Article

Bioprospecting and Biotechnology: some policy issue

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Introduction

Bioprospecting, defined as the systematic search for valuable, molecules, genes and organisms in nature, has the potential to developing countries a means to use biodiversity without disrupting nature; to add value to their natural resources; to ensure that such resources are protected and used in a sustainable manner; and to build the necessary skills to apply biotechnology in improving quality of life (Sittenfeld and Villers 1993; Sittenfeld and Lovejoy, 1999). Today, important developments in biotechnology are rapidly generating new financial opportunities derived from the use of biological resources. However, such biotech opportunities that impact on managing the economy and the environment will in this century depend on how issues between biotechnology and biodiversity are treated and implemented within the principles of the Convention on Biological Diversity (CBD).

Because of its nature, bioprospecting is at the intersection of biodiversity conservation a the use of biotechnology and thus has consequences in the areas of legal and regulatory frameworks; technology transfer and business development; intellectual property rights and facilitation of local, national and international collaborations (Sittenfeld, 1996; Tamay et al., 1997; Sittenfeld and Lovejoy, 1998). Though the bioprospecting principle may be simple, the interaction between biotechnology use and biodiversity conservation and its sustainable does require a careful designed strategy to complement other aspects of biodiversity protection and socio-economic development.

The screening of samples from the wild has always been a prominent activity in ancient and modern pharmaceutical industries. Almost half of the best-selling pharmaceuticals are directly extracted from nature or have active components in natural products that serve as the lead compounds, the majority of them having been obtained from microbial sources (Demain, 1998). Currently, the incorporation of automated selection and assay screens, i concert with the development of robust molecular biology techniques and information systems for application in the pharmaceutical and agricultural sectors, has allowed the bioprospecting process to rapidly analyse a large number of samples obtained from nature Nevertheless, even with the new technologies; the frequency of discovery of target molecules per sample is low. Also, a new pharmaceutical or a new genetically modified (G plant variety may require 10- 15 years to bring to market and cost more than $300 million in research and development (ten Kate, 1995; Shear, 1999; Thayer, 1998). These barrier severely limit possibilities for many developing countries, and particularly small island countries to fully bioprospect biodiversity and subsequent product development on their own, thus rendering imperative cooperative agreements with industries and research centers in the developed nations (Sittenfeld, 1996).

Any consideration of biodiversity and biotechnology use is framed by its dependence on larger natural systems in interaction with human systems. The consequences of biotechnology, as any other technology, entail both opportunity and risk (Dale et al., 2002). The current debate between environmental activists and biotechnology industries is also preventing tropical countries, from implementing fundamental and balanced decisions for bioprospecting biodiversity.

BIOPROSPECTING FRAMEWORKS

Bioprospecting is notably complex and should incorporate benefits in terms of capacity building and technology transfer for the country as a whole, direct financial benefits and potential royalties for conservation; and the involvement of a country's national and local institutions and entities, the creation of industrial incentives, and the attraction of potential industrial activities in general. Supportive macro-policies, combined with an integrated set of biological research, business development and technology transfer options are needed to create a bioprospecting program that yields these long-term benefits for conservation and for developing countries as a whole (Sittenfeld and Lovejoy, 1998). In this respect, bioprospecting requires the creation of appropriate frameworks and the co-operation and involvement of governments, intermediary institutions, private enterprise, academia, and local communities and entities (Sittenfeld and Villers, 1993). The development of bioprospecting agreements in Fiji has been described in a case study that dwelt with the drawing up on an equitable bioprospecting

agreement and developing community activities involving the University of the South Pacific (USP), pharmaceutical companies, the Fiji government, non-goverrnment organizations and local communities (Aalbersberg, 1996). Added benefits were that the USP, serving 12 Pacific islands, is in a position to disseminate the educational aspects of bioprospecting, to enrich the understanding of fragile ecosystems and sustainable use of ecosystems, and to share models and lessons learnt.

Bioprospecting frameworks integrate four elements: macro policies, biodiversity inventories and information management systems, technology transfer and business development and strategic planning (Sittenfeld and Lovejoy, 1998). At the same time, bioprospecting include interactions with many disciplines, from humanities, law and business to basic and applied sciences. Macro policies represent the fundamental point of departure for a bioprospecting framework and comprise the set of governmental and international regulations, laws and economic incentives that determine biodiversity ownership, land use patterns, access to and control of biological resources, implementation of intellectual property rights (IPR), technology promotion, and industrial development (see *Box 1*).

Box 1 **Bioprospecting of Biodiversity**

Bioprospecting is a targeted exploration and search for as yet undiscovered chemical compounds, genes and their products within wild species and biological organisms for a certain use with potential for commercial development. Bioprospecting is linked to conservation of biodiversity by sharing part of the benefits with the caretakers of the wild bio-resources.

Bioprospecting, often downstream screening, testing and development activities following discovery of a potentially useful substance, gene or organism.

- Biotechprospecting of biodiversity for new medicines involves

1. *Discovery*.identification and collection of material by random, bio-rational and traditional (medicinal) approaches, followed by screening for particular .bio-activities.*, and elucidation of novel molecular form
2. *Intellectual property rights*: Protection of intellectual property through patenting of new genes and/or bioactive principles with novel antibiotic, insecticidal or anti-tumour properties
3. *Process technology*: Isolation, synthesis and purification of new bioactive chemicals for laboratory, clinical and field trials to demonstrate and compare the effectiveness and biosafety of the newly discovered product with contemporary market products
4. *Manufacturing* and *Marketing Strategies:* Development of techniques for larger scale industrial production of the final bioactive product and its market availability and accessibility to the public

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e.g. the Samoan species *Mamala Homolanthus acuminatus* from which Prostratin was isolated for potential use to combat HIV

Macro-policies are formed on the international, national and social levels. International agreements, conventions and other mechanisms provide guidance for sharing biological resources between countries and leave major responsibilities of designing adequate legislature and regulations to each individual country (Sittenfeld and Lovejoy, 1999). *Box 2* provides the difficulties and challenges of implementing legal frameworks in the case of Costa Rica that has been a pioneering force in bioprospecting.The experiences presented may have implications for the bigger island countries whereas the smaller island countries on account of their vulnerability arising from their small size and geographic remoteness have to draw lessons more on a collective basis rather than on a stand alone approach.

Box 2 **Difficulties and challenges of implementing Legal Frameworks, the case of Costa Rica:**

Costa Rica enacted in 1998 the Biodiversity Law. The Law regulates the access to genetic and biochemical resources and the sharing of the benefits arising out of their utilization. This Chart summarizes the main difficulties and challenges that Costa Rica has faced in the process of developing the Biodiversity Law.

Uncertainty and value

- Bio-prospecting is very uncertain; the word bioprospecting has been derived from prospecting for oil and minerals, but bioprospecting, or prospecting for biological or genetic resources and even of indigenous knowledge, is quite different, because it presents even greater risks; only a few products have reached the clinical or even pre-clinical stage,

even though a lot of samples have been collected from all over the world since the mid-1980s.

- When determining the value of genetic resources, it should furthermore be born in mind that the significance of one sample in the overall chain of efforts and costs to develop a new product or a new drug is very limited. Unless a country can add value to these resources, for instance by scientific research, their value, and therefore the benefit that can be obtained has the potential to increase.

§ Technology has had a paradoxical impact on the value of biological resources. On one hand, new technologies increase the potential commercial use, and therefore the economical value, of biological resources, while the cost of screening these materials and/or isolating active ingredients is decreasing. On the other hand, technological developments have reduced the amount of material needed for research purposes, and may thereby have facilitated illegal collection and use. So while, in general, the economic value of genetic resources is increasing, the commercial value of any particular extract or sample is not.

Rights and ownership

Property rights and ownership: the CBD does not address the question of ownership; it only establishes (Article 3) that states are sovereign over their genetic and biological resources. But sovereignty, national patrimony and ownership are different concepts; therefore, it is important to clearly define ownership in the national law. In fact some of the most common problems arising when negotiating benefit- sharing agreements are related to the lack of clarity on ownership. In Costa Rica, the Law divides the property rights of biodiversity into genetic and bio-chemical properties and the biological resources *per se*: the biochemical and genetic properties belong to the State, therefore are under the administration of the Ministry of the Environment and Energy, while, biological resources are the property of the land owner, a situation that causes confusion and debates around definitions and intention of use.

Over-regulation

Another notorious pitfall is over-regulation:

§ The complexity of access regulations creates problems; if nobody can comply with the regulations, most likely they will be not enforced. High transaction costs and bureaucratic procedures contribute to a lack of enforcement.

§ Access legislation may negatively affect basic research; it may have negative impact on local universities and research institutions, as basic research is important for conservation purposes and for sustaining biodiversity.

Defeating the purpose?

The ultimate goal of access and benefit sharing should be clear. If the main aim is to make money, it is bound to fail. In case the objective is to create national capacity, a value added industry, or the conservation of natural biological resources, then it is necessary to make the right connections, and develop coherent policies on access, biodiversity conservation and sustainable use. These policies should include access to knowledge and traditional use of medical products. Considerations on different treatments or regulations according to the initial nature or purpose of research: non commercial versus research intended for commercial development, has produced discussions on whether or not to consider all kinds of intended research with a potential for sending sooner or later, products to the market place.

For island countries the implications, rights and duties of the United Nations Convention of The Law of the SEA (UNCLOS) are quite relevant and important. In practice, producing legislation and regulatory measures, in accordance with the guidelines provided by the Biodiversity Convention, has proven to be a lengthy and complex task by itself. Intrinsic characteristics of biological resources such as the capacity of biodiversity to reproduce differently with or without human intervention, offers problems in terms of regulating access and use in domesticated or wild biodiversity. Animals, and marine organisms that move from one region or country to the other, present difficulties for the definition of ownership and the application of sovereign rights by individual countries. Because of the complexities of the issue, the VI Conference of the Parties of the CBD (The Hague, April 2002), approved the Bonn Guidelines On Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising Out of Their Utilization, with the final aim of .serve as inputs when developing and drafting legislative, administrative or policy measures on access and benefit sharing with particular reference to provisions under Article 8 J, 10 C, 15, 16, and 19; and contracts and other arrangements under mutually agreed terms for access and benefit-sharing..

Implementing the provisions of the Convention that relate to sovereign rights and access to biological resources depends on the capacities to transform the resources into useful products and to advance the well being of source countries. The issue is not so much whether countries have sovereign rights, but is whether the countries have the capacity and institutional systems to add value and generate new and better-priced products. By nature, bioprospecting is an intensive scientific and technological activity, therefore, the

creation of incentives favouring research and development to properly increase biotechnology and ensure that their development promote industrial learning and socioeconomic development, merits careful analysis by countries trying to assert its sovereign rights in effective manners.

BUILDING ON TO MACRO-POLICIES: BIODIVERSITY INVENTORIES, BUSINESS DEVELOPMENT AND TECHNOLOGY ACCESS

Supported by international and national macro-policies, three basic elements: biodiversity inventories and information management; business development; and technology transfer, which guide the rational and productive use of genetic resources in prospecting activities

- **Inventories and Information Management**

Biodiversity prospecting begins by searching for chemicals or genes in living organisms. This will only be successful through the development and management of biological, ecological, taxonomic, and related systematic information on living species and systems. Biodiversity inventories create catalogues of available resources and their location. Not all taxa inventories need to be complete and accurate before screening for potential products; however inventories prevent damage to ecosystems, areas, species and populations by indicating what resources are available, and where they can be collected without damaging the environment (Raven and Wilson, 1992). Microbial gene prospecting, for example, does not require previous taxonomic knowledge of the resource, but if information is available, this facilitates the selection of collecting sites and sampling procedures. Bioprospecting for microorganisms and their components -which represent possibly the largest component of biodiversity on any ecosystem-, has been and will be in the future an alternative worthy of exploration and exploitation for island and developing countries. However this will require much more than a traditional biotic inventory. Microbial biodiversity surveys must include an understanding of the distribution, abundance, and community structure of microbial biodiversity with respect to latitude, biomes, and other ecological gradients, including comparison with patterns of distribution and abundance of plant and animal species (Newman and Banfield, 2002). Under this ecological scope, molecular technology and bio-informatics play an important role. Genomics has provided a means for conduct more extensive surveys of microbial diversity and community structure analysis; and, has revealed an extraordinary genetic plasticity and horizontal exchange in the microbial world. Microbial genome sequencing projects are expected to result in the discovery of novel microorganisms and functions, including new tools for bioremediation and bio-restoration, for the development of potential new commercial products; and for to biological resource and environmental conservation (Stahl and Tiedje, 2002).

- **Business Development and technology access**

Business development, building from inventory-generated knowledge, defines markets, market needs, major actors, national capacities in science and technology as well as institutional or community strategies and goals. Important requirements for starting a bioprospecting negotiation process include knowledge of one's assets and debilities, applications for traditional knowledge, market surveys and evaluation of conservation needs. As an example, currently, there is little commercial interest in the etnnobotanical approach to drug discovery by the big drug industries (Balick and Cox, 1996), since other technologies, such as combinatorial chemistry are bringing new alternatives to find drugs (Cox, 2001).

- **Technology Transfer**

Capacity-building in the use of intellectual property rights, taxonomy, biotechnology, ethnobotany, negotiation of bioprospecting agreements will go a long way in ensuring a fair and equitable transfer of technology. Bioprospecting collaborations should make use of negotiation processes and contractual agreements. In general, contract negotiation is divided into three basic sets of issues: scientific, business and legal issues. The typical source-country needs are: generaton of income to support protected areas and conservation activities; and local community development through direct contributions and royalties; the transfer of technologies and guaranteed future just and equitable profit-sharing if commercial products are forthcoming for all participants and according to its contribution. In this respect, the definition of fairness comes to be a difficult one and a source of debate in all negotiation processes. Sampling must be done under Best Ecological Practice without damaging the ecosystem. For bilateral contracts industrial partners, exclusivity and time limitations are furthermore required. Lessons from INBio (Instituto Nacional de Biodiversidad) in Costa Rica are indicated in Box 2 and are of relevance to bioprospecting in sland countries with fragile economies.

Box 2 The following Chart summarize some of the lessons learned by INBio in the contract negotiation process:

1. It is essential to have a clear and defined institutional policy on the requirements and criteria to be negotiated for a bioprospecting research agreement.

2. The incorporation of national scientific capacity is important to add value to raw biodiversity, and enhances the country.s position in the negotiation of benefits (e.g. higher royalty rates).

3. It is necessary to develop a good understanding of the operation and evolution of biodiversity markets and to be aware of the technical and scientific changes that support these markets.

4. The presence of institutional capacity in multidisciplinary teams, for the negotiation process in terms of legal, scientific and business areas, is a requirement. The terms of the agreements are often challenging and complex.

5. Innovation and creativity add considerable weight to compensation and benefit sharing negotiations.

6. Mastering of key issues is crucial: IPR regimes, warranties, determination of royalty rates, transfer of materials to third parties, definitions (products, extracts), ownership of IPR, joint research, confidentiality, dispute resolution, survival of obligations, etc).

7. Proactive approaches to business development according to a defined institutional policy and needs (bioprospecting strategy) enhances the opportunities for new and innovative agreements. The existence of a Business Development Office at INBio, with a highly qualified staff; attending seminars and activities with industry and research centers and making direct contacts with potential users, all enable in a positive manner institutional challenges. The current policy is based on the idea that it is not enough to wait to be contacted, or be available at the behest of the company but to have and maintain a proactive approach. Even if no formal market survey has been made, the identification of potential partners in the field of biotechnology has to be developed.

8. Coordination with other national and international institutions devoted to biodiversity R&D, and understanding the technology transfer needs and capacity building at the country level, are important requirements to build expertise in biotechnology.

9. Good political support, an appropriate legal framework, and legal certainty (e.g. who is entitled to grant permits) create a positive environment for success.

10. The development of macro-policies such as national biodiversity inventories, information management systems, investment in biotechnology, and well-defined and well managed protected areas provide a smoother scenario for biodiversity prospecting.

Source: Cabrera, 2002.

Access to technology through its development, transfer or other form of acquisition that converts the raw biological materials into higher value added products is a complex undertaking. It is important for institutions representing the source country to develop a strategic plan for technology development and capacity building that is tailored to the country's needs and capabilities and is responsive to market opportunities. Strong scientific capacity will attract research collaborations because it reduces investment risks (Sittenfeld and Lovejoy, 1999), at the same time that these collaborations must in turn provide additional technology, training, and information to build upon that base, becoming a cycle of benefits for developing countries, which in many cases represents the only valuable contribution in the absence of monetary returns.

CONCLUDING REMARKS

In a number of cases it is still nearly impossible to control and monitor the illegal transfer of genetic material. Microorganisms can be cultivated from much less than a handful of soil and genes can be cloned from minute amounts of DNA or RNA or isolated from biological material that easily fits into an airmail envelope. Genes do not have tags designating their country of origin, and once cloned, it is possible that are no longer controlled by their source country (Tamayo et al., 1997). Authorized access permits as mechanisms to create and oversee a regulatory regimen are important tools, but not enough to guarantee good bioprospecting practices. If bioprospecting, is to be performed under ethical principles and guidance, requires from the source country the creation and implementation of difficult tasks by all means: regulations on access to genetic resources, together with an infrastructure that provides full support and approval from government and adherence to national or local regulations on access to resources; acquire technology that adds value to genetic resources wherever possible (from extracts, partially purified or pure compounds to gene sequences or recombinant plants); take advantage of local capabilities and resources; create interdisciplinary and multidisciplinary teams of scientists, lawyers, conservation managers and business developers and a good capacity to distribute benefits from bio-products, using fair and effective procedures; develop a reputation as a reliable business partner over time; and reinvest part of the revenues in biotechnology development and biodiversity management and conservation.

The Biodiversity Convention envisions harmonious links between conservation, intellectual property, environmental protection, research and development and economic advancement for developing countries. This is a complex and long-term undertaking by any standard. However, it is important to consider that raw materials obtained for bioprospecting have a low market value, and in order to increase their value the transformation into products is a long and expensive process, that requires tremendous inputs from science and technology. Finally, the economic impact of bioprospecting should not be overestimated: modern bioprospecting can only complement other activities, designed to improve standards of living and conservation of biodiversity.

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