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Bioprospecting, Benefit Sharing, and Biotechnological Capacity Building

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Summary. — Substantial attention has been given to the obligations of developed countries to share benefits and transfer technology in exchange for access to biodiversity. There has been comparatively little discussion of measures that developing countries can take to attract and fully benefit from bioprospecting endeavors. Efforts in Costa Rica and South Africa to promote value-added bioprospecting and national programs in Korea, Taiwan, Singapore, and Cuba to develop biotechnological capabilities are analyzed for insights into the components of successful strategies for sustainable development of biochemical resources. Potential synergies between national programs to promote biotechnology and value-added bioprospecting are also discussed.

Key words — bioprospecting, biotechnology, biodiversity, sustainable development, natural products

1. INTRODUCTION

Bioprospecting, defined as the purposeful evaluation of wild biological material in search of valuable new products, has always been a central activity in human development. In its modern form, bioprospecting involves the application of advanced technologies to develop new pharmaceuticals, agrochemicals, cosmetics, flavorings, fragrances, industrial enzymes, and other products from biodiversity. Until recently, organizations engaged in bioprospecting were under no obligation to compensate countries from which biological material had been collected. With the entry into force of the convention on biological diversity (CBD), open access to biological resources was replaced by a recognition of the sovereign rights of each country to control access to the biodiversity existing within its borders. In accordance with the CBD, bioprospecting organizations are now expected to share benefits and transfer technology in exchange for access to biochemical resources. [1]

The doctrines of sovereign control and equitable benefit sharing expressed in the CBD have also been incorporated in national and subnational legislation, a principal objective of which is the creation of regulatory processes to ensure that equitable benefit sharing arrangements are negotiated prior to granting access to biological resources (Glowka, 1998). Efforts to define and foster equitable benefit sharing from bioprospecting activities have also been supported by a steady stream of case studies and policy guidelines (Aalbersberg, Korovulavula, Parks, & Russell, 1998; Chasek *et al*., 1999; Glowka, 1998; Guérin-McManus *et al*., 1998; Laird, 1993; Mays, Duffy-Mazan, Cragg, & Boyd, 1997; Moran, 1997; Mugabe, Barber, Henne, Glowka, & Viña, 1996; Rosenthal, 1997; ten Kate, 1997). This body of research has provided a useful catalog of alternative benefit sharing arrangements but, as evidenced by the continuing debates by the conference of the parties to the CBD, there remain widely divergent views on what constitutes fair and equitable benefit sharing and how best to promote it (UNEP, 1995, 1997–1999).

One source of continued misunderstanding is the disparity between the market value of products derived from biological resources and the compensation provided for the raw materials themselves. Several publications have utilized more rigorous economic models as a means of estimating the value of biological samples as inputs for pharmaceutical research

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and development, R&D, (Artuso, 1997a; Aylward, 1993; Barbier & Aylward, 1996; Simpson, Sedjo, & Reid, 1996). The analysis by Simpson, Sedjo and Reid (SSR) injected a bit of reality into the benefit-sharing debate by reminding policy makers that, like all other goods, the demand curve for biological samples is downward sloping. Given this basic economic fact, the market price for randomly collected biological samples is likely to be little more than the cost of collecting them. But SSRs conclusion that "the expected pharmaceutical value of preserving any given plant species or hectare of threatened habitat are negligible" is based on two simplifying assumptions; (a) that plant samples can be treated as uniform commodities and (b) that samples of all plant species are readily available for pharmaceutical screening. These assumptions are helpful in constructing a tractable mathematical model, but for purposes of policy analysis they are misleading oversimplifications.

A model involving monopolistic competition for a differentiated product more accurately reflects the complex reality of the market for biological samples, extracts and derivative products (Artuso, 1997b). Source country suppliers that can provide biological samples and derivative products which combine relatively rare ecological characteristics with associated cultural and scientific knowledge, low production costs, a stable political environment, etc., have the potential to obtain significant rents. It is the interaction of the biological and associated abiotic characteristics of biological resources that can give rise to value-added bioprospecting.

It is also important to note that analysis by SSR does not take into account the potential effect of investments in research and capacity building on the market value of a country's biochemical resources. The interaction between conservation of biological resources, bioprospecting, and knowledge generating investments has been explored by Brazee and Southgate (1992) and Barbier and Aylward (1996). Rausser and Small (2000) have also modeled the potential effects of scientific and ethnobotanical research on the expected value of plant samples. The general conclusions reached in all of these articles are however limited by their dependence on formal optimization models. The studies are unanimous in recognizing that the optimal bioprospecting strategy will include some level of knowledge generating investment. But they do not contain any analysis of the potential benefits of specific policies or programs that could be used to promote bioresource development.

In the hopes of providing more practical guidance for policy makers, I have sought to combine insights provided by theoretical economic models with empirical analyses of value-added bioprospecting endeavors and biotechnology development programs. I analyze national biotechnology programs in Korea, Taiwan, Singapore, and Cuba, as well as value-added bioprospecting programs in Costa Rica and South Africa, for insights into the components of successful strategies for sustainable development of biochemical resources. Potential synergies between biotechnology and bioprospecting are discussed, as well as obstacles to coordination of national programs aimed at promoting these activities.

2. BIOPROSPECTING AND SUSTAINABLE DEVELOPMENT

I use the term sustainable development to refer to widespread, long-term improvement in economic opportunity and well being that is realized without significant damage to the environment. Bioprospecting activities can theoretically contribute to sustainable development by providing incentives for conservation while developing technological capabilities that enhance long term opportunities for economic growth. The problem is how to transform this theoretical potential into reality.

Table 1 presents data on total revenues, percentage of revenues attributable to products derived from biological material, and R&D expenditures for several industries that utilize biochemical resources. These data provide some indication of the current and potential size of various markets for biochemical resources. The data also highlight the distinction between the value of finished products containing or derived from biochemical resources and the significantly lower value of raw biological material as an input in the research or production of these products. The pharmaceutical and cosmetic industries provide two representative examples of this discrepancy.

Global sales of prescription pharmaceutical products are estimated to exceed $330 billion and one recent study found that 57% of the top 150 prescription drugs contain active ingredients that are pure natural products, synthetic derivatives or chemical analogs of natural

Table 1. *Data on markets for biochemical resources ($ billions)*

Product category	Global sales	Sales derived from biochemical resources	Market value of biological inputs	R&D expenditures[a]
Pharmaceuticals	330	188[b]	14	46
Phytomedicines	14	14	8	N/A
Agrochemicals	30	N/A	N/A	1.8
Seeds	30	30	N/A[c]	1.5
Enzymes	12	1.8	0.02	0.25
Personal care	64	7.6	1.2	1.0
Flavors & Fragrances	14	2.2	N/A	1.0

Sources: Boswell (2001), Brown (1998), Brown and Walsh (2000), FIS (1999), Glaser (2000), Grifo, Newman, Fairfield, Bhattacharya, and Grupenhoff (1997), IMS (1998), Marley and Thomas (1999), Mathieu (1998), Mirasol (1998), Ortega (1998), Parkinson (2001), Sauer (2000), company financial reports.

[a] All estimates of R&D expenditures except pharmaceuticals are based on R&D as percentage of sales for top companies multiplied by global sales.

[b] Includes purified natural products, derivatives, and synthetic analogs of natural products.

[c] Private seed companies generally rely on their own germplasm collections. In addition, genetic resources for plant breeding programs can still be obtained at little or no cost from national and international seed banks.

products (Grifo *et al*., 1997). [2] But, the value of plant, animal, and microbial products directly used in the manufacture of prescription pharmaceuticals is estimated to be less than $12 billion (Ortega, 1998). Biodiversity is also a source of novel compounds for the discovery of new drug leads, and pharmaceutical companies annually spend more than $45 billion on R&D (Mathieu, 1998). But screening of natural and synthetic compounds accounts for less than 12% of the pharmaceutical industry's R&D expenditures and most of these resources are expended on equipment and personnel costs rather than acquisition of compounds (PhRMA, 1999).

A similar analysis applies to cosmetic and personal care products. Sales of personal care products in the US, Europe, and Japan exceeded $64 billion in 1999. Skin care products containing biologically derived antioxidative, analgesic, antibacterial and anti-inflammatory agents are a growing segment of this market (Brown & Walsh, 2000). One study estimated US sales of naturally derived personal care products to account for $2.5 billion of the $28 billion US market. But, the value of the biological source material used in these products was estimated at less than $500 million (Brown, 1998).

Although markets for products derived from or containing biochemical resources are substantial, competition between suppliers of biological material, low probabilities of developing a new product from any given sample, and continued advances in alternative R&D technologies will continue to limit the compensation bioprospecting organizations are willing to provide for unevaluated biological samples (Artuso, 1997b; Simpson *et al*., 1996). Still, many biochemical compounds cannot easily be synthesized. In addition, some consumers prefer to use natural products instead of synthetic substitutes. This creates opportunities for developing commercial-scale operations for production and extraction of biochemical material. The bulk supply of raw materials and purified natural products can provide a source of revenue and a means of developing technical and management capabilities. But, the laws of supply and demand still hold; unless the commodity can be differentiated on the basis of quality or other characteristics, prices and profits will be limited by the ability of other suppliers to enter the market.

Some commentators have suggested that a multilateral regulatory system is needed to ensure that developing countries receive appropriate levels of compensation in exchange for access to biodiversity (Mulligan, 1999; Vogel, 1994). Unfortunately, some proposals intended to benefit developing countries could actually do more harm than good. If global demand for biological resources is elastic, an international regulatory system that attempted to enforce above market rates of compensation, in exchange for access to biochemical resources, would reduce source country benefits. One possible solution to this problem is to provide compensation from an international tax on sales of broad classes of products (e.g., seed sales) that contain or were derived from biochemical resources (Barton & Christensen,

1988). The critical issue in this case is political feasibility.

Multilateral compensation arrangements have been a continuing point of contention in the ongoing negotiations to update the International Undertaking on Plant Genetic Resources. Some indication of the lack of consensus that still exists on this issue can be seen from the amount of bracketed text that remains in the latest draft of the benefit sharing sections of negotiating text. [3] With respect to the access and benefit sharing provisions of the CBD, even relatively modest proposals to develop a protocol or code of conduct for bioprospecting activities have found little support from the US, Great Britain, and other developed countries. [4] It would seem that for the foreseeable future, countries hoping to benefit from the chemical and genetic value of their biodiversity cannot pin their hopes on international regulatory systems or multilateral compensation arrangements.

In a competitive market environment, generating significant long-term benefits from bioprospecting activities will require the development of differentiated products and services that combine access to biodiversity with associated knowledge, technical capabilities, and marketing arrangements (Artuso, 1997b, 1999; Rausser & Small, 2000). This highlights the necessity for countries seeking to benefit from bioprospecting to move beyond a "gatekeeping" approach designed to control access to biodiversity, toward a more proactive strategy aimed at promoting sustainable development of biochemical resources. The importance of this issue is underscored in Article 10 of the CBD, which calls upon each contracting party to "encourage cooperation between its governmental authorities and its private sector in developing methods for sustainable use of biological resources."

3. LESSONS FROM NATIONAL BIOTECHNOLOGY DEVELOPMENT EFFORTS

The entrepreneurial and institutional capabilities required to develop and market new biologically derived products are quite similar whether the product is recombinant interferon, a plant derived anti-cancer agent, or a novel industrial enzyme derived from microbial diversity. It is therefore interesting to contrast the generally reactive approach that countries have taken toward bioprospecting activities with the relatively ambitious national programs that many developing countries have implemented to promote investment in biotechnology. [5]

Biotechnology is an expanding set of technical and scientific capabilities that has the potential to increase innovation and productivity across a wide range of industries. The potential for positive spillovers from biotechnological R&D provides the theoretical rationale for government investment and incentive programs (Jaffe, 1986; Mansfield, 1991). While national biotechnology development efforts vary significantly due to differences in technical capabilities and political systems, an analysis of relatively successful programs in Singapore, Taiwan, Korea, and Cuba, highlights four common features: (a) a high level of political support; (b) increased government funding for R&D, with a focus on specific products and commercial applications; (c) promotion of collaborative R&D activities between public, academic, and private sector organizations; and (d) provision of financing and business development services to support the development of new biotechnology companies.

In Taiwan, biotechnology was designated by the Prime Minister's office in 1985 as one of four key industrial sectors for future development. Political support for Korea's biotechnology development program was provided through the passage of national legislation, and in Singapore, the Economic Development Board (EDB) targeted biotechnology as one of two priority industry sectors for the 21st century. Singapore, Taiwan, Korea have also demonstrated their commitment to developing scientific and technical capabilities in biotechnology by establishing national centers of excellence (Acharya, 2000; Gonsen, 1998).

In addition to increased public funding for biotechnological research, successful national programs have included a variety of mechanisms to ensure that publicly supported research eventually leads to new commercially valuable technologies and products. In Taiwan, the government sponsored Development Center for Biotechnology was established at National Taiwan University. Collaborative efforts with local pharmaceutical companies to develop products for controlling hepatitis B and C were designated as priority research targets for the Center. The focus on hepatitis is understandable since in Taiwan, and other countries of Southeast Asia, prevalence rates of hepatitis B and C exceed 10% of the popula-

tion, and current treatment options are too costly for most people to afford (WHO, 2000).

In Singapore, the National Institute of Molecular and Cell Biology (IMCB), was established on the campus of the National University. Public funding for IMCB has been supplemented since 1989 by more than $50 million in contributions from Glaxo–Wellcome. Singapore also provides tax incentives for university–industry collaborations and IMCB has forged a number of collaborations with national and multinational firms, including Pfizer, Boehringer Mannheim, Lynks Therapeutics, and Applied Genetics. IMCB has also created several start-up companies to commercialize its inventions. (ATIP, 1997; Gonsen, 1998; The-Yung Liu, 1999). In Korea, the Ministry of Science and Technology and the Ministry of Trade and Industry, promoted private sector involvement in biotechnology by providing the initial support needed to create the Korean Genetic Engineering Research Association and the Korean Bioindustry Association (Acharya, 2000).

National biotechnology development programs have also included public sector support for a variety of business promotion activities including venture capital financing, tax incentives, and creation of science and technology parks. One of the more innovative examples of proactive business development and technology transfer is Singapore BioInnovations (SBI). Singapore's EDB established SBI in 1990 to commercialize local biotechnology inventions and identify foreign companies willing to transfer technology to Singapore in exchange for equity investments. SBI offices are located in six US cities that are considered centers of biotechnology. SBI staff actively seek out companies with technological capabilities and research programs that address the most pressing needs of Southeast Asia. Singapore also provides income tax exemption for a period of 5–10 years to newly established local biotechnology firms (ATIP, 1997).

Cuba's successful biotechnology program provides evidence that even a small country with limited industrial capacity can succeed in developing internationally competitive products. A key to Cuba's success was its decision to focus on the development of recombinant interferon as the initial goal of the program. Production of interferon was selected as the initial objective because it would require gaining competence in key biological techniques. In addition, administration of recombinant interferon had proven to be effective against several viral diseases, such as dengue fever and hepatitis that are endemic to developing countries. Interferon also showed promise as an anticancer agent. The interferon effort was spearheaded by a group of policy makers and scientists from relevant ministries and research institutes. This group reported directly to Cuba's State Council and operated largely outside the traditional government bureaucracy (Billard, 1993; Pilling, 2001; Satz, 2000).

Immediately following the initial production of interferon in Cuba in 1981, the government established the Center for Biological Research which was later expanded and renamed the Center for Genetic Engineering and Biotechnology (CIGB). Cuba's biotechnology capabilities were then expanded into other product areas and technologies including the development of vaccines, immunosuppressants, and anti-cancer agents derived from natural products, as well as agricultural biotechnology. In 1987, the CIGB formed a wholly owned international marketing subsidiary, Heber Biotec SA, which by 1999 had sales of $45 million with operations in 38 countries (Satz, 2000). The majority of these sales have been to other developing countries, but this may soon change. Glaxo–SmithKline recently licensed the rights to test and market the Meningitis B vaccine developed by Cuba's Finlay Institute. York Medical, a Canadian company is also paying for clinical trials in the UK of an anticancer vaccine developed in Cuba (Pilling, 2001).

4. NATIONAL BIOPROSPECTING PROGRAMS

Bioprospecting projects conducted in accordance with the access and benefit-sharing provisions of the CBD are being conducted in numerous countries around the world, including Argentina, Australia, Bermuda, Cameroon, Chile, China, Costa Rica, India, Indonesia, Jamaica, Malaysia, Mexico, Nigeria, South Africa, and Suriname. The bioprospecting activities underway in most of these countries, however, were initiated by foreign organizations and the host countries have not responded by developing more proactive efforts to promote bioprospecting. Costa Rica and South Africa are two countries that are using the experience and technical capabilities gained from initial bioprospecting endeavors to develop

more comprehensive value-added bioprospecting programs. A comparison and critical analysis of the two programs, in relation to the national biotechnology development efforts reviewed above, can provide some insights for other countries seeking to benefit from bioprospecting.

For more than two decades biodiversity conservation has received strong support from both of Costa Rica's major political parties. Over 20% of the country have been set aside as national parks and nature reserves. In 1987, the Ministry of Natural Resources, Energy, and Mines (MIRENEM) with financial support from the MacArthur Foundation, established a Biodiversity Office to develop a new strategy for biodiversity conservation. MIRENEMs Biodiversity Office initiated a planning process which led to the creation in 1989 of a "private, non-profit, public-interest association," La Associacion Instituto Nacional de Biodiversidad (INBio). INBio's initial objectives focused on the development and distribution of information on Costa Rica's biodiversity, including the execution of a 10 year National Biological Inventory (Gamez *et al.*, 1993; Hunter, 1997).

In 1991, INBio entered into its first bioprospecting agreement with the US pharmaceutical company Merck, Sharpe, and Doame. The agreement included over one million dollars in equipment, training, and operational funding for INBio, a $120,000 contribution to the National Park Service, and an undisclosed royalty on any resulting products that would be shared equally between INBio and the National Park Service (Sittenfeld & Gamez, 1993). [6] INBio used the capabilities and recognition it received from its agreement with Merck to implement bioprospecting projects with several other foreign corporations, including Bristol–Myers Squibb and Eli Lilly (pharmaceuticals), Indena (natural products and drug discovery), Givaudan Roure (cosmetics), Diversa (industrial enzymes) and Akaddix (agricultural biotechnology).

The general structure of the benefit-sharing arrangements in each of INBio's bioprospecting agreements has followed the pattern established in its original project with Merck; some up-front compensation, royalties on any new products to be shared equally with the Ministry of Environment and Energy, and provision of training and technology. INBio indicates it has obtained over $2.5 million in funding from its bioprospecting activities since 1991. Some of these funds have been used to establish a laboratory to screen and evaluate compounds for antimicrobial activity. In addition, INBio has established collaborative natural product research projects with the Universidad de Costa Rica, Universidad Nacional, and the Instituto Tecnológico de Costa Rica. [7]

In response to INBio's initial bioprospecting agreement with Merck, Costa Rica passed several pieces of legislation which affected access and use of biodiversity. But it was not until 1996 that Costa Rica, began to draft a Biodiversity Law intended to address comprehensively issues involved in commercial utilization of biodiversity. The first drafts of this legislation were the subject of widespread public debate that continued until a final version of the law was passed in 1998. The Biodiversity Law outlines the basic requirements for granting bioprospecting access permits including prior informed consent and equitable benefit sharing. The law also created the National Commission for Biodiversity Management (CONAGEBIO), which is composed of officials from the ministries of environment and energy, agriculture, health, and trade; a representative from the Costa Rican Institute for fisheries and aquaculture; the Executive Director of the National System of Conservation Areas, and representatives from business, farmer, indigenous, and environmental organizations. CONAGEBIO provides policy advice to the government and reviews bioprospecting permit applications through its Office for Technical Support (Solis Rivera & Madrigal Cordero, 1999).

INBio has been relatively successful in developing bioprospecting collaborations with foreign companies through which it has received significant monetary compensation, training, and technology transfer. There has however, been relatively little involvement from Costa Rica's business community in INBio's bioprospecting activities. In an effort to catalyze local private investment, INBio recently obtained $1.7 million from the Inter-American Development Bank (IDB) to provide technical assistance and market analysis to small businesses seeking to develop new products from biodiversity. The funding from the IDB was designed to initiate an ongoing biobusiness development program by INBio financed through fee for service arrangements and a share of the revenues from successful new products (IDB, 1998).

South Africa's efforts to develop the chemical and genetic value of its biodiversity can be traced to the early 1990s when several

multinational companies entered into bioprospecting agreements with South African institutions (Laird & Wynberg, 1996). Based upon experience gained from these projects, the Bio/Chemtek division of South Africa's Commission on Scientific and Industrial Research (CSIR) launched its own pilot bioprospecting effort which lead to the discovery of an anti-obesity agent (known as P57) from an indigenous South African plant (Horak, 1998). Even though P57 is a mixture of phytochemicals, CSIR has been able to obtain a patent and license its discovery. The success of this pilot project led to the formation, in 1998, of a bioprospecting consortium consisting of CSIR, the South African Medical Research Council, the Agricultural Research Council (ARC), the National Botanical Institute, and several universities. One of the primary objectives of the consortium is to evaluate the pharmaceutical potential of all 23,000 species of vascular plants native to South Africa.

The consortium's bioprospecting efforts have been structured to establish collaborations with foreign research organizations and multinational companies that can provide a high level of competence in key technologies or provide critical assistance with regulatory approval, production, or marketing (Horak, 1998). This strategic outlook has led to several bioprospecting projects involving consortium members and foreign organizations. These include a collaboration with the US National Cancer Institute, which has provided CSIR with technology for screening biological extracts for anti-cancer activity, and a microbial bioprospecting agreement with the US biotechnology company, Diversa. CSIRs Bio/Chemtek division has also recently completed construction in South Africa of a manufacturing facility to produce sufficient quantities of P57 to proceed with expanded clinical trials (Milmo, 1999). The facility, which was constructed with technical assistance from UK-based Phytopharm and funding from the US-based pharmaceutical company, Pfizer, was designed to meet FDA manufacturing guidelines. If the clinical trials are successful, a commercial scale manufacturing facility will be constructed in South Africa and CSIR will receive a portion of any revenues. CSIR has also entered into a bioprospecting agreement with a Swiss based company to develop "over the counter" consumer health care products from South African plants. [8] Another member of the bioprospecting consortium, the ARC, has initiated discussions with several agrochemical companies to expand the ARCs ongoing program of screening plant extracts for pesticidal properties.

In a break from CSIRs traditional role as a contract research organization, the Bio/Chemtek Division has also established several new programs to promote the formation of small technology and community-based businesses. These include the establishment of an incubator facility for new biotechnology companies and the provision of technical assistance and market assessment to local producers of essential oils and botanical extracts.

A particularly interesting aspect of South Africa's bioprospecting initiative is the collaboration that has developed between traditional healers and the CSIR. Working with a council of traditional healers, the Bio/Chemtek Division of CSIR has developed a database of information on traditional uses of South African plants. Information in the database is used to prioritize the selection of plants for screening both by CSIR and its partners. CSIR essentially treats the information it receives from the healers as a trade secret. [9] It is necessary to pass through several layers of physical and on-line security before accessing the database in which the information is maintained. In addition, a formal agreement obligates CSIR to negotiate benefit-sharing arrangements with traditional healers before commercializing any discovery developed using information contained in the database. While this agreement is commendable, CSIR has not yet developed a specific plan for allocating benefits from a new product across communities and tribal groups. [10] One approach to this problem, that has been utilized in Suriname and Cameroon, is the creation of locally controlled trust funds from which bioprospecting benefits are disbursed according to priorities and definitions of equity defined by the affected communities (Guérin-McManus *et al*., 1998; Iwu & Laird, 1998; Moran, 1997).

INBio's origins in the Biodiversity Office of the Ministry of Natural Resources and Energy helps explain the clear linkage between bioprospecting and biodiversity conservation that has developed in Costa Rica. But in contrast to the biotechnology development programs in Cuba, Singapore, Korea, and Taiwan, INBio's efforts to develop biotechnical capabilities have not been supported by a well-defined national program of technology development and business promotion. In South Africa's bioprospecting program, the situation is reversed, technical and industrial development has received greater

emphasis than conservation efforts. The relatively high pre-existing technical capacity of CSIR and its mission to support industrial development have provided fertile ground for the development in South Africa of commercially oriented bioprospecting capabilities. In a relatively short period of time, CSIR has been able to isolate, produce, and initiate clinical trials on a potentially lucrative new phytomedicine. What has not yet developed in South Africa are any benefit sharing arrangements linking bioprospecting with biodiversity conservation.

As outlined above, several of the more successful national biotechnology capacity-building programs have included active involvement of private sector organizations and government-supported efforts to promote the formation of new biotechnology companies. Both INBio and CSIR have developed a number of collaborations with foreign corporations, but there has been relatively little involvement of domestic business interests in the early stages of either Costa Rica's or South Africa's bioprospecting programs. Recently, INBio and CSIR's Bio/Chemtek division have initiated programs to promote small businesses involved in the extraction and processing of biological materials. This is an encouraging recognition of the need to stimulate private sector investment. Still, it appears that both programs will need to provide greater access to venture capital funding and facilitate technology transfer arrangements between local companies and foreign firms in order to promote the development of value-added products from biodiversity.

5. STRATEGIC PLANNING BIOTECHNOLOGICAL CAPACITY BUILDING

The experiences of Costa Rica and South Africa highlight the benefits of proceeding with pilot projects while working to develop a comprehensive bioresource development program. [11] Experience gained in managing individual bioprospecting projects can be of great benefit in identifying technology transfer requirements, designing appropriate access and benefit sharing policies, and catalyzing more broad based investment. Of course, a succession of separate projects does not in itself amount to an effective bioresource development program. Many potentially beneficial projects may never be developed due to an inhospitable policy environment or a lack of institutional or technical capacity within the country. Formulating a national strategy for development of biochemical resources can promote bioprospecting investments, facilitate successful technology transfer, and support the formation of a profitable industrial sector that is linked with the conservation of biodiversity.

Formulating a national strategy for value-added bioprospecting requires an assessment of biological resources and scientific capabilities in relation to specific market opportunities. Strategic planning for development of biochemical resources also demands an integrated approach to a broader set of policy issues than normally addressed in access and benefit-sharing legislation. These include foreign investment guidelines, tax treatment of start-up companies, intellectual property rights, and import and export procedures. A strategic plan should also seek to expand relevant scientific and technical education programs, while promoting collaboration between government research institutes, academia and domestic and foreign companies. Using public funding as seed capital for collaborative R&D projects that involve the domestic private sector is one means of ensuring that capacity building includes business development, project management, and marketing skills a well as scientific and technical training.

The appropriate scale and scope of a national bioresource development program will vary depending on historical factors and economic and political conditions. Costa Rica's success in promoting bioprospecting is attributable in part to the country's stable political environment, longstanding ties with foreign research institutions and foundations, and a long-term commitment to conservation and sustainable development. For its part, South Africa has a level of technical capability that rivals some developed economies. Many developing countries do not enjoy these advantages. For countries struggling to provide basic services, an expansive national strategy to promote value-added products from biodiversity is unlikely to be the most efficient use of scarce resources. Yet even in lower income countries, a targeted bioresource development program that builds upon traditional uses of biodiversity can benefit local communities while creating opportunities for technical development.

One promising example of this approach is an ongoing program in Nigeria and Cameroon, which has focused on scientific evaluation and standardized production of traditional medi-

cines as well as screening of plant materials for activity against a number of tropical diseases endemic to the region (Chasek *et al*., 1999; Iwu & Laird, 1998; Schuster *et al*., 1999). Initial funding for the Nigeria and Cameroon program was provided through the NIHs ICBG program. Control of the program is firmly maintained by a locally based nongovernmental organization (NGO) whose director has developed close ties with nonprofit research institutes in the US. These ties have enabled the Nigeria–Cameroon program to focus its attention on technical capacity building and local public health issues. What is not yet clear is whether the accomplishments of the Nigeria–Cameroon program will be sufficient to catalyze national bioresource development initiatives after the ICBG funding has been exhausted.

In response to the CBD and with support from the Global Environment Facility (GEF), many developing countries, have formulated national biodiversity action plans that emphasize both conservation and sustainable uses of biodiversity. [12] Some of these same countries have also implemented ambitious biotechnology development programs. Yet very few countries have integrated bioprospecting and biotechnology development efforts to any significant degree, even though there are a number of potential linkages that could yield synergistic benefits. These linkages and potential synergies are summarized in Table 2.

At the most basic level, a critical mass of scientists and technicians trained in biochemistry and molecular biology is essential for R&D activities involving bioprospecting or biotechnology. Bioprospecting and modern biotechnology also overlap in more specific ways. For example, bioprospecting for genetic material that codes for agronomically valuable traits is an essential first step in the production of transgenic crop varieties. The newly developed "golden" rice variety that many hope will help reduce vitamin A deficiency in developing countries was developed using genes from daffodils and two species of bacteria. The Diversa corporation, a rapidly growing biotechnology company that has entered into bioprospecting agreements not only in Costa Rica and South Africa but also in Indonesia, Iceland, and Bermuda, uses microbial DNA extracted from soil samples to genetically engineer common microorganisms to produce novel chemical compounds. Biotechnological techniques are also used as a means of producing commercial quantities of complex natural products that were discovered through bioprospecting activities, but have proven too difficult or costly to synthesize chemically. Examples include the anti-cancer drug taxol, which was originally derived from the bark of the Pacific Yew tree but is now produced using tissue culture techniques, and the anti-coagulant hirudan, which is a chemical isolated from the saliva of the common leech, *Hirudo medicinalis*, but is now produced in commercial quantities from transgenic strains of bacteria as well as from transgenic plants (Walsh, 2000).

Biotechnology development strategies and value-added bioprospecting programs also share many of the same policy and business development issues. Policies and programs pertaining to foreign investment, intellectual property rights, and technology transfer are equally important for companies seeking to develop

Table 2. *Potential synergies between biotechnology development and value-added bioprospecting*

Scientific and technical linkages	Common policy and programmatic issues	Reciprocal benefits
Biochemistry	Foreign investment policies	Creation of conservation incentives
Genetics	Technology licensing arrangements	Additional sources of funding and technical assistance
Cell & tissue culture	Intellectual property rights to isolated biochemicals	Broader allocation of policy and program development costs
Fermentation techniques	Coordination of public–private R&D activities	Diversification of market opportunities
Recombinant production of natural products	Finance and business development for start-up enterprises	
Prospecting for genes conferring valuable agronomic traits or coding for valuable enzymes and other products	Access and benefit sharing for use of wild biodiversity	

recombinant products from the human immune system as for companies seeking to discover anti-HIV compounds from indigenous plants. The same is true of programs designed to provide favorable tax treatment and expanded access to capital for research intensive start-up enterprises. Recognizing these intersections provides a stronger justification for expending resources on policy formulation and program development in support of value-added bioprospecting. Incorporating bioprospecting activities into biotechnology development programs can also generate a more diversified mix of market opportunities and joint venture partners.

A well-defined bioprospecting program, conceived as part of a broader strategy to create incentives for conservation of biodiversity, can also generate new sources of funding and technical assistance for biotechnology capacity-building efforts. Multilateral development agencies such as the World Bank, the United Nations Development Program, the IDB, and the GEF, as well as private foundations and NGOs, such as the MacArthur Foundation and the World Wildlife Fund, provide funding for bioprospecting activities designed to promote sustainable uses of biodiversity. In addition, the United Nations Industrial Development Organization, the UN supported International Centre for Genetic Engineering and Biotechnology, and the United Nations Educational, Scientific and Cultural Organization have developed technical assistance programs targeted toward sustainable development of biochemical resources.

One of the most significant challenges involved in developing linkages between national programs to promote sustainable development of biochemical resources and efforts to promote biotechnological industries is the need for cooperation between environment and development coalitions. The network of scientists, policymakers, and environmental NGOs that has been involved in implementation of the CBD has evolved into what Haas (1990) has termed an epistemic community. This community has been successful in keeping the issue of biodiversity conservation on the international agenda. But, sustainable use of biodiversity, together with access and benefit sharing legislation, has come to be viewed as primarily a conservation as opposed to a development issue. At the national level, environment ministries have generally taken the lead in formulating regulatory policies pertaining to bioprospecting, often with little or no involvement from development, trade and science ministries, or from the private sector. In some cases, this has led to a "gatekeeping" approach to biodiversity access that does little to promote, and can even deter, the development of value-added bioprospecting activities. [13] National biodiversity strategies and action plans, despite the CBD's emphasis on sustainable use, technology transfer and biotechnology, have not been well integrated into sectoral planning and decision making (Wells *et al.*, 2000). In a similar way biotechnology development programs are generally the province of ministries of science and technology, trade and industry. There is often little involvement from organizations seeking to promote conservation and sustainable use of biodiversity.

A national task force with high level representation from both the environmental and development communities can serve as a focal point for exploring common policy concerns and potential synergies between sustainable use of biochemical resources and development of biotechnological capabilities. Ideally, this task force would coordinate its activities with both the steering committee for the country's biodiversity action plan and the coordinating body for the country's biotechnology development efforts. One means of promoting more expanded interaction would be to implement a few pilot projects with clearly defined, commercially oriented success criteria that illustrate the common scientific and policy linkages between bioprospecting and biotechnology.

6. CONCLUSIONS

The preamble to the CBD states that "sustainable use of biodiversity is of critical importance for meeting the food, health and other needs of the growing world population." Acquisition of relevant technologies, in particular biotechnology, is recognized in Articles 16 and 19 of the CBD as essential for achieving these goals. While substantial attention has been given to the obligations of developed countries to share benefits and transfer technology in exchange for access to biochemical resources, there has been comparatively little discussion of measures that developing countries can take to attract and fully benefit from bioprospecting investments. Countries seeking to derive significant benefits from their biological resources must develop capabilities to pro-

vide value-added combinations of biological material, associated knowledge, and technical services. This requires moving beyond a gatekeeping approach to access and benefit sharing, toward a more comprehensive strategy focusing on benefit creation.

The generally cautious approach that developing countries have taken toward bioprospecting contrasts with the integrated proactive programs many countries have developed to enhance biotechnological capabilities. A review of several of the more successful of these programs indicates the importance of combining publicly supported initiatives to develop scientific and technical capabilities with a concerted effort to promote private investment and commercialization of new products. There are numerous potential linkages and synergies between value-added bioprospecting and biotechnology capacity building. Recognizing these connections can provide an expanded array of market opportunities on which to justify public investments in research, technical training and policy formulation. In addition, a bioprospecting program that is developed as part of a broader strategy to create incentives for biodiversity conservation can provide access to additional sources of development assistance, foreign direct investment, and technology transfer.

NOTES

1. Although the term genetic resources is used in the access and benefit-sharing articles of the CBD, countries have placed controls on a much broader range chemical products derived from biological material. I shall therefore use the term biochemical resources to include genetic material as well as other chemical compounds that can be derived from biodiversity. As used in this article, biochemical resources should be understood to exclude conventional agricultural commodities, timber products, and biochemicals derived from the human body.

2. The top prescription drugs were ranked by number of prescriptions, not by total revenues. The percentage of drug revenues obtained from natural products or their derivatives is likely to be somewhat less since many commonly prescribed drugs are less costly on a per prescription basis.

3. See http://www.fao.org/WAICENT/FAOINFO/AGRICULT/cgrfa/IU.htm. The difficulties involved in multilateral compensation arrangements for use of plant genetic resources are also discussed by Frisvold and Condon (1998).

4. The author has participated in official meetings of United Nations Conference on Trade and Development and the Organization for Economic Cooperation and Development in which proposals for development of protocols and guidelines for bioprospecting projects were opposed by delegates from the US, UK, and Japan.

5. I use the term biotechnology to refer to both "modern" biotechnologies such as genetic engineering as well as older biotechnologies such as tissue culture and fermentation processes.

6. The net financial benefit INBio received from its original agreement with Merck was significantly less than $1 million since INBio was responsible for the cost of collecting biological samples and preparing extracts for shipment to Merck.

7. Personal communication with A. Sittenfeld and N. Mateo former directors of INBio's Bioprospecting Division August, 2000.

8. Personal communication with M. Horak, Director of Bioprospecting, Bio/Chemtek Division, CSIR, 2000.

9. See Gollin (1993) for a discussion of the potential application of the legal doctrine of trade secrets to traditional knowledge of plant uses.

10. CSIRs collaboration with Phytopharm and Pfizer are not covered under the agreement since P57 was not discovered with the assistance of traditional knowledge.

11. The state of Western Australia is another example where promising results from an initial bioprospecting effort have prompted the development of a more extensive bioprospecting activities (Surry, 2000; ten Kate & Wells, 1997).

12. The UNDPs Biodiversity Planning Support Program provides a central clearing house of information for national biodiversity strategies and action plans. See http://www.undp.org/bpsp for national planning guidelines, funding sources and status reports.

13. For a cautionary tale that highlights the need to include a wide range of stakeholders in the promotion and evaluation of bioprospecting activities see the Colombian case study in (Chasek *et al*., 1999).

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