS and its opportunistic infections, tuberculosis, malaria, central nervous system disorders, contraception and sexually transmitted diseases, and cardiovascular and pulmonary diseases. Applications that propose, in addition to pharmaceutical drug discovery, research and training related to phytomedicine analysis and natural product-based crop protection or veterinary agents are also encouraged.

For the purposes of this joint biodiversity and drug development program, the National Institutes of Health (NIH) will be allocated funds from the National Science Foundation (NSF). The Foreign Agricultural Service (FAS) will review all applications that contain agricultural components for possible co-funding in countries where they have available resources. Participating NIH components are the Fogarty International Center, the National Cancer Institute, the National Institute of Allergy and Infectious Diseases, the National Institute of Mental Health, the National Institute of Child Health and Human Development, the Office of Alternative Medicine and the National Heart, Lung and Blood Institute. It is possible that other organizations may join the program at a later time. The Fogarty International Center (FIC) of the NIH will administer this program under the authority and regulations of the Public Health Service (PHS).

There are no plans to reissue this Request for Applications (RFA) at this time.

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■ A. HEALTHY PEOPLE 2000

The PHS is committed to achieving the health promotion and disease prevention objectives of Healthy People 2000, a PHS-led national activity for setting priority areas. This RFA, INTERNATIONAL COOPERATIVE BIODIVERSITY GROUPS, is related to the priority needs of several diseases of interest to the National Institutes of Health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington DC, 20402-9325 (telephone 202-512-1800).

■ B. SUMMARY

This RFA calls for the development of interdisciplinary programs through the establishment of International Cooperative Biodiversity Groups (ICBGs), with active and substantial participation by U.S. and developing country scientists and institutions. It is the intent of this RFA to promote the conservation of biological diversity through the discovery of bioactive agents from natural products, and to ensure that equitable benefits from both the research process and any discoveries accrue to the country of origin. Benefits that accrue to the country of origin may take a variety of forms but will include economic benefits and enhancement of research capacity. The RFA is seeking proposals that will build institutional relationships with developing countries that will continue to grow beyond the life of the RFA and will serve as effective models for others to develop similar relationships.

■ C. BACKGROUND

This RFA represents a recompetition of the International Cooperative Biodiversity Groups program following its first five years of funding. The unifying theme underlying this RFA is the concept that the discovery and development of pharmaceutical and other useful agents from natural products can, under appropriate circumstances, promote sustained economic growth in developing countries while conserving the biological resources from which these products are derived. This theme reflects the partnership between the National Institutes of Health, the National Science Foundation and the U.S. Agency for International Development that was the genesis for the original ICBG program.

Natural products that hold promise for the development of pharmaceutical agents, as well as those that form the basis for many traditional herbal remedies and serve as leads for agricultural and other uses, are often found in ecosystems that are seriously threatened. These include terrestrial ecosystems such as tropical forests as well as marine ecosystems such as coral reefs, and mangroves. Predominantly found in developing countries of the tropics, these ecosystems are rich in biological diversity. Tropical forests, for example, cover only seven percent of the earth's surface, but they are thought to contain at least one-half of all plant and animal species. Deforestation is apparently proceeding at a rate of 20 million hectares per year, resulting in the loss of species at rates estimated to be 100 to 1000 times greater than background extinction. Cultural diversity is also seriously threatened by habitat conversion and the loss of biological resources on which many traditional societies depend.

Recent experience demonstrates that diverse plant, microbial and animal resources, contain a wealth of potentially useful compounds. For example, the demonstrated clinical utility of the Vinca alkaloids, vinblastine and vincristine, of the camptothecin analogues, and the effectiveness of taxol in treatment of ovarian and breast cancers, have generated enthusiastic support for a thorough exploration of natural products. In addition to cancer, natural products are proven and/or possible sources of drugs for malaria, parasitic diseases, diarrheal disorders, AIDS and its opportunistic infections, cardiovascular diseases, respiratory diseases, hepatitis, central nervous system disorders, and other serious illnesses prevalent in developing countries. Natural products have also been a valuable source of crop protection agents such as pyrethrins and of veterinary medicines such as ivermectin.

The terrible irony is that as advances in biology expand our ability to use genetic diversity to combat these diseases, the raw material is being lost to extinction. Perhaps even more urgent than the losses of genetic and chemical diversity as sources of potential pharmaceutical and agricultural protection agents, are the immediate repercussions of biodiversity loss in many developing countries where herbal remedies from diverse biota are a primary source of health care. Simultaneous with these biological losses to extinction are accelerating losses of traditional knowledge associated with the biota. This knowledge of the identity and utility of specific organisms for medicinal and other uses has intrinsic value as part of our cultural patrimony, is currently important as a source of health care for many people, and may offer important leads for future treatments of numerous human ailments.

The underlying causes of biodiversity loss are many and complex, and involve interwoven social, economic, and political elements. It is clear, however, that poverty, unemployment, and lack of economic opportunities are significant contributing factors. In developing countries struggling to meet the most basic human needs, efforts to protect biological diversity will succeed only if implemented in the context of promoting sustained economic growth. Likewise, to be effective, efforts to protect biological diversity must include the active participation of affected local communities, which ultimately will determine the success or failure of those efforts. Biological resources must benefit local populations if the resources are to be conserved. Consequently, the sustainable economic potential of biological resources, such as developing pharmaceuticals from natural products, can be used to promote biodiversity conservation by providing an economic return from sustainable use of the resources while improving quality of life through better human health. Experience suggests that the development of significant conservation incentives is most likely when both near and long term benefits accrue to stakeholders.

D. ELIGIBILITY REQUIREMENTS

Public and private non-profit institutions, for profit institutions, Governments and their agencies, and foreign institutions are eligible to participate as members of a Group. However, the Group Leader must be located in a public or private non-profit institution, Government or Governmental agency of the United States. Foreign and for-profit institutions may participate in an ICBG as Associate Programs.

E. MECHANISM OF SUPPORT

1. Awards will be made as Cooperative Agreements (U01). Assistance via Cooperative Agreement differs from grant awards in that sponsoring Government components anticipate substantial programmatic involvement in achieving the goals and objectives of the project. The nature of the U.S. Government's assistance is described in Section J, Part 3 of this RFA under "Terms and Conditions of Award." There is no intent, real or implied, for Government staff to direct Group activities or to limit the freedom or scientific creativity of investigators.
2. The estimated starting date for the initial year of award under this RFA is August 1, 1998. This RFA is a one-time solicitation. However, should the Government determine that there is continuing program need, the Government may issue a new RFA.
3. An award will be made only to the Group Leader's institution, which will subcontract with the other participating institutions. All Group activities will be coordinated through the Group Leader's institution. Applicants must comply with PHS policies concerning allowable costs. Particularly pertinent to this RFA is the non-allowability of indirect costs to organizations outside the U.S. Any questions about allowable costs may be directed to Ms. Silvia Mandes, Grants Management Officer, FIC.
4. Under the Cooperative Agreement, a relationship between the awardee and the Government is established in which the Group is responsive to the requirements and conditions set forth in the RFA. Specifically, the Group Leader defines the details for the project in response to the RFA, retains primary responsibility for the performance of the Group, and agrees to coordinate with the assistance of the Government in all aspects of scientific and technical management of the project in accordance with the terms and conditions outlined in Section J., Part 3. "Terms and Conditions of Award."
5. Awards pursuant to this RFA are contingent upon availability of funds. Subsequent to receiving awards, the awardees may request supplemental support from the Government to expand their activities. Funding for such expansion must be provided from sources other than the FIC, but should be administered through the FIC if they originate from one of the agencies sponsoring this RFA. In making such a request the applicant must identify the source of the funds and certify that the funds are committed prior to submission of the supplemental request. Complementary funds could also be supplied, for example, from a non-governmental organization or a U.S. Governmental agency, not currently participating in this RFA. Applicants are encouraged to apply for funds from corporate partners or non-profit foundations to supplement conservation and development activities in the host countries, perhaps utilizing trust funds in those countries for management of such resources. Regardless of the source, any supplemental support for Group activities must be reported to FIC.
6. All policies and requirements that govern the grant program of the U.S. Public Health Service apply, in particular, PHS Grants Policy Statement, DHHS Pub. No. (OASH) 90-50.000 (Rev), October 1, 1990.

■ F. FUNDS AVAILABLE

The Government anticipates making four to six awards (Cooperative Agreements) for project periods of up to five years. Approximately \$2.5 million (total costs) for the initial year's funding has been set aside to cover direct and indirect costs of all awards. Therefore, the cost effectiveness of program design in relation to proposed budgets will be a very important funding criteria, and the limits of overall program funding should be kept in mind.

All currently funded Groups that wish to be eligible for funding beyond their fifth year of support under their initial ICBG award must apply under this RFA.

■ G. DEFINITIONS

■ **COOPERATIVE AGREEMENT:** An assistance mechanism in which substantial Government scientific and programmatic involvement with the recipient is anticipated during performance of the planned activity.

■ **INTERNATIONAL COOPERATIVE BIODIVERSITY GROUP:** A consortium of Associate Programs, at least one of which is located in a developing country institution, representing diverse scientific disciplines and organizations which join together under guidance and direction of a single Group Leader (Principal Investigator) and which function as a unit with a common goal: to promote, through multidisciplinary approaches, drug development, biodiversity conservation, and sustained economic growth. In this RFA the terms International Cooperative Biodiversity Group, ICBG, and "Group" are used synonymously.

■ **DEVELOPING COUNTRY:** It is the responsibility of the applicant to demonstrate that the country (ies) that would host the proposed ICBG qualifies as a developing country with significant biological diversity. In addition, the proposed country must be one that maintains diplomatic relations with the United States Government. While no absolute distinctions are made, it is unlikely that a country that has a per capita gross domestic product greater than \$9000 per year would qualify. Applicants are encouraged to examine the data on their proposed country in the [statistical summary table](#), Economic Development and Biodiversity. Applicants are also strongly encouraged to consult with the FIC Biodiversity Program Director regarding their proposed collaborating country.

■ **ASSOCIATE PROGRAM:** A component of the overall Group with a separate, detailed program plan and budget, that brings to the Group a unique resource, capability or expertise.

■ **CENTRAL OPERATIONS OFFICE:** An administrative unit located at the Group Leader's institution, which is responsible for coordinating and/or providing administrative support for all Group activities including budgets from the Group's associate programs.

■ **NATURAL PRODUCT:** In the context of the ICBG, a term used broadly to encompass any naturally occurring bioactive agent selected for preclinical evaluation against a disease or for another medical, agricultural, cosmetic or industrial need. This, of course, excludes materials which are synthesized de novo as well as any semi-synthetic derivatives which do not require the collection of material from nature.

■ **GROUP LEADER:** The Principal Investigator identified in the application who assembles the ICBG, submits the single application in response to this RFA and who is responsible for the performance of the Group as a whole and of each Associate Program Leader. The Group Leader will coordinate Group activities both scientifically and administratively, and in addition, may lead one of the Associate Programs of the Group. The Group Leader's institution is legally and fiscally accountable for the disbursement of funds awarded. The Group Leader's institution must be a not for profit institution in the United States.

■ **ASSOCIATE PROGRAM LEADER:** The director of one of the Associate Programs of the ICBG.

■ **TECHNICAL ADVISORY GROUP (TAG):** A committee of advisors with relevant expertise from the Participating Agencies and Institutes, including the Director of the Fogarty International Center (FIC). The TAG reviews applications to make funding recommendations following the initial peer review, and meets several times per year, as necessary, to review developments in the ICBG program as a whole and progress of individual Groups.

■ **FIC BIODIVERSITY PROGRAM DIRECTOR:** A representative of the Fogarty International Center, a member of the TAG, and the Government program administrator for all funded Groups. The Program Director has lead responsibility for day to day funding and policy decisions in coordination with the Director of the FIC and the Technical Advisory Group. In conjunction with the Government Scientific Coordinator for each ICBG, the Program Director supports the activities of the Groups where possible through policy and program functions.

■ **U.S. GOVERNMENT SCIENTIFIC COORDINATOR:** A representative of the TAG who assists a specific ICBG, attends Group meetings, interacts scientifically with the Group, and facilitates the role of the Government as a participant in the Group. The U.S. Government Scientific Coordinator serves as the chair of his or her respective Advisory Committee.

■ **ADVISORY COMMITTEE:** A subset of two or more U.S. Government scientific advisers from the TAG to assist the work of the Group by providing advice and assistance and through the Scientific Coordinator (Committee Chair), to the Group. The Advisory Committee assists in such matters as reviewing the Group's progress reports and suggesting mid-course corrections and future directions for the Group. The Advisory Committee assembled for each Group is determined by the TAG. Each committee, including the Scientific Coordinator, attends groups meetings, where possible, meets separately at least once per year and maintains ongoing communication regarding group progress.

■ **PATENTABLE INVENTION:** Any new and useful process, machine, manufacture or composition of matter, or any new and useful improvements thereof, as defined under the U.S. Patent Statute (35 USC 101).

■ **CONTRACTUAL AGREEMENT:** Any formal written agreement negotiated among participating institutions in an ICBG, or between the ICBG and other organizations, that stipulates the rights and responsibilities of the parties with respect to the research process, the treatment of intellectual property and the sharing of benefits.

■ H. RESEARCH OBJECTIVES

■ **1. The overall goals** of the International Cooperative Biodiversity Group Program are drug discovery, biodiversity conservation, and economic development. The following cross-cutting approaches should guide the research and capacity-building efforts toward these goals: a) assisting with the discovery of drugs that address priority health needs of the United States and the participating developing country; b) parallel assistance with research on other natural products-based materials such as herbal medicines, crop protection agents, veterinary medicines, or other useful products; c) developing inventories of native species and indigenous knowledge; d) training, targeted toward achieving the research goals of this RFA and meeting the needs of the participating country; and, e) enhancing the scientific infrastructure within the host country. Specifically, the program objectives are to:

a) Discover, isolate, and preclinically evaluate agents from natural sources to treat or prevent diseases of importance to developed countries as well as those primarily important in developing countries.

Particularly relevant disease areas and health needs include cancer, HIV-AIDS and its opportunistic infections, tuberculosis, malaria, central nervous system disorders, contraception and sexually transmitted diseases, and cardiovascular and pulmonary diseases. It should be noted that studies required for the later stages of drug development (e.g. formulation development, toxicology, etc.) and the conduct of clinical trials are beyond the scope of this RFA.

b) Discover, isolate, and/or evaluate other natural-product based entities such as phytomedicines, crop protection agents, animal veterinary medicines, or other useful products with the potential to provide near to medium term economic benefits to local communities and other developing country partners through product earnings or stimulation of local industries. Such efforts should address local health and development priorities. It is probable that in many cases research in these areas can be carried out in parallel with drug discovery work with minimal additional cost to Groups. This may be achieved by incorporating academic, governmental or commercial partners with the appropriate scientific resources and by utilizing the same or similar samples to those collected for drug discovery.

c) Undertake inventories of biological diversity and develop collection practices compatible with conserving biodiversity, and produce documentation of all collected material in the form of museum catalogues, published works, and/or databases, reporting specific locality and all features of biology relevant to standard botanical and zoological collections; assure accessibility of inventory specimens to the public by housing them in public institutions (such as universities and national museums), and accessibility to inventory databases through publication on the Internet.

d) Support research training targeted to meet the needs of the developing country represented within the Group and related to the scope of work of the RFA, and to augment field experience and training of U.S. scientists in areas of knowledge unique to the developing country. Support for local health needs would concentrate on joint research and training, focusing on disease prevention and control using locally available resources, and discovery of appropriate therapeutics and other useful products.

Examples of relevant areas of training could include systematics, information science, ethnomedicine, chemistry, cell biology, biotechnology, or production methods, data management and quality control in pharmaceutical development. Incumbent Groups should plan to advance the level of training of developing country scientists beyond initial efforts to include advanced field and laboratory work such as the development and conduct of locally appropriate bioassays, isolation chemistry, database development, ecology and biodiversity management techniques.

Research training supported through this award may take place in the host country or in the United States and may be linked to degree-earning programs. Types of training may include, but are not limited to: i) practical and applied short-term courses or workshops for professionals or technicians; ii) course work, laboratory, or field training in essential research skills for technical assistants, graduate degree candidates, or professionals; and iii) fellowships for 1 or more years for degree candidates or post-doctoral trainees to conduct research related to the goals of the Group. Training costs and plans, must be specified in the text of the proposal and in the proposal's budget request.

e) Assist in enhancing the scientific infrastructure within the participating developing country(ies) where the biodiversity resources are found. Infrastructure support could include both social and physical infrastructure. Social infrastructure might be enhanced through strengthening of networks of scientists or local healers. Physical infrastructure support could include assistance for herbaria, museums, and laboratories, the supply of necessary equipment in these facilities, and the enhancement of collecting and screening capabilities in the host country. Limited renovation of existing facilities, but not construction of new facilities, is allowable under this RFA. All renovation of facilities must be strictly relevant to the research objectives of the Group and requires prior approval of the Government.

It is likely that some element of all five approaches (a-e) will be included in successful applications. Without a comprehensive and multi-disciplinary approach, it would be difficult to meet the requirement that drug discovery, biodiversity conservation, and sustained economic growth be addressed.

■2. **Applications for funding** as an ICBG should stress creative, synergistic approaches to biodiversity conservation, drug discovery, and sustainable economic growth. Experience has shown that synergy among these goals is more likely when the varied activities of the ICBG have significant geographical overlap than when they are widely dispersed among different regions and countries. However, legitimate scientific or other considerations may lead to less geographically localized programs.

■I. COMPOSITION OF GROUPS

Groups should be multi-disciplinary, including individuals and organizations with expertise in various relevant disciplines of the biological and physical sciences, as well as areas such as economics and sociology, and may include those who have not collaborated in programs of this type in the past.

In addition to being multidisciplinary, it is expected that Groups will be international in scope with participation of developing country institutions to the greatest extent possible. Since it is unlikely that all of the required capabilities will be located within one institution, Groups likely will be multi-institutional as well.

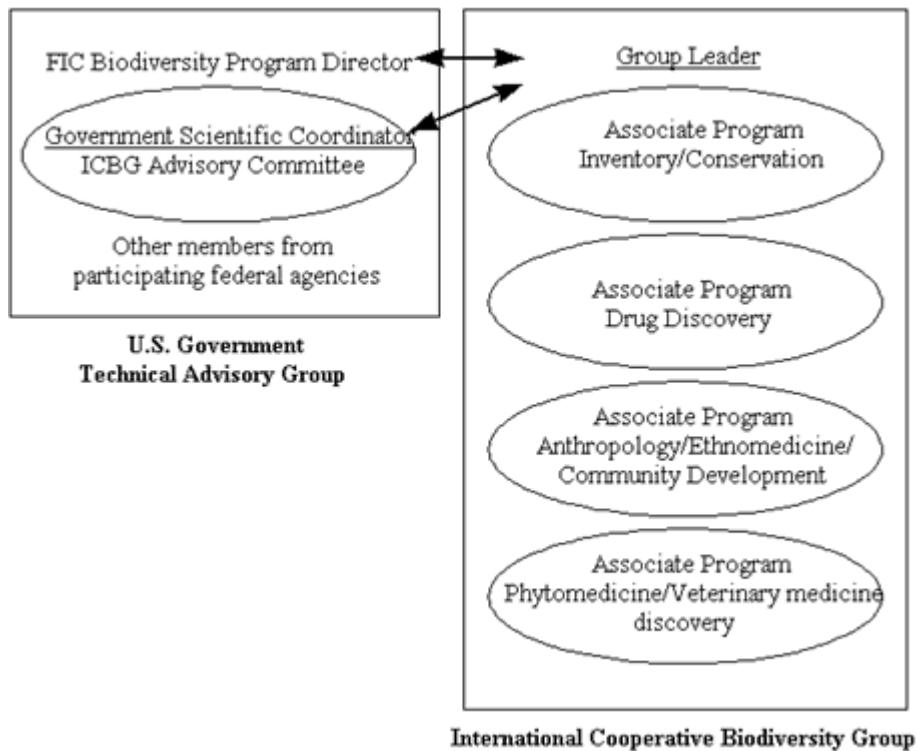
The active participation of the private sector is encouraged because it: 1) will allow this segment of the scientific community to contribute its considerable intellectual and material resources; 2) will promote private sector participation in conservation; and 3) will facilitate efforts to negotiate conditions for the equitable distribution of profits and other benefits to all parties, including developing country institutions involved in conservation and sustainable resource use. Furthermore, the interaction of academic and non-profit institutions with industry and Government will encourage the creation of novel, interdisciplinary approaches which may not otherwise develop.

■1. The composition of an ICBG is envisioned as follows:

- a) A Group Leader who is likely to also head an associate program.
- b) Associate Programs, each headed by an Associate Program Leader, in diverse scientific disciplines, such as ecology, microbiology, cell biology, ethnobiology, sociology, anthropology, botany, zoology, entomology, pharmacology or chemistry, that may be appropriate to the realization of Group objectives. A predominance of developing country and U.S. institutions composing the Associate Programs is strongly encouraged. At least one of the Associate Programs must be located in a developing country and directed by a scientist or program administrator in a developing country institution.
- c) The U. S. Government Coordinator (Advisory Committee Chairperson) appointed by the Technical Advisory Group to provide assistance to the Group.

The following diagram is a sample representation of possible relationships among scientists that might form an International Cooperative Biodiversity Group. It is shown as an example only and depicts some of the scientific disciplines that may be included. No specified number of associate programs should be inferred by this sample, nor is a requisite inclusion of a particular discipline implied. Different ICBGs will vary considerably with respect to the number and kinds of scientific disciplines required.

ILLUSTRATIVE EXAMPLE FOR ICBG ORGANIZATION



■2. **The Group Leader**, in addition to providing scientific and administrative leadership, may head an Associate Program. Associate Program Leaders will be directly responsible to the Group Leader. The formation of the Group, submission of the application in response to this RFA, the overall management of the Group, and the allocation of funds to the various Associate Programs based on anticipated needs, past performance and the overall Group needs at any given time will be the responsibility of the Group Leader and the Group Leader's institution in accordance with PHS policies.

■3. **The composition of the Group** and its Associate Programs should depend on the talents required to accomplish its scientific and technical objectives as perceived by the Group Leader and Associate Program Leaders. The major consideration in structuring an ICBG should be the maximum utilization of intellectual, physical, and financial resources to carry out the proposed research. If the Group includes more than one Associate Program on a specific topic, each should be capable of contributing high quality, necessary, and non-overlapping talents.

■4. **An individual scientist** or a single institution may be proposed as a Group Leader in only one application. However, an individual scientist may be an Associate Program Leader in more than one application, or a Group Leader and an Associate Program Leader on separate applications. If a scientist appears on more than one application, it is the responsibility of the Group Leader to demonstrate in their applications that there are no scientific or budgetary overlaps or proprietary conflicts with each individual's proposed activities. Likewise, individuals currently receiving funding via contracts, grants, gifts, commercial arrangements, or Cooperative Agreements may be funded under this RFA providing that there is no scientific or budgetary overlap or proprietary conflict in funded activities.

Any Associate Program Leader must complete their portion of the overall application in detail even if no funds are requested for his or her specific project. NSF Staff or intramural scientists at the NIH or the Department of Agriculture may participate in an ICBG as collaborators or consultants, but may not submit a formal application as an Associate Program Leader, assist in developing other portions of the application, or receive funds from this program. Such a government scientist must obtain appropriate

clearances prior to submission, and in the application, provide a letter of commitment, a current curriculum vitae, and documentation of the required clearances. The Group Leader must incorporate into the application, in the usual grant format, a full description of the project, including technical details and methodology. The participation of an intramural scientist is independent of and unrelated to the role of the Advisory Committee or the U.S. Government Scientific Coordinator as described in Section J, Part 3. "Terms and Conditions of Award."

■ **5. More than one Associate Program** of a Group might be derived from a single institution. However, the varied talents and technologies required for the effective attainment of the objectives described in this RFA are not likely to be present in an individual institution. It is anticipated that the Associate Program Leaders within a Group will therefore likely be derived from several institutions.

■ **6. No prescribed number of Associate Programs** per Group is stipulated. However, the Group Leader could experience difficulty in providing the desirable level of guidance, and Group members might communicate and collaborate less efficiently, if the Group were to contain more than five or six Associate Programs. In addition, to ensure the most effective use of resources, the number of institutions collaborating in a Group should be considered carefully.

■ **7. In forming Groups, potential Group Leaders** should remain cognizant of the need for communication, including regular meetings of members, and transfer in a timely manner of data and materials to Group members located in all the participating countries. A plan for communication and material transfer, including all permits and other legal documents required to assure this transfer, must be supplied.

■ **8. Under the provisions of assistance** via a Cooperative Agreement, the U.S. Government Scientific Coordinator will assist the ICBG and participate in the Group in a manner specified in Section J. 3 "Terms and Conditions of Award ", and carry out the scientific responsibilities required. The U.S. Government Scientific Coordinator will not conduct Associate Program activities.

■ **J. SPECIAL REQUIREMENTS**

■ **1. Award Monitoring and Evaluation**

Progress of each funded Group will be monitored and evaluated using regular technical progress and financial reports prepared by the Group. Detailed reporting instructions are being developed in response to ongoing program reviews, and may be available from the Program Director following the deadline for receipt of a Letter of Intent.

The U.S. Government Scientific Coordinator or the ICBG Program Director, with advice from the Advisory Committee, may also elect to conduct site visits or enlist the technical assistance of external consultants to review progress and work with investigators to suggest mid-course changes or recommendations for non-competitive renewal of awards. 🏹

■ **2. Intellectual Property and Benefit-Sharing**

Because the discovery of bioactive agents from natural products is one objective of this effort, along with ensuring an equitable economic benefit accrues to developing country organizations or communities associated with ICBG research, it is essential that applicants develop appropriate research plans and contractual agreements for the treatment of intellectual property. These plans must ensure that inventions and the various intellectual and material contributions that lead to their development are properly

protected and compensated. Experience has shown that the development of these plans and agreements is frequently complex and challenging because multiple institutions and countries are involved, often with very different objectives, perceptions and expectations, and occasionally from very different legal environments.

In the application each applicant Group must, therefore, provide a detailed description of its approach to intellectual property and to the sharing of benefits from ICBG sponsored research. Descriptions should encompass both the conduct of collaborative research activities and the nature of contractual agreements among the collaborators. The research plan and contractual agreements among Group members must be designed such that they address the [program principles that are detailed in Appendix 1](#).

Prior to receiving an award formal agreements specifying the rights and responsibilities of each Group member institution must be signed and dated by the organizational official authorized to enter into such arrangements, and must be on file at the Fogarty International Center. (See Section M., "MINIMUM REQUIREMENTS FOR APPLICATION"). Proposals that represent continuation from previous ICBG awards must also provide updated, revised or new agreements prior to receiving an award. The above applies to all research carried out under this RFA, including any that may involve U.S. Government laboratories. ▲

■3. Terms and Conditions of Award

The following terms and conditions will be incorporated into the award statement and provided to the Principal Investigator (Group Leader) at the time of award. The "Terms and Conditions of Award" described in this section are in addition to, and not in lieu of, otherwise applicable OMB administrative guidelines, HHS Grant Administration Regulations at 45 CFR Parts 74 and 92, and other HHS, PHS, and NIH grant administration policy statements.

a) Awardee Rights and Responsibilities

Assistance via Cooperative Agreements differs from that of grants in that, in addition to programmatic and administrative stewardship responsibilities, the U.S. Government in awarding the Cooperative Agreement anticipates substantial scientific involvement during performance of the project. However, the Group must define its objectives and its approaches to attain these objectives in accord with its own interests, scientific creativity, capabilities and perceptions. In this process, Groups are invited to use novel and effective approaches to the interdependent program areas of drug development, biodiversity conservation and sustained economic growth. The Group must develop the details of the program design following the guidance given in this RFA. It is the primary responsibility of the Group Leader to state clearly the objectives of the Group, to direct the research and other activities stipulated in the proposal, and to ensure that the results obtained are properly disseminated, and published. It is anticipated that decisions will be reached by consensus of the Group under the leadership of the Group Leader and that the U.S. Government Scientific Coordinator will have the opportunity to offer input to this process.

The Group Leader is responsible for organizing meetings of all Group members at least once per year to review progress, plan and design research and technical activities, and establish priorities.

Each project is expected to contribute to the achievement of three classes of benefits: health benefits through the discovery of natural products which may lead to new pharmacologic and possibly agricultural agents, benefits in the understanding and conservation of biological diversity, and potential economic benefits. The following three sections describe responsibilities of the awardee relating to the realization of these benefits.

i. Drug Discovery

One principal end product of the ICBG is the identification of bioactive natural products with potential for biomedical use. Other possible end products include information toward the development of phytomedicines of local importance as well as agricultural agents and other natural product based materials. Research toward these products should utilize the important resources of indigenous knowledge where relevant and acceptable to local participants. The awardee is responsible for developing strategies to insure that profits derived from those agents or from the knowledge which provides access to those agents are equitably distributed to the appropriate participating organizations and communities, as described in Principles for the Treatment of Intellectual Property (Appendix 1).

The Government will retain the option to cross-file or independently file an application for investigational clinical trial [e.g. an Investigational New Drug Application (INDA) or an Investigational New Device] to the United States Food and Drug Administration of any invention resulting from these Government supported Cooperative Agreements. It is the responsibility of the Group Leader to submit to the U.S. Government Scientific Coordinator upon request reports of data generated by the Group or any of its members required for cross-filing purposes. Such reports will include background information, methods, results, and conclusions. They will be subject to approval and revision by Government staff and may be augmented with test results from other Government-sponsored projects prior to submission to the appropriate regulatory agency.

The awardee will retain custody of and rights to the data, and timely publication or dissemination of major findings by the Group members is encouraged. Publications or oral presentations of work done under this agreement will require appropriate acknowledgment of joint support from NIH and NSF, and FAS as applicable, under this RFA. The Government will have access to all data generated under this Cooperative Agreement and may periodically review the data. It is the responsibility of the Group Leader to provide this data to the FIC Program Director and the Government Scientific Coordinator upon request.

ii. Biodiversity Conservation

The primary products of biodiversity conservation efforts should include:

1) strengthened host country capabilities to implement sustainable resource use policies and programs; 2) the establishment of biotic inventories and collections of preserved or living specimens of plants, animals and microbes; and 3) enhancement of the value of biodiversity to communities affected by conservation efforts through benefit-sharing activities, educational programs, sustainable use income opportunities, or other approaches. Additional end products could include floral and faunal lists, identification keys, and computerized databases. These should be made available for use by the host-country natural resource management authorities as soon as possible.

Projects must comply with all national and international regulations regarding collection and importation of organisms. Assurance must be provided that all requisite permits from the relevant governments will be procured. Requests to collect species that have been declared threshold or endangered by the Convention on International Trade in Endangered Species (CITES) must be especially well justified, and all regulations regarding these species must be scrupulously followed.

Collection of biological materials for inventories, assays, chemical analyses or commercial development must be conducted with close attention to the potential impact of collection on natural populations of target or associated organisms.

Voucher specimens should be collected for all taxa. These must be preserved in a manner suitable to allow subsequent identification and scientific analysis of the specimens. Specimen collections must be placed in appropriate depositories, such as natural history museums, herbaria, and living organism stock collections. It is especially important to deposit specimens in the host country, and plans for the eventual deposition of all collections made during the life of the proposed ICBG should be included in the proposal. Strengthening host country capabilities in these areas is encouraged as a component of any ICBG.

Floral and faunal lists and identification keys should be published in English and in the major language(s) of the host country. When ethnobiological studies are involved, results should also be published in the language(s) of the indigenous people(s) where possible.

The development of biodiversity databases, such as computerized keys, inventory lists, and geographic information systems, is strongly encouraged. Where possible, these databases should be located at the host country institution where collections from ICBG activities are deposited. In any case, the institutions where collections are housed must have ready access to the data, and where possible, the biodiversity (biological inventory) database should be accessible via the internet. If these databases are linked to drug discovery databases with proprietary information appropriate attention to security of those data is expected.

iii. Economic Development

ICBG efforts must provide for both near and long term benefits to the source country and communities from the research process and any discoveries which emerge from it.

It is strongly recommended that Groups hold a public meeting or workshop in the host country during the formative or very early working stage of the project. Experience has shown that such fora involving individuals from local communities as well as from university, government, and private voluntary organizations are an extremely valuable means of gaining early feedback on working plans and broad-based support for future project efforts.

For projects that will have substantial interactions with indigenous and local communities Groups are advised to consult social scientists with local expertise, at a minimum during project planning and periodically thereafter.

End products of special concern for economic development include training targeted to the specific needs of the research program and the participating country, enhancement of the scientific infrastructure of the participating country, and identification of new natural products suited for sustainable microenterprise development and/or health promotion in the participating country. In respect to these products the following guidelines must be observed:

In the enhancement of scientific infrastructure, project managers must specifically consult with participating country officials to assure that the enhanced research capabilities can be sustained after completion of the project, using locally available resources. In so far as possible and appropriate to the research needs of the program, equipment procured will be of U.S. source and origin. Major equipment procurements which are not from U.S. sources or origins must be justified in writing and are subject to U.S. Government approval.

Where information is generated that would be useful to developing countries in meeting development objectives, such as information useful in establishing sustainable natural products-based industries or novel and important approaches to partnership frameworks, such information will be made available to the Government of the developing country partners and to the U.S. Government. Moreover, within the Cooperative Agreement, a plan to disseminate this information should be developed and implemented. The dissemination plan may include such elements as publication of results in appropriate journals; presentations at conferences; the transfer of relevant information to agricultural and industrial extension services; and direct publication and extension efforts by the collaborators.

In the licensing of a product for advanced development and/or commercial production, the licensee must be required to use the participating country and/or communities as the first source of raw or processed material, subject to the negotiation of mutually acceptable terms.

b) Nature of U.S. Government Assistance

The U.S. Government shall assist in the activities of the ICBG principally through the U.S. Government Scientific Coordinator and the FIC Biodiversity Program Director. The Program Director shall be the primary Government contact with the Group Leader for issues relating to program administration, funding and policy.

The Coordinator will be the primary Government contact with the Group Leader for scientific and technical issues. The Coordinator will be appointed by the Government from one of the participating agencies. During performance of the award, the Coordinator may provide appropriate assistance in the design of

activities; in the identification of scientific resources; and in the collection of materials or information. In all cases, the role of the Coordinator will be to assist and facilitate, and not to direct activities.

The U.S. Government Scientific Coordinator, as well as any other Group member, may assist in research planning; may suggest studies within the scope of the Group's objectives; may present to the Group findings from published sources or from grant or contract projects in support of these suggestions; may participate in the design of project activities and experiments as agreed to by the Group; and may participate in the analysis of results.

When appropriate and with prior knowledge of the Advisory Committee to the Government Scientific Coordinator, U.S. Government laboratories or contractor laboratories may be available for training related to the specific research efforts of the ICBG. Prior written approval from the laboratory director must be obtained. Funding for this training must be within the ICBG's approved budget.

The *in vitro* human cancer cell line screen of the NCI will be available for testing of all ICBG materials, including extracts, either in the form of a primary screen or for confirmatory secondary testing, as appropriate.

Upon recommendation of the U.S. Government Scientific Coordinator, and with appropriate prior mutual agreement, other Institutes of the NIH, including NIAID, NICHD, NIMH, may use their contract-based resources in support of Group research activities. The following is a list of resources that may be available. It cannot be assumed that any specific resource will be made available, and accordingly they should not be included as part of the application unless formally agreed upon prior to submission, and documentation of such a commitment is provided with the application. All compounds and information exchanged between awardee and the Government will be governed by confidentiality agreements among the parties involved. These resources include:

- i. Reference compounds for standardization of test systems, as analytical standards, and for related purposes.
- ii. Needed resources such as test materials and research results and other information that may not otherwise be available to the Group.
- iii. Laboratory testing capacity, whenever appropriate and possible, in the current contract-based preclinical therapy-related laboratory testing program. The Group is expected to provide sufficient test material for such testing.
- iv. Searches of computer files of materials, chemical structures and biological activity, if requests for such searches are sufficiently focused to avoid excessive costs. Information given to an ICBG will be restricted by any standard confidentiality agreements between the Government and suppliers of test material to the Government.
- v. Experimental animals and other biological resources (e.g. cell cultures), if available, to Groups whose main research activities do not require these materials on a regular basis, and if fully justifiable. Note: in all cases Groups whose experimental approach involves studies that require animals must 1) meet all PHS animal protection requirements (see below) and 2) budget for anticipated associated costs in their application.
- vi. Computer processing and statistical evaluation if costs are not excessive.

The Government will have access to data generated under this cooperative agreement and may periodically review the data.

These "Terms and Conditions of Award" require that the U.S. Government Scientific Coordinator approve the following: reports intended for inclusion in INDAs and Clinical Brochures; redistribution, outside the ICBG, of biological and chemical materials received from the U.S. Government; and dissemination of research or project findings resulting from the use of such materials to assure conformity to existing confidentiality agreements with suppliers.

c) Collaborative Responsibilities

At least twice during the five year duration of awards under this RFA representatives of all funded Groups and all available TAG members will attend a joint meeting to share important information, to review the overall progress of the program and establish future priorities.

d) Arbitration

Disagreements pertaining to approval by the U.S. Government Scientific Coordinator on scientific and technical programmatic matters will be arbitrated by a panel composed of one Group designee, one Government designee assigned by the Government Scientific Coordinator, and a third designee with expertise in the relevant area chosen by the other two. This arbitration procedure in no way affects the awardee's right to appeal an adverse action in accordance with PHS regulations at 42 CFR Part 50, Subpart D, and HHS regulations at 45 CFR Part 16.

■4. Inclusion of Women and Minorities in Research Involving Human Subjects

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This new policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43) and supersedes and strengthens the previous policies (Concerning the Inclusion of Women in Study Populations, and Concerning the Inclusion of Minorities in Study Populations), which have been in effect since 1990. The new policy contains some provisions that are substantially different from the 1990 policies.

All investigators proposing research involving human subjects should read the "NIH Guidelines For Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513) and reprinted in the NIH Guide for Grants and Contracts, Volume 23, Number 11, March 18, 1994.

Investigators also may obtain copies of the policy from the program staff listed under INQUIRIES. Program staff may also provide additional relevant information concerning the policy.

■K. LETTER OF INTENT

Prospective applicants are asked to submit, by October 15, 1997, a short letter of intent that includes a descriptive title of the proposed project, a short (one paragraph) description of the intended components, and to the extent known, names of members of the proposed Group (Group Leader and Associate Programs) and their institutions. The letter of intent is requested in order to provide an indication of the number and scope of applications to be reviewed and to assist in the formation of an initial peer review group. The letter of intent does not commit the sender to submit an application, nor is it a requirement for submission of an application. Letters of Intent should be sent directly to:

Dr. Joshua Rosenthal
International Cooperative Biodiversity Groups Program
Fogarty International Center
National Institutes of Health
31 CENTER DRIVE MSC 2220
BETHESDA, MD 20892-2220

■ L. APPLICATION PROCEDURES

■ 1. Receipt Date

The deadline for receipt of applications at the Division of Research Grants is JANUARY 22, 1998. APPLICATIONS RECEIVED AFTER THIS DATE WILL BE CONSIDERED AS NOT RESPONSIVE TO THIS RFA AND WILL BE RETURNED WITHOUT REVIEW. Please note, the Division of Research Grants will not accept any application to this RFA that is the same as one currently being considered by any other review group or awarding unit of the National Institutes of Health.

■ 2. General

a) The regular research grant application Form PHS-398 (Rev. 5/95) must be used in applying. General instructions for completing the Form PHS-398 are contained in the application package. Apply additional instructions as outlined in this RFA. The Form PHS-398 is available through the NIH pages on the World Wide Web (<http://www.nih.gov/grants/funding/phs398/phs398.html>), from sponsored projects offices at most institutions or from the Division of Research Grants. One completed original and five (5) copies total, including appendices, are required.

Submit a signed, typewritten original of the application, including a single Checklist, and three (3) signed, single sided photocopies in one package to:

Division of Research Grants
National Institutes of Health
Suite 1040
6701 ROCKLEDGE DR MSC 7710
Bethesda, Maryland 20892-7710

To ensure that your application receives appropriate consideration, it is essential to send the two (2) remaining copies of your application with all appendices directly to:

Dr. Joshua Rosenthal
International Cooperative Biodiversity Groups Program
Fogarty International Center
National Institutes of Health
31 CENTER DRIVE MSC 2220
BETHESDA, MD 20892-2220

b) To expedite the review of the application, and to assure its identification with this RFA:

The application form should state "TW-98-001 International Cooperative Biodiversity Groups" on line 2 of the face page of the application form; personalized titles more fitting for your application should be listed on line 1 and not on line 2.

The RFA label available in the application form PHS-398 (Rev. 5/95) must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review.

■ 3. Organization of Application and Suggested Modifications of Form PHS-398 (Revised, 5/95)

This RFA requires the submission of a single application for each proposed International Cooperative Biodiversity Group. Applicants should follow the instructions given in the Form PHS-398 (Rev. 5/95) package unless otherwise indicated in this announcement or in supplemental instructions. Because of the

multi-institutional nature of an ICBG and the special requirements in this RFA, additional instructions regarding format and some modifications are given to guide the writing of a comprehensive application.

The application will be reviewed as a whole, and in addition each Associate Program will receive an individual critique. Therefore, the application should contain separate sections for each Associate Program, preceded by a Group Plan section.

■a) GROUP PLAN

This section should contain the following portions of the PHS-398: Face Page; Description, Performance Sites, Key Personnel; Research Grant Table of Contents; Budget for Entire Period of Proposed Support; Research Plan; Checklist. The 25 page limit described in the PHS-398 applies to this Group Plan section individually.

Complete the FACE PAGE for the application as in a regular research grant proposal.

For the Group Plan section, KEY PERSONNEL should list the Associate Program Leaders for the whole Group. The TABLE OF CONTENTS should number pages for the entire application consecutively, with the FACE PAGE as page 1.

The BUDGET page in this section (Form EE) should reflect the consolidated TOTAL DIRECT COSTS, by category, of the entire proposed ICBG. A summary page of the TOTAL DIRECT COSTS, by Associate Program, by year, must be included on a separate page. The Group Plan section should also provide, from the applying institution, a Detailed Budget for the First Twelve Month Period and a Budget for the Entire Proposed Project Period for Direct Costs for the management and coordination of Group activities through a Central Operations Office and all travel including the cost of annual Group meetings.

Often the various research tasks necessary to reach the Group's goals may need to be phased in, at least in part, in sequential fashion. For example, isolation chemistry will not likely begin until samples have been collected and samples with biologically active constituents have been identified and verified. In such cases, the budgets for the individual Associate Programs should, logically, reflect an appropriate change in relative emphasis among tasks until an operational steady state situation is attained. Justification for phase-in budgets also should be provided.

Inasmuch as the Group Leader may also function as an Associate Program Leader for his/her Associate Program, detailed budget information that duplicates information provided in the section describing the Group Leader's Associate Program need not be included in the Group Plan Section.

The RESEARCH PLAN in the GROUP PLAN section should summarize and synthesize the associate programs to illustrate a coherent Group effort, e.g., how the projects are mutually reinforcing and how collectively they will further the goals of the proposed research. This should include a description of the interrelationships among members of the Group and organizational charts in accordance with Sections H. and I. of this RFA. It is important to discuss any prior collaborative efforts among the investigators as evidence of the ability to work together in multi-disciplinary and/or international projects.

The Group Plan section should not repeat details that are provided in the Associate Program sections, however, it should contain any additional information about the proposed Group Leader or his/her institution that is evidence of the capability to carry out the scientific and administrative duties required in this RFA and the functions of the Central Operations Office.

In addition, the Group Plan Section must include the following elements to be considered responsive to minimum requirements.

- i. A statement assuring compliance with the Program Principles for the Treatment of Intellectual Property and assuring adequate patent coverage of new inventions that may issue as a result of Government funding in accordance with Appendix 1.
- ii. A statement of acceptance of the provisions of "Terms and Conditions of Award," as described in Section J, Part 3.
- iii. A plan to assure maintenance of close collaboration and effective communication among members of the Group in accordance with Section I, Part 7.

■b) ASSOCIATE PROGRAMS

Each of the Associate Programs, including the Associate Program (if any) of the proposed Group Leader, should be numbered consecutively (AP 1, AP 2, ...). Use Form PHS-398 for each Associate Program but omit the checklist for the individual program. The 25 page limitation stipulated in the PHS-398 application package applies to each of the individual Associate Programs.

Each Associate Program section should begin with its own TITLE PAGE (in front of the application FACE PAGE). The TITLE PAGE should state "International Cooperative Biodiversity Groups", the overall project title, and the Group Leader at the top of the page. The Associate Program Leader, the Associate Program number within the group, and its general field(s) of study should be stated in the lower right hand corner.

The "Title of Project" (line 1) on the FACE PAGE should list the overall Group title and should be the same for all associate programs in one Group application, but should end with the Associate Program number (e.g., - AP 1). The remainder of the FACE PAGE should be completed as in a regular grant application.

The TABLE OF CONTENTS for these sections should be consistent with the GROUP PLAN TABLE OF CONTENTS, and should be detailed enough to enable reviewers to find specific information readily.

It is also suggested that the "Description" (grant application form page BB) of each of the Associate Programs, in addition to describing the work proposed, provide a statement of relevance to the overall objectives of the proposed ICBG.

The remaining parts of the PHS-398, except the CHECKLIST for each Associate Program section should be completed as in a normal grant application, detailing the proposed work of the Associate Program, and where relevant, the interactions with other Associate Programs within the Group.

■c) APPENDICES

- i. Incumbent Groups must describe, in 10 pages or less, the progress they have attained toward the original goals of their program, including a list of publications, workshops and any other accomplishments of the Group.
- ii. If internal or external advisory groups will be used in addition to those specified in this RFA, list their membership and describe their roles.
- iii. List in a separate table all consultants, both paid and unpaid. Include a signed letter of agreement from each consultant.
- iv. If the applicant has an approved assurance covering the research (multiple project assurance for human subject/full assurance of compliance for animal subjects), the applicant should provide with the application, an indication of certification of institutional review board (IRB) approval if humans are involved and verification of the institutional animal care and use committee (IACUC) approval if animals are involved in any Associate Program (domestic and foreign). These reviews and approvals should occur PRIOR TO SUBMISSION OF the applications for award and the certifications and verifications should be SUBMITTED WITH the applications. Failure to provide required certifications and verifications within applications could result in deferral of award or rejection of application. If animals or humans will be subjects of the research at PERFORMANCE

SITES OTHER THAN THE APPLICANT ORGANIZATION, the applicants must identify, with the application, the assurance status of each participant. Failure to provide this information within the applications could result in deferral of award or rejection of application. Questions concerning use of human or animal subjects in research should be referred to the Office of Protection from Research Risks, National Institutes of Health, Bethesda, MD 20892 (Telephone: (301) 496-8101 for Human Subject Protections and (301) 496-7163 for Animal Welfare).

■ M. MINIMUM REQUIREMENTS FOR APPLICATION

Applications to the International Cooperative Biodiversity Groups must meet a set minimum requirements, listed below, in order to be considered by the peer review panel. These requirements are each described elsewhere in this RFA and should be addressed in the relevant portions of the application:

1. Identify a single Group Leader from a U.S. non-profit institution who will be responsible for the application, for Group research and technical activities, and for the disbursement of funds in support of Group activities.
2. Structure the Group to include at least one Associate Program located within a developing country institution.
3. Identify the Group Leader's institution that will assume legal and financial responsibility and accountability for the use and disposition of funds awarded on the basis of this RFA; show availability of personnel and facilities capable of performing and supporting the administrative and scientific functions of this ICBG.
4. Present, for each Associate Program, research and technical approaches, as specified in Sections H and J.3. of this RFA, and detailed budget requirements.
5. Provide a description of the Group's plan for assuring adequate protection of intellectual property and sharing of benefits that may result from Government funding of the proposed work. The application requires an outline for the basic framework of an agreement or agreements among all Group members and their institutions, including local community organization representatives, signed and dated by the organizational official authorized to enter such arrangements for each Group member and member institution. The outline or plan need not list specific terms of agreements, but must indicate correspondence of the basic plan with relevant national and international laws and the program principles described in Appendix 1. Finalized, signed agreements among all Group members must be submitted to the FIC for review prior to award.
6. Provide a clear, concise plan in narrative and diagrammatic form that depicts the interrelationships among the members of the Group and the contribution of each to the fulfillment of Group objectives; provide an organizational chart of the Group showing the name, organization, and scientific discipline of the Group Leader and Associate Program Leaders; provide an organizational chart for each Associate Program within the Group showing relationships among the key personnel.
7. Provide a plan to assure the maintenance of close collaboration and effective communication among members of the Group and between the Group and host country government and community leaders. The application must include letters of commitment to the plan by all Associate Program Leaders.

8. The application should include a general letter of support for the project from the relevant developing country Government agency(ies), acknowledging the multiple goals of the program. The application must include a list of the documents that will ultimately be necessary to satisfy local institutional and governmental requirements, and a statement of commitment from the Group Leader to provide these before an award is made. Copies of all permits and legal documents and certifications of governmental authorizations required to assure collaborations must be provided before an award is made.
9. Describe the ways in which the Group Leader and the Associate Program Leaders possess the outstanding scientific and technical skills and leadership qualities to conduct the proposed research successfully, including relevant research programs, experience, unique competencies, and pertinent publications, peer recognition or other evidence of accomplishment.
10. Outline the capacity and plans to cooperate with and to provide research training for developing country nationals (eg. scientists, students).
11. Describe the competence of the Group Leader to manage comprehensive research projects and to coordinate and integrate research and project activities of diverse Associate Programs.
12. Describe how each component Associate Program is required for the attainment of the Group's objectives and that each has available the professional and technical personnel to permit efficient and successful conduct of the proposed research; documentation should include curricula vitae for all key professionals involved in the Group.
13. Indicate that all key personnel have the time available for this project and show for all key professional personnel: 1) title, identifying number, percentage of effort devoted to the project, direct costs, and project period of all awarded and pending grants, contracts, Cooperative Agreements, and industrial commitments regardless of source of funding; and 2) identify and explain areas of potential scientific and/or budgetary overlap with active and pending grants, contracts, and Cooperative Agreements and what support would be relinquished if this Cooperative Agreement award is made.
14. Describe, for each component Associate Program and the Group as a whole, the facilities available for conduct of the proposed research. Funds will be provided for alteration or renovation only for facilities in developing countries under this RFA.
15. Provide a plan for scheduling at least one Group meeting per year with active participation of all Associate Program leaders, notifying Group members, and disseminating Group meeting proceedings. Include plans for information exchange and discussions among Group members between Group meetings.
16. Provide a research training plan which includes types of training, numbers of trainees, in-country courses and workshops, if any, and letters of commitment from institutions where training will take place. Costs associated with training activities must also be specified in the Budget section of the application.
17. Submit an overall work scope and schedule for the specified time frame of the application.

■ N. REVIEW CONSIDERATIONS

■ 1. Review Procedures

Applications will be received by NIH Division of Research Grants (DRG) and reviewed by the DRG and FIC for completeness. Incomplete applications will be rejected without further review and returned to the applicant.

The FIC will evaluate proposals for their responsiveness to this RFA. Applications will be analyzed to determine if they meet the goals and objectives of the program as described in this RFA. Applications that are judged to be non-responsive will be administratively withdrawn, and the proposed Group Leader and institutional official will be notified.

The Government may conduct an initial peer review to eliminate applications that are clearly not competitive for award. The Government will withdraw from further competition those applications judged to be noncompetitive and notify the Group Leader and institutional official.

Those applications judged to be both competitive and responsive will be further evaluated, using the review criteria below, for scientific and technical merit by a peer review group convened by the National Institutes of Health. The peer review group will consist of members with the necessary scientific disciplines to evaluate the applications received. Secondary review will be provided by the FIC Advisory Board. Based on recommendations from the peer review process, the ICBG Technical Advisory Group and Participating Agencies will recommend funding levels and priorities. The Agencies will critically examine the submitted budget and will recommend an appropriate budget and period of support for each approved application. Final funding decisions will be made by the Director, FIC, considering the outcome of the above process.

■ 2. Review Criteria

■ Significance

a) Potential impact on human health, biodiversity conservation, and sustainable economic development.

■ Approach

b) Technical merit of proposed methods in response to this RFA.

c) Degree of multidisciplinary cooperation among associate programs and potential for synergy of activities toward the three goals of the program. Adequacy of plans for effective intra-Group communication and for assuring Group cohesiveness, accounting for the special requirements of an international collaboration.

d) Adequacy of plans to build capacity for biodiversity and biomedical research, and applicability of those plans to local and international scientific needs beyond the specific targets of the proposed work.

e) Extent and level of developing country participation, and documentation of local community involvement.

■ Innovation

f) Originality of proposed approaches in response to this RFA.

■ Investigators

g) Adequacy of the scientific disciplines and specific competencies represented by the Group Leader and Associate Program Leaders; experience, competence, commitment, and time availability of the Group Leader, Associate Program Leaders, and other key personnel. Previous success relevant to this RFA and demonstrated past support from NIH, NSF or other sources.

h) Ability, as measured by previous success, to cooperate with and train developing country nationals in the scientific and technical disciplines considered critical to meeting the objectives of the proposed programs.

i) Administrative experience and competence of Group Leader in the development, implementation, and management of comprehensive research programs and the demonstrated commitment of the applicant institution to support these activities.

■ Environment

j) Extent to which the proposed work takes place in a country or region that is a priority for biodiversity conservation and economic development efforts, and takes advantage of the unique biological and intellectual resources (including indigenous knowledge, where appropriate) of that country or region.

k) Adequacy of existing physical facilities, research and training resources available to the Group Leader and Associate Program Leaders. Evidence of availability and competence of the applying institutions to carry out all required legal, fiscal and policy responsibilities.

Special Considerations

This RFA does not cover clinical trials or collection of samples of human tissue. However, research that involves obtaining data through 1) intervention or interaction with a living individual, or 2) collecting private information that identifies a living individual, shall be undertaken only in accord with Department of Health and Human Services regulations for protection of human subjects (Title 45 Code of Federal Regulations Part 46). Investigators proposing such research should consult their local Institutional Review Boards or the Office for Protection from Research Risks (OPRR), National Institutes of Health, 6100 Executive Boulevard, MSC 7508, Rockville, Maryland 20852-7508. In this regard, applicants must be sure to meet the requirements of obtaining single project assurances from OPRR for all projects involving human subjects at foreign sites unless otherwise covered by a multiple project assurance.

The involvement of informants in the collection of information on traditional uses of biota for ethnomedical or other uses requires strict adherence to the Principles for the Treatment of Intellectual Property outlined in Appendix 1.

■ O. INQUIRIES

It is strongly advised that prospective applicants contact the FIC early in their planning process to discuss their applications and to obtain any clarifying information or instructions that may be developed. Written or telephone inquiries concerning the objectives and scope of this RFA or inquiries about whether or not specific proposed research would be responsive to this RFA are encouraged and should be addressed to:

Dr. Joshua Rosenthal
Director, Biodiversity Program
Fogarty International Center

National Institutes of Health
31 CENTER DRIVE MSC 2220
BETHESDA, MD 20892-2220
Telephone: 301-496-2516
FAX: 301-402-2056
Email: joshua_rosenthal@nih.gov

Direct inquiries regarding fiscal matters to:

Ms. Silvia Mandes
Grants Management Officer
Fogarty International Center
National Institutes of Health
31 CENTER DRIVE MSC 2220
BETHESDA, MD 20892-2220
Telephone: 301-496-1653
FAX: 301-402-0779
Email: mandess@ficod.fic.nih.gov

Direct inquires regarding peer review of applications to:

Dr. Kirt Vener
Chief, Review Logistics Branch
Division of Extramural Awards
National Cancer Institute
Executive Plaza North
Room 622B
BETHESDA, MD 20892
Telephone: 301-496-7173
FAX: 301-402-0275
Email to: kv5n@nih.gov

■ P. AUTHORITY AND REGULATIONS

Awards are made under authorization of the Public Health Service Act, Title III, Part A, Sections 301 and 307, and Title IV, Part A of Section 482 (P.L. 78-410, as amended by P.L. 99-158, 42 USC 241, 242I, and 287b) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. The participation by other agencies in funding the program is authorized under the Economy Act (31 U.S.C. 1535).

APPENDIX 1

PRINCIPLES FOR THE TREATMENT OF INTELLECTUAL PROPERTY AND THE SHARING OF BENEFITS ASSOCIATED WITH ICBG SPONSORED RESEARCH.

In developing both research plans and intellectual property agreements it is important that all involved understand the differences between patent coverage and benefit-sharing agreements. While legal protection of the right to commercialize an invention is generally accomplished through the patent system, agreements among collaborators are generally required to designate the terms of partnerships including, among other things, the licensing of an invention and the sharing of any financial benefits that accrue from it.

The conduct of ICBG sponsored research and the agreements among the collaborators must address the following principles to be eligible for funding.

a) **Protection of inventions using patents or other legal mechanisms.**

Non-profit organizations (including universities) and small business firms retain the rights to any patents resulting from U.S. Government contracts, grants, or Cooperative Agreements. P.L. 96-517, through regulation, extends to businesses of any size the first option to the ownership of rights to inventions made in the performance of a federally-funded contract, grant, or Cooperative Agreement. All group members, therefore, including businesses of any size, might be full partners in the research of the Group and in rights to file patents for any inventions resulting therefrom as specified in the Group's research agreement. This includes communities organized into or represented by an appropriate legal entity.

The specific intellectual property arrangements among the institutions may vary and could include joint patent ownership, exclusive licensing arrangements, etc. Valuable intellectual resources that cannot or will not be patented, such as novel assays or traditional medicinal techniques, may require alternative protection methods such as trade secrets. Applicants are encouraged to develop an arrangement that best suits the particular circumstances of their Group.

b) **Clear designation of the rights and responsibilities of all partners.**

i. This is principally done through the design of adequate contractual agreements. Agreements should be among all collaborating organizations, whether or not they are recipients of government funds. These may include commercial drug developers, source country and US research institutions, and indigenous and local peoples whose resources, biological or intellectual, are utilized in the research process.

ii. It is strongly recommended that all parties to agreements have separate, competent legal counsel to represent their interests.

iii. Useful contractual tools for the designation of rights and responsibilities include material transfer agreements, research and development agreements, license options agreements, know-how licenses, benefit-sharing agreements, and structured trust funds.

iv. Unless stipulated otherwise in agreements among source country institutions and their collaborators, biological samples and associated information collected under ICBG sponsored research is the property of the source country institutions. The Government retains "march-in" rights to require licensing if the inventing organization(s) fail to pursue development of the process or invention, as described in the "Terms and Conditions of Award".

v. The ownership and compensation terms of first generation and subsequent inventions based upon a lead discovered in ICBG work should be clearly stipulated in agreements.

vi. Agreements should specify that the basic goals of the collaboration include the drug discovery, economic development, and the conservation and sustainable use of biological diversity.

vii. Agreements should also indicate how a sustainable source of materials for follow-up analysis of a lead compound will be developed, and should preferentially use the participating country and/or communities as the first source of raw or processed materials.

c) **Sharing of benefits with the appropriate source country parties.**

- i. Equitable distribution of benefits should accrue to all those who contribute to a commercialized product, whether they are members of the consortium or not, including research institutions and local or indigenous people who provide useful traditional knowledge.
- ii. Benefits should flow back to the area in which the source plant, animal or microorganism was found, in such a way that they at least indirectly promote conservation of biological diversity.
- iii. The selection of beneficiaries must be justified in terms of program goals, as well as local and international laws and customs.
- iv. Benefits should be structured such that they are appropriate to the needs of the communities and the resources of the other collaborators. For example, trust funds managed by a community or community-project board may be more effective in support of conservation and health or education services than cash payments to a single individual or authority. Note that direct cash compensation may even have injurious effects on non-money economies.
- v. Ideally, compensation begins flowing early in the collaboration through initial payments, training, equipment or services, to provide near term conservation incentives.

d) Disclosure and consent of indigenous or other local stewards.

- i. Arrangements for the use of traditional knowledge or the collection of samples from the lands of local peoples should be based upon full disclosure and informed consent of those peoples.
- ii. Indigenous concepts of intellectual property should be respected. If for instance, cooperating indigenous groups, on the basis of religious or other concerns, object to specific uses, widespread dissemination or other treatments of the knowledge they provide, these concerns should be respected in the conduct of ICBG projects.
- iii. The process of disclosure and informed consent should be as inclusive and formal as is possible and culturally appropriate. The best practice is the development of written agreements with a community following complete and formal presentation of the Group's goals and methods. Presentations should provide realistic descriptions of the type, amounts and probabilities of benefits as well as any costs or risks that may accrue to cooperating communities.
- iv. Arrangements with individuals who cooperate or provide information should be based upon prior community-level agreements whenever possible or appropriate.

e) Information flow that balances proprietary, collaborative and public needs.

- i. Agreements and research plans should anticipate the tension between the traditional scientific ethic of public access to information, including publication of results, and the understandable desire of indigenous or commercial partners for confidentiality of information with potential commercial value, pending protection through patenting or other means.
- ii. Sharing of information among collaborating institutions should be as complete as possible to maximize efficiency of research and equity in partnerships while recognizing the proprietary concerns of those partners.

f) Respect for and compliance with relevant national and international laws, conventions and other standards.

- i. Relevant international conventions such as the U.N. Convention on Biological Diversity and national laws regarding study, use and commercialization of chemical, biological and cultural resources should be observed rigorously in the development of agreements and the conduct of research.
- ii. An essential goal of this program is to develop models for sustainable and equitable commercial use of biodiversity-rich ecosystems. As such ICBG research agreements and activities should, wherever possible, go beyond the minimum legal standards regarding international research collaborations, looking to codes of conduct and other standards for guidance.