THE ECONOMIC VALUE OF PHARMACEUTICAL PROSPECTING AND ITS ROLE IN BIODIVERSITY CONSERVATION

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1. INTRODUCTION[1]

Biodiversity - the variation between groups of living organisms and their ecological conditions - is an immense reservoir of chemical diversity. Within the pharmaceutical industry, there is currently a resurgence of interest in exploring biodiversity as a source of novel chemical compounds for use in the development of new pharmaceuticals, or "pharmaceutical prospecting."[2] A growing number of pharmaceutical companies are initiating or upgrading research programs that screen microbial sources, higher plants and other taxonomic groups for useful activity against disease targets. On the supply side, developing country governments, development agencies and non-governmental organizations are increasingly interested in assisting developing country institutions to *capture* the "pharmaceutical value" of biodiversity.

This paper examines pharmaceutical prospecting from an economic perspective. In Section 2 the economic nature of the prospecting process is explored emphasizing the use of biodiversity in pharmaceutical applications and its potential as a renewable resource. Two important distinctions underpinning the paper are presented in this section. First, the "pharmaceutical value" of biodiversity is disaggregated into "prospecting" and "production" components. Second, the section outlines the difference between biodiversity as the "raw material" in the production process and information about biodiversity - the "intellectual property" that drives innovation.

Section 3 moves on to a review of previous efforts to estimate the pharmaceutical value of biodiversity. The wide range of results generated by prior studies is examined and the conclusion drawn that initial studies probably far over-estimated the pharmaceutical value of biodiversity. Nevertheless, one of the studies does demonstrate that society may derive important benefits from new drugs based on biodiversity that cannot be captured in financial revenues.

In Section 4 the difficulties experienced by biodiversity-rich countries in capturing the prospecting value of biodiversity and returning a share of the returns to conservation activities are investigated. Issues of market failure and the structure of economic incentives across three stages of the prospecting process - biodiversity protection, the generation of taxonomic information and pharmaceutical R&D - clarify the root causes of the problem. As a raw material input to the prospecting process, biodiversity is typically treated as a *free good*. Pharmaceutical prospecting, therefore, provides little in the way of financial incentives for a developing country to invest in biodiversity protection. In addition, the use of publicly-

[1]I would like to thank Ana Sittenfeld, Sarah Laird and the many other people who contributed to the research effort behind this paper. I am grateful to Edward Barbier, Joshua Bishop and Gardner Brown for their comments on a draft of this paper. Comments on earlier versions of Section 2 and 4 were also received from Jo Burgess, Walt Reid and David Simpson. All remaining errors, misinterpretations, etc. remain my exclusive property.

[2]Reid *et al.* (1993) define "biodiversity prospecting" as the exploration of biodiversity for commercially valuable genetic and biochemical resources. This definition may be rephrased to reflect the objective of prospecting - the derivation of valuable genetic, chemical, and biological products from biodiversity Pharmaceutical prospecting would, therefore, join a list of activities including agrochemical, genetic, and industrial materials prospecting that fall under the rubric of "biodiversity prospecting."

provided taxonomic services and reference collections makes an important contribution to the commercial collection of biotic samples, yet receives none of the returns from this activity. The ability to patent novel chemical compounds, however, does provide a means for capturing the value of biodiversity and information included in the final product of pharmaceutical R&D - a new and marketable drug.

Nevertheless, the paper argues that a preoccupation with the question of how to *capture the value of biodiversity* may overlook an important development question - that of how to *invest in the generation of information about biodiversity*. The economic link between biodiversity and new drugs is the development of information about species and their chemical constituents. In these activities lies an opportunity for developing countries to add value to biodiversity and thus appropriate a share of pharmaceutical prospecting value-added.

With these points in mind, the valuation issue is revisited in Section 5. Two methods of modeling the net returns to biodiversity and species information are developed. The first model explores the allocation of net returns according to the full social costs of the activities included in pharmaceutical prospecting. The second model builds on earlier efforts in estimating the expected returns from royalty agreements. In Section 6 the question of whether pharmaceutical prospecting is a sufficient rationale for "saving" biodiversity is evaluated - along with an analysis of whether the likely returns to a biodiversity-rich developing country will cover the full costs of biodiversity protection.

The two models indicate that biotic samples are a valuable component of the pharmaceutical prospecting process. However, the level of current demand in the market for biotic samples is simply not enough to allow prospecting activities to make a significant contribution to protection - even under the application of the most promising of current contractual forms. Nonetheless, prospecting may provide a profitable means of funding in-country development of taxonomic knowledge and reference collections.

In the concluding section, the findings and policy implications are summarized and recommendations made for areas of future research.

2. PHARMACEUTICAL PROSPECTING AS AN ECONOMIC ACTIVITY

There are a number of activities involved in the pharmaceutical prospecting process:

i) protection of biodiversity
ii) collection of biotic samples
iii) taxonomic classification of biotic samples
iv) chemical extraction of biotic samples
v) primary screening
vi) bioassay, isolation and structural determination of potential lead compounds
vii) pre-clinical development including formulation, toxicology and animal testing
viii) clinical research
ix) application for regulatory approval

Pharmaceutical prospecting does not necessarily proceed in a linear, step-wise fashion as outlined above. However, the process generally involves adding information to the "raw material" of biodiversity and its subsequent derivative forms. Along the way large numbers of potential candidates are discarded. A flow chart of the steps leading up to the derivation of a lead compound - activities (i)-(vi) - is presented in Figure 1. For synthetic compounds, 1 in 10,000 is often cited as a rough estimate of the odds for deriving a lead compound in screening programs. Comparable figures for natural products are not common knowledge, thus considerable uncertainty surrounds just how long the odds of success are in pharmaceutical prospecting.

Typically, activities (iv)-(ix) take place in developed countries which have established pharmaceutical R&D capacity. Over the past 30 years, 90 percent of new pharmaceuticals originated from just ten countries - the US, Japan and eight European countries (Ballance, Pogány and Forstner 1992). Developing countries engage in biodiversity protection, (i), and, depending on local taxonomic expertise, may be involved in collection and identification activities, (ii) and (iii). Eisner (1990) suggests that since the extraction and initial bioassay of natural product material is technique-oriented and relatively labor-intensive, a logical site for additional extraction and screening facilities would be in biodiversity-rich developing countries.

For the purposes of this paper, investment in pharmaceutical prospecting is segregated according to three major types of activities:

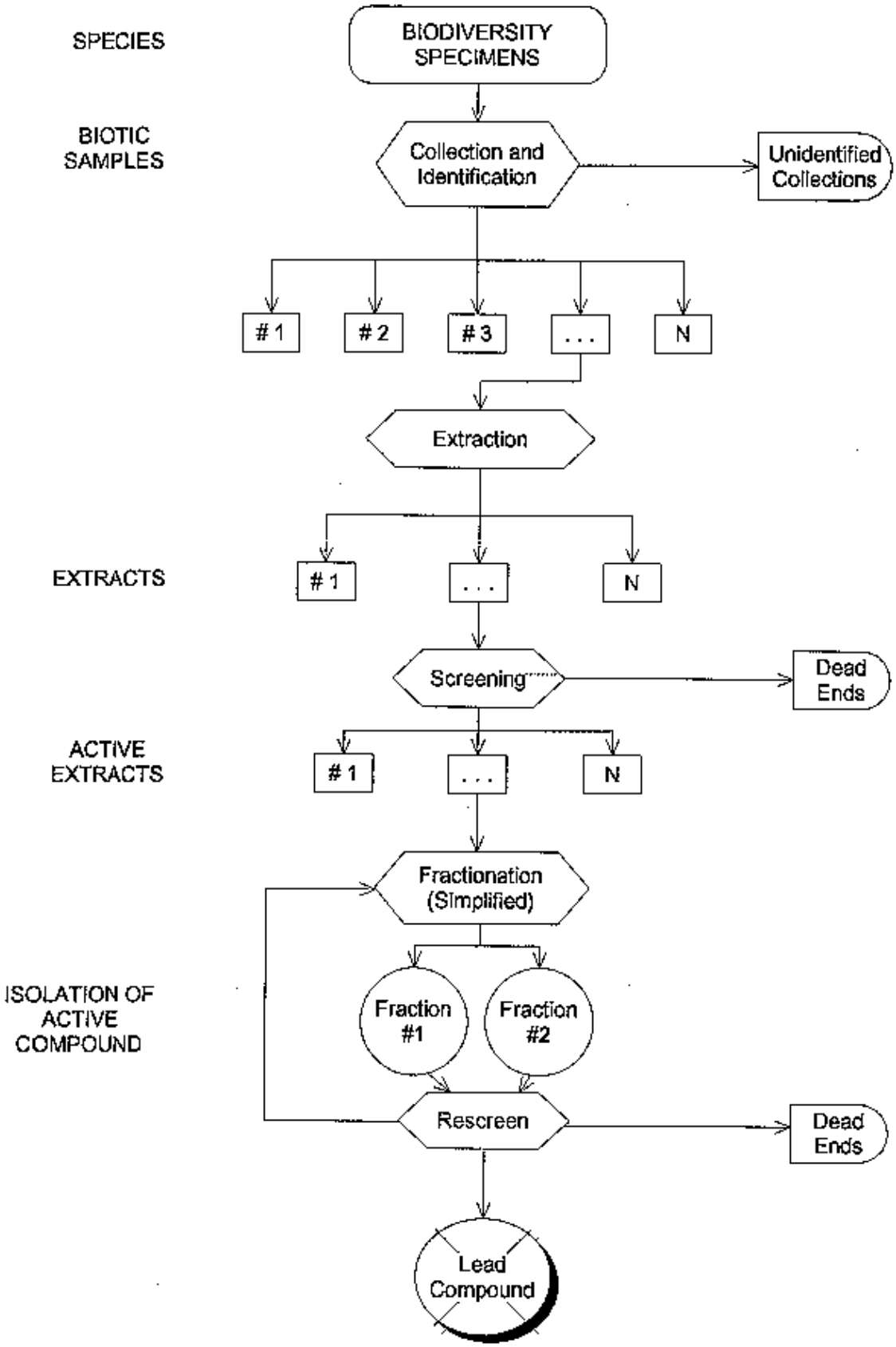
- protection of biodiversity - i.e (i)
- collection and identification of biotic samples - i.e. (ii) and (iii)
- pharmaceutical R&D - i.e. (iv)-(ix)

Typically, these activities are conducted by different sectors of society such as parks personnel, taxonomists and pharmaceutical companies. The respective economic outputs of these activities or investments are:

- the "raw material" for pharmaceutical prospecting - biodiversity

- species information and the "processed product" - biotic samples

Figure 1 PHARMACEUTICAL PROSPECTING: FROM BIODIVERSITY TO LEAD COMPOUND



- information about a species' biochemical properties and the "final product" of pharmaceutical prospecting - a marketable compound

Thus, the paper focuses on the principal economic ingredients of pharmaceutical prospecting - *biodiversity* and *species information*.

pharmaceutical prospecting involves only those activities up to and through the completion of the research and development phases - when approval of a new pharmaceutical product is obtained. Pharmaceutical prospecting is separate from the activity of mass production or harvesting of biodiversity and its subsequent transformation into a product of mass consumption. This distinction implies that the overall "pharmaceutical value" of species information and biodiversity consists of two components:

- its "prospecting value" - value generated by the use of the "raw material" of biodiversity and the development of species information during prospecting process

- its "production value" - e.g. the value of biodiversity for the purpose of mass production and marketing of pharmaceuticals

This disaggregation reflects the distinction between two markets for biodiversity and species information in the production of pharmaceuticals - first as a source of new, approved medicinal compounds and, second, as the "raw material" used in the mass production of marketed pharmaceuticals. As the objective of this paper is to explore the economic issues behind the process of acquiring knowledge about biodiversity, the emphasis in this paper is on the prospecting component of pharmaceutical value.[3]

Biodiversity as a Source of Novel Pharmaceuticals

Naturally-occurring chemical compounds that are of interest to the pharmaceutical industry are drawn from the secondary metabolites produced by living organisms. Primary metabolites are the principal chemical constituents - such as amino acids - that are common to all living organisms. Secondary metabolites are more complex compounds that are generally common only to a particular family, genus or even species (Balandrin *et al.* 1985). As secondary metabolites of different types are present in all organisms, the full range of biodiversity has potential for yielding new compounds of medicinal interest.

Plants. Discussion of the use of natural products in developing new pharmaceuticals is largely associated with the use of plants. In the 19th century, prior to the advent of the "pharmaceutical" industry, all medicinal preparations were derived directly from nature, mostly from plants. Since then, however, the pursuit of plant-based pharmaceutical applications has been of a cyclical nature (Findeisen and Laird 1991). As a result of the lack of interest by major players in the industry during the 1970s and 1980s, major new drugs developed from plant sources in the past 20-30 years are limited in number. The only major

[3] *See* Aylward et al. (1993b) for a brief analysis of the production benefits of biodiversity prospecting.

plant screening program during this period took place at the publicly funded US National Cancer Institute (NCI).[4]

In the past few years, new technological developments - including advances in high throughput screening techniques - have rekindled the interest of pharmaceutical companies in the exploration of plants for novel chemical compounds. In addition, popular concern over the richest source of plant chemical diversity - the tropical rainforests - may have added to the impetus to explore the potential of plants.

However, plants are not the only component of biodiversity rich in secondary metabolites of potential interest to the pharmaceutical industry. Despite its neglect in the popular press, microbial diversity has long been an important and well-known source of lead compounds for the pharmaceutical industry. Marine diversity has also been targeted by drug researchers, although its potential remains largely unexplored. Finally, a large reservoir of species diversity - insects - is almost completely unexploited.

Microbes. Microbial diversity is a rich source of natural products chemistry - a source which has seen a consistent level of exploitation by industry R&D departments since the Second World War. Penicillin - the wonder drug of World War II - and a host of subsequent antibiotics and many other products have been produced from microbial sources. Mevacor - a breakthrough cholesterol-lowering drug with sales of over $1.5 billion in 1992 - is just one of four products recently developed by the microbial screening program at Merck & Co (Merck & Co 1992; The Economist 1993). While the extent of microbial diversity is largely unknown - the World Conservation Monitoring Centre (1992) suggests that probably less than 3 percent of the world's microorganisms have been described - microbial diversity may equal or exceed that of all other forms of biodiversity. Recent improvements in screening technologies complement the "chemical inventiveness" of microorganisms in generating many new leads for drug development (Nisbet 1992).

Collection of microbial samples is accomplished by sampling different microenvironments such as soils, detritus, etc. A few small scoops of material may yield thousands of different species. Once collected there is little reason to return to the original site as microorganisms can normally be cultured through fermentation processes. Freedom from the difficulties of resupply is, no doubt, an important factor in explaining the sustained level of interest shown by the pharmaceutical industry in fermentation products relative to other natural products. The need to return for additional supplies of plants or marine organisms as research continues and as full-scale production becomes necessary, can be a costly, risky and frustrating experience for researchers.[5] The use of microbial diversity avoids these complications and keeps the research and development process in-house.

Marine Organisms. As with microbial species, the full diversity of marine organisms is largely unknown. Current species estimates imply that only 20 percent of species are of

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[4]Aylward (Forthcoming) provides an evaluation of the plant screening activities undertaken by the National Cancer Institute.

[5]*See* Suffness, Newman and Snader (1989) for an account of difficulties encountered by the National Cancer Institute in developing the bryostatins

marine origin, however, this may reflect a bias towards terrestrial research in systematics. Grassle (pers. comm. in Ray 1988) suggests that deep sea fauna may rival tropical forests in species diversity. Rinehart (1992) reports that marine macroorganisms and microorganisms produce a "dizzying array" of secondary metabolites. The hunt for drugs at sea is likely to be constrained by the relatively large cost of obtaining specimens, the lack of techniques for *ex situ* reproduction of marine invertebrates and the difficulty of locating the source of activity. Many of the compounds isolated from macrospecies actually are produced by microorganisms - thus confusing attempts to reproduce activity from subsequent samples.

Despite these limitations, considerable interest in the pharmaceutical potential of marine diversity exists. NCI incorporated marine organisms in its early program, screening approximately 3,000 different species during the 1972-80 period (Suffness and Douros 1982). Although no commercial products have yet emerged from the early program, NCI resumed collection of marine samples in 1986. In addition, Reid *et al.* (1993) cite a number of major pharmaceutical companies that have initiated marine screening programs, including SmithKline Beecham, Bristol Myers Squibb, Merck & Co., Rhone-Poulenc Rorer and Glaxo Group Research.

Insects. Insect diversity is a new and unexplored area in natural products chemistry. Eisner (1990) suggests that arthropods may hold considerable amounts of material of interest to medicinal chemists. As a source of species diversity, arthropods far outstrip their terrestrial plant and animal counterparts. Wilson (1988) reports that arthropods make up just over one-half of the 1.4 million species described to date. As indicated in Part II of this report, Merck & Co. recently agreed to pay $1 million to Costa Rica's National Biodiversity Institute for the right to investigate the chemical properties of not only plant and microbial species, but those of insects as well.

As a result of the broad base of experience in plant conservation, plant taxonomy and phytochemistry (literally the chemistry of plants) much of the material in this paper is derived from experience with plants. However, the economic activities involved in prospecting for new drugs using marine organisms and insects are not dissimilar from those of plants. Thus, the analysis in this paper may be of relevance to prospecting activities carried out with these organisms as well as with plants. On the other hand, the economic and policy issues associated with prospecting using microbial diversity are likely to be significantly different from those in the case of plants. This is a result of the ease with which microbial diversity is obtained, the lack of a need to return to the resource for resupply, the likelihood of in-house classification of species and the in-house manipulations performed with microbial species in order to obtain new products. This paper, therefore, *may not* bear directly on prospecting with microbial species.

Biodiversity for Pharmaceutical Prospecting: A Renewable Resource

Farnsworth and Morris (1976) point out that although "guesstimates" can be made about the untapped potential of biodiversity, it is practically impossible to determine when a particular species has been fully investigated for its pharmaceutical properties. For example, Douros and Suffness (1980) report that in NCI's first natural products screening program 35,000

species of plants were tested for anti-cancer activity. Current estimates of higher plant diversity range from 250,000-500,000 species. In other words, in the most extensive pharmacological investigation of plants ever recorded, only a fraction of the total number of plant species were evaluated for a single type of biochemical activity against a single disease (Farnsworth and Morris 1976). In addition, these plants were only tested against a limited set of cancer screens - tests that are now regarded as relatively unsophisticated. In its new program initiated in 1986, NCI is testing natural products against a revised set of disease-oriented screens (Suffness, Newman and Snader 1989). Hence, it is possible to conclude that due to improvements in NCI's screening technology the original 35,000 species of plants are once again virtually *unexplored* sources of anti-cancer compounds.

Improvements in screening technology and the development of new screens clearly extend the potential applications of the chemical diversity in natural products. New screens are a response not only to scientific and technological advances in isolating disease targets, but to the continued evolution of disease. Increasing levels of disease resistance to commonly-used drugs is of particular concern in the case of tuberculosis, pneumonia, meningitis, malaria and other infectious diseases. In addition, new disease targets are continually developing. AIDS is a "new" disease of global reach and of epidemic proportions. In the United States, population shifts to outer-edge suburbs and rural areas combined with increasing deer and tick populations have lead to a rapid upswing in cases of Lyme disease (US News and World Report 1992). In sum, there is no shortage of disease targets for the pharmaceutical R&D community to tackle.

The sheer scale of the resource - on the order of 10 to 100 million species - and the continuing evolution of screens, screening technologies and disease targets implies that biodiversity will never be fully explored or exploited for its pharmaceutical potential. This suggests that the chemical properties of biodiversity represent a potentially limitless (relative to demand) renewable resource "pool" for use in the development of new pharmaceuticals. The real threat to this resource is on the supply side - the competing uses of land and natural habitat and the failure to protect areas rich in biodiversity, particularly the biodiversity-rich regions in the tropics.[6]

The implication of biodiversity's renewability in prospecting activities is that species - and hence protected areas - are economic assets that may provide a steady stream of economic benefits over time. Unlike exhaustible resources, the stock of which must inevitably be drawn down over time, a renewable resource is capable of sustaining continued economic use without actually sacrificing its physical stock. This is an important factor in the case of protected areas that produce a number of other "joint" benefits such as ecotourism and ecological functions. Unfortunately, renewable biological resources are notoriously prone to overuse and degradation due to market and policy failures. Following a review of the literature on the pharmaceutical value of biodiversity, Section 4 takes up the issue of how market failure and economic policies may impact on the economic incentives to invest in pharmaceutical prospecting.

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[6]See Swanson and Barbier (1992) for an overview of the potential role of biodiversity in economic development and the factors contributing to the loss of biodiversity.

3. HOW MUCH IS BIODIVERSITY WORTH?

The rekindling of interest by pharmaceutical companies in exploring the biochemical potential of biodiversity has gone hand in hand with renewed claims by conservationists that biodiversity's value as a source of new drugs makes protection of biodiversity a critical component of sustainable development strategies. In this section previous attempts to indicate the value of using biodiversity in the drug discovery process are reviewed and evaluated. These studies provide the quantitative estimates of the pharmaceutical value of biodiversity that underpin the popular impression that biodiversity and drug development go hand-in-hand.

Estimates of the Pharmaceutical Value of Biodiversity

Perhaps the most oft-quoted figure regarding the importance of natural product-derived drugs is that one-quarter of US prescription drugs contain one or more active constituents obtained from higher plants. Another figure frequently encountered is that one-half of US prescriptions contain one or more natural products. Both of these estimates derive from a pioneering attempt by Farnsworth and Morris (1976) to demonstrate the pharmaceutical value of plants using 1959-73 US National Prescription Audit data on the sources of community pharmacy prescriptions in the US.[7] Using an average prescription price for 1973 of $4.13, the authors arrived at a subtotal of $1.59 billion. Assuming that non-community pharmacy prescriptions represent one-half of total US prescriptions, the authors suggest that $3.0 million was the total US pharmaceutical value of higher plants in 1973.

Using an average prescription price of $8.00 for 1980, Farnsworth and Soejarto (1985) updated this analysis of the total value of US prescriptions - as shown in Box 1. Extrapolating from the 1973 data, the authors suggest that 507 million community pharmacy prescriptions contained active principles from plants. In accounting for non-community pharmacy prescriptions, the authors gross up the value of community pharmacy prescriptions by a multiplier of two to arrive at $8.11 billion as the total value of US prescriptions. Employing data indicating that plant drugs in 1980 were derived from just 40 plants, Farnsworth and Soejarto (1985) conclude that the pharmaceutical value lost by the extinction of a single species that would yield a marketable drug is $203 million.

Farnsworth and Soejarto (1985) also estimate that only 5,000 species of plants had been exhaustively researched for their pharmacological properties. Given that 40 plants were employed in making drugs in 1980, the authors calculate that of every 125 plants evaluated for their pharmacological potential, one would eventually yield a marketable drug. By inference, *the annual revenues from a single untested plant species are $1.6 million.* The authors prefer to gross up the figures. They estimate the value that will be lost to be $3.25 billion due to the loss of 2,067 species (10 percent of all US flowering species) by the year 2000.

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[7]The figure for higher plants is derived from 1973 data and the figure for natural products from 1959 data. The latter figure fell to 41 percent by 1973 due to a decrease in the share held by microbial products from 21 percent to 13 percent. Animal-derived products contributed roughly 2-3 percent.

Box 1 Pharmaceutical Value of Plant-Derived Prescriptions #1 - US

1.	Number of US community pharmacy-dispensed prescriptions	2.0 billion
2.	Percent of prescriptions containing one or more active principles from plants (1959-73 average)	25.4%
3.	Number of community pharmacy prescriptions containing active principles from plants	507 million
4.	Average US prescription price (1980)	$8.00
5.	Total value of community pharmacy prescriptions derived from plants	$4.06 billion
6.	Multiplier to gross up the value of community pharmacy prescriptions to total US prescriptions:	2
7.	Total value of prescriptions from plants	$8.11 billion
8.	Number of plants used in prescriptions	40
9.	Total value per successful plant species	$203 million
10.	Success Rate per plant species investigated	1 in 125
11.	Annual value of revenues per untested plant species (US)	$1.62 million
12.	Converted to 1990 dollars	*$2.58 million*

Notes: All figures in 1980 dollars except (12). All other data for 1980.

Source: Derived from Farnsworth and Soejarto (1985)

Farnsworth and Soejarto (1985) admit that they are uncertain about the accuracy of their results. A review of their methods reveals a number of limitations. A basic flaw is the authors' failure to distinguish between the volume and value of production in their translation of the US National Prescription Audit data into market values. The authors supply no evidence in support of the implicit contention that plant-derived prescriptions have the same value - on average - as non-plant or non-natural product prescriptions.

Farnsworth and Soejarto (1985) also stretch the imagination by ascribing the total market value (at the point of consumption) of plant-derived drugs to the plant species. If there were no available substitutes for plant material in pharmaceutical prospecting or drug production it would be possible to argue that the full pharmaceutical value would be lost if the species was lost. However, this is simply not the case. As pointed out in the previous section of this paper a number of alternative sources of natural diversity are under investigation. In addition, other methods of drug development - such as "rational" drug design - actually predominate in R&D departments of the major pharmaceutical companies.[8] In the case of drug production, Farnsworth and Morris (1976) indicate that although many plant compounds are still obtained from natural sources, artificial synthesis in many cases is feasible. Due to plentiful supply of natural material and technological constraints on production of synthetic compounds, however, it is often simply unattractive from a commercial standpoint to mass-

[8]See Aylward (Forthcoming) for a discussion of issues of health care cost-effectiveness and alternatives for the development of pharmaceutical products

Box 2 Pharmaceutical Value of Plant-Derived Prescriptions #2 - OECD

1. Annual value of a plant-derived drug (US)	$200 million
2. Multiplier extending US data to OECD	3
3. Value of a plant-derived drug (OECD)	$600 million
4. Probability of success	1 in 2,000
5. Annual value per untested species	$300,000
6. Converted to 1990 dollars	*$474,000*

Notes: Item (1) is derived from Farnsworth and Soejarto (1985). All figures except (6) are, therefore, in 1980 dollars.

Source: Derived from Principe (1989b)

produce synthesize compounds. Thus, it is likely to be the exception, rather than the rule, that society is unable to find alternative therapies for the maladies that plant drugs address.

Plant material gathered for pharmaceutical prospecting and drug production is just one of the inputs that contributes to the net final value of these activities. In other words, the major drawback of the Farnsworth and Soejarto (1985) study - and other similar efforts that follow - is that it fails to examine the net (or even gross) returns to biodiversity *per se*. The total gross returns from pharmaceutical prospecting and drug production are attributed solely to biodiversity instead of being apportioned across the various factor inputs including other forms of capital - physical, technological and human - and labor.

Principe (1989a; 1989b) also attempts to calculate the value that would be lost by plant extinctions through the year 2000. By and large Principe uses data from Farnsworth and Soejarto (1985). An exception is the estimate of the probability of success in deriving a marketable drug from untested species. Principe (1989b) reports that a panel of experts in plant-based drug development suggested that the probability of a given plant yielding a marketable drug was between 10 in 10,000 and 1 in 10,000. Principe chose to work with the midpoint of this range - 5 in 10,000.

As shown in Box 2, Principe (1989b) uses a multiplier of three in order to obtain $600 million as the annual value of plant-derived drugs in the OECD using US data from Farnsworth and Soejarto (1985). Because of the lower success rate, Principe's implicit estimate of the *annual value of an untested species is $300,000* - far less than the $1.6 million predicted by Farnsworth and Soejarto (1985). Based on expected extinctions of 50,000 plant species word-wide by the year 2000, Principe (1989b) suggests that the market value foregone will be $15 billion (in 1984 dollars) annually by 2000. As with the previous studies, Principe does not examine the net returns to biodiversity. In general, this study suffers from the same limitations as Farnsworth and Soejarto (1985).

Given the continued frequency of its citation, it is worth questioning whether data on the composition of US community pharmacy prescriptions ostensibly from the 1959-73 period continues to be a valid indicator of the prevalence of global use of natural product-derived

Box 3 Value of Tree-derived Pharmaceuticals

1.	Percent of Canadian trees with medicinal properties	38 in 134
2.	Percent of these trees that are likely to be marketable	10%
3.	Percent of Canadian trees with marketable medicinal properties	3 in 100
4.	Average annual global value of a tree-derived pharmaceutical	$250,000
5.	Annual value per untested tree species	*$7,500*

Notes: As the relevant price level is not indicated in the original article all figures are assumed to be in US 1990 dollars.

Source: McAllister (1991)

pharmaceuticals in the 1980s and 1990s. Farnsworth and Morris (1976) reveal that in 1973 one category of products - steroids derived from diosgenin found in the Dioscerea (yam) family - made up almost 15 percent of the 25 percent share of total prescriptions ascribed to plants. Codeine (2.02 percent), atropine (1.50 percent), and reserpine (1.45 percent) were the only other plant-based compounds whose prescription rates exceeded one percent of total prescriptions. Clearly the value of higher plants in 1973 as calculated by Farnsworth and Morris (1976) rested largely on one specific compound - diosgenin - which owed much of its market power to its use in oral contraceptives.[9] Huxley (1984) implies that the contribution of total prescriptions made by the Dioscerea family is likely to be far less in later decades by reporting that in the Western World such contraceptives are now derived from synthetic sources.

Between 1954-59, Farnsworth and Morris indicate that eight new drugs from higher plants were introduced as prescription items, including the famous anti-cancer agents vinblastine and vincristine derived from the Rosy Periwinkle. However, in the period leading up to the 1970s, investment in higher drug plant research decreased substantially. The authors suggest that by the mid-1970s only three pharmaceutical companies in the US were engaged in meaningful research on higher plants with an estimated total annual expenditure between them of $150,000. Farnsworth and Soejarto (1985) assert that by 1980 not a single US pharmaceutical company had an active plant research program. Even the extensive natural products program at the US National Cancer Institute was phased out in the early 1980s, having apparently failed to produce any useful products.[10]

[9] In addition, the final drugs - steroids such as progesterone - are actually semi-synthetic forms of diosgenin. Thus, these are not even "pure" natural products and, therefore, dilute their claim to the entire returns, or net returns, of the prospecting or production activities.

[10] At least one marketable drug has resulted from the early work at NCI. In late 1992, taxol (from *Taxus brevifolia*) was approved for use against ovarian cancer in the US. Meanwhile, topotecan reached Phase II clinical trials in early 1992 in the US. Topotecan is a modified form of the compound camptothecin (from *Camptotheca acuminata*) discovered by NCI.

Box 4 Value of Lives Saved by Plant-Derived Drugs - OECD

1.	Annual mortality due to cancer in the US	500,000
2.	Percent of deaths prevented by anti-cancer drugs	15%
3.	Percent of anti-cancer drugs derived from plants	40%
4.	Annual lives saved by plant anti-cancer drugs	30,000
5.	Value of a statistical life saved	$8 million
6.	Annual value of plant anti-cancer drugs (US)	$250 billion
7.	Multiplier extending US data to OECD	3
8.	Annual value of plant anti-cancer drugs (OECD)	$750 billion
9.	Multiplier to reflect all plant drugs	2
10.	Annual value of all plant-derived drugs (OECD)	$1.5 trillion
11.	Number of plant-derived drugs	40
12.	Annual value per successful species (OECD)	$37.5 billion
13.	Probability of success	1 in 2,000
14.	Annual value per untested species (OECD)	$18.8 million
15.	Converted to 1990 dollars	*$23.7 million*

Notes: All figures in 1984 dollars except (15).

Source: Derived from Principe (1989b)

Moreover, Farnsworth and Morris (1976), indicate that during the period 1959-1973 no new plant-derived drugs were introduced in the US. Given the apparent lack of interest in phytochemical research up until the late 1980s, and the long lead times required to develop, test and gain approval for new drugs, it is likely that very few of the new drugs introduced after 1973 were derived from plants. It is, therefore, probably a large overstatement to continue to suggest that 25 percent of prescriptions - whether by value or volume - are derived from plants. An evaluation of the recent history of patent applications and regulatory approvals is proposed in Appendix A. This would provide data on past and current trends in plant research and the use of plant drugs in therapy.

McAllister (1991) applies a somewhat similar methodology to that employed by Farnsworth and Soejarto (1985) in estimating the financial value of Canadian tree species for pharmaceutical purposes. As shown in Box 3, McAllister's implicit conclusion is that the *annual value of an untested tree species is $7,500.* While McAllister's result may not overstate such values as do the previous studies, his analysis is prone to the same limitations. The low monetary value obtained is simply a result of the rather "conservative" estimate of the global end use value.

In order to carry out some rough calculations of the economic value of plant-derived pharmaceuticals, Principe (1989a;1989b) combines US data on mortality due to cancer and statistical estimates of the value of human life with estimates of the effectiveness and prevalence of plant anti-cancer drugs (see Box 4). Principe admits that this calculation is

only an attempt to derive a broad indicator of the order of magnitude of the total economic benefits generated by drugs derived from plants. However, given that global sales of all pharmaceuticals in 1992 are estimated to be around $150 billion, the suggestion of a total economic value of $1.5 trillion for plant-derived drugs may be excessive (Ballance, Pogány and Forstner 1992).

Using this data it is possible to work back to a value (in terms of lives saved) of $37.5 billion per successful species (as shown in Box 4). Using Principe's (1989b) estimate that 1 in 2,000 species will produce a marketable drug, the expected *annual value of a single untested species would be $18.8 million.* Note that this figure is some sixty times larger than the comparable figure derived from Principe (1989b) for the pharmaceutical value of an untested species.

While the assumptions in the analysis are heroic, the point remains that new, life-saving drugs derived from natural products are extremely valuable to society. Huxley (1984) reports that vinblastine, in combination with other drugs, now produces a remission rate of 80 percent in Hodgkin's disease compared with 19 percent from a previous treatment. Vincristine provides over 90 percent remission in acute lymphocytic leukemia, which frequently attacks children. Taxol has also shown remarkable, curative powers in clinical trials for ovarian cancer and offers hope it may prove equally useful in the treatment of other cancers (Edgington 1991).

If plant drugs can make such vast improvements on current levels of treatments, the full value of such drugs to society as a whole may not be adequately reflected in value estimates based on market prices. First, individuals may be willing to pay considerably more than the going market price for the drug. Second, such improvements may generate benefits that accrue to society as a whole - rather than to the individual. These may include a reduced health care cost burden, improved productivity of the work-force and the alleviation of grief and suffering of those close to the patient.

While Principe's (1989b) work is important in highlighting this issue, it still suffers from many of the methodological weaknesses of the Farnsworth and Soejarto (1985) study. The actual results must, therefore, be regarded as a large overstatement of the value of plant-derived drugs.

The Value of a Research Discovery

In appraising the Korup project in Northern Cameroon, Ruitenbeek (1989) makes a number of important methodological advances in his treatment of the "genetic value" of the project. Ruitenbeek insists that for the purpose of project appraisal the relevant figures are expected, not actual, production values, and that expected values should be adjusted by a factor that describes the ability of a host country's institutions to actually capture this value. In addition, Ruitenbeek suggests that the "genetic" value of biodiversity can be represented by the value of a new research discovery instead of the value of the end product - e.g. a drug. Thus, Ruitenbeek is the first to implicitly focus on the value of the end product of the prospecting process rather than the value of the final pharmaceutical product.

Ruitenbeek (1989) assumes that on an annual basis the project would generate 10 research discoveries with potential commercial applications. As each of these discoveries are valued at $7,500, the total expected economic value is $75,000 per year. In net present value terms, the "genetic" contribution credited to the project is $722,000. Due to the further assumption that the aforementioned "institutional factor" is 0.1 for Cameroon, the cash value of these discoveries to Cameroon amounts to only $7,500 per year or $72,200 in present value terms. Ruitenbeek does not give any indication of the likelihood of such discoveries per species; thus it is not possible to compare his results directly with those of the previous studies. However, if we assume that Ruitenbeek was simply concerned with plants and that half of the 1,000 plant species inhabiting the Korup and adjoining Oban (Nigeria) forest areas find their principal home on the Cameroonian side of the border, it is possible to suggest that the *annual per species value would be in the region of $150.* Of this only $15 would be capturable by Cameroon (Ruitenbeek 1990).

In order to understand why Ruitenbeek's estimates are drastically lower than those cited earlier, it is necessary to review his method for valuing a research discovery. The intuition that the value of a research discovery can be approached by using estimates of the value of patent rights is, perhaps, the single most innovative aspect of Ruitenbeek's work. Early in the R&D process pharmaceutical companies seek patent protection for promising compounds. Regulatory approval of a new drug essentially gives the company the go ahead to cash in on the patent value of the compound for its prescribed use.[11] At the end-point of the prospecting process - the point of approval - a patent will obviously have significant value as it guarantees the holder the right to exclusive production of the drug for the remainder of the patent period. In financial terms, the value of the patent at approval is likely to be a fairly accurate representation of the value of the pharmaceutical prospecting process. Patent values, however, will not provide an accurate picture of the *economic* value of the prospecting process as post-patent returns and spin-off benefits will not be internalized in the price of a patent.

The value of a research discovery employed by Ruitenbeek came from Schankerman and Pakes (1986). As this piece of work - and indeed the literature on the economic value of inventions and R&D - covers all patents, not just those of pharmaceutical products, it is important to consider whether the results generated by this literature are valid in the case of pharmaceutical prospecting.

Schankerman and Pakes (1986) construct a model of patent renewal that generates estimates of the value of patents held in the United Kingdom, France and Germany during the post-1950 period. Each of these countries has a system of annual renewal fees for patents. The idea underlying the authors' valuation of patent rights is that patent holders will decline to pay the renewal fees when the next set of annual fees exceed the expected discounted net returns from future revenues generated by retention of the patent. Using estimates of decay rates (percentage of patents renewed from one period to the next), assumption about the distribution of patent revenues and data on renewal fees, the authors' generate a distribution

[11]Note that companies often develop more than one therapeutic use for a given compound. If the patent is simply on the compound, then the subsequent identification of additional therapeutic uses of the compound will add to the value of the compound - but only to the extent that approval and hence marketing can be attained prior to patent expiration (or at least before generic competition whittles away intellectual property rents).

Box 5 Value of a Pharmaceutical Prospecting Royalty Agreement #1

1.	Drug with peak year sales (million):	$1,000 million	$500 million
2.	Net Present Value of sales (million)	$5.06 million	$2.53 million
3.	Royalty percentage	5%	5%
4.	NPV per discovery	$253,000	$127,000
5.	Probability of success	1 in 10,000	1 in 10,000
6.	NPV per untested species	*$253.00*	$127.00

Notes: Sales build to peak year figure (for years 4-6) and then drop off of through year 10 at which point a "terminal value" is posited. A discount rate of 5% is used to obtain present values. Probability of success is assumed from the figure mentioned in the text. All figures assumed to be in 1990 dollars.

Source: Derived from Harvard Business School (1992)

of the estimated value of patent rights for each of the three countries.

Schankerman and Pakes' (1986) findings indicate that the distribution is extremely skewed. Their calculations show the median value of patent protection to be roughly $900 in France, $1,900 in the United Kingdom and $6,000 in Germany.[12] Just 10 percent of the patents exceed $13,000 in France, $16,000 in the United Kingdom and $45,000 in Germany. Estimates of the value for the top one percent of patents range from $80,000 to $270,000 depending on the country.

Phillips and Firth (1990) reveal that only half of UK patents are renewed into their eighth year. This confirms that most patents are of low value. Given maximum renewal fees of $525 per year (starting with the fifth year) Phillips and Firth (1990) suggest that is unlikely that such trivial patent renewal fees actually inhibit renewal in the case of commercially valuable patents.

This observation leads to the criticism that efforts to value patents may not be particularly revealing in the case of marketable pharmaceuticals. Schankerman and Pakes (1986) admit that renewal data will not be very informative on the value of patents that are maintained for the entire period. Due to the need to patent compounds showing initial promise and the ensuing length of time necessary to obtain regulatory approval, the pharmaceutical R&D process tends to take up at least one-half of the 16 to 20 years of patent protection available in industrialized countries. In the post-approval scramble to rapidly recoup R&D investment costs, it is unlikely that companies pay much attention to such small renewal fees. An additional limitation to using patents values to value the output of pharmaceutical R&D is that some countries - most notably the US - do not charge patent renewal fees. As a result, it

[12]All figures are based on the 1970 cohort of patents and calculated in 1980 dollars. As year five is the first year in which renewal fees must be paid in these countries the estimates reveal the net returns after year five for those patents reaching year five.

is possible to suggest that the figure used by Ruitenbeek (1989) would tend to understate the potential value of pharmaceutical discoveries.

These criticisms do not imply that Ruitenbeek's intuition is faulty, only that the application is of limited significance. An accurate valuation of all patents, whether successful or not, would be a useful indicator of the value of intermediate products in the R&D process. Unfortunately, in the case of pharmaceutical prospecting, the data generated by Schankerman and Pakes is likely to provide information only on the value of research discoveries that fail to make it through to regulatory approval and the marketplace. This leads to a downward bias in the attributed value of all research discoveries. Given the practical difficulties involved in valuing patents, it is preferable to stick to the task of trying to estimate the expected value of successful products and then allocate the returns across all inputs.

Value of Royalty Agreements

Three recent efforts to calculate pharmaceutical value build on the idea of examining the value of research discoveries by using royalty payments as a means of valuing biodiversity's contribution to pharmaceutical prospecting.

A Harvard Business School (1992) case study examining the Merck/INBio agreement takes a simple, but elegant approach to examining the potential financial benefits that a country - in this case Costa Rica - stands to gain from research discoveries. The conclusions of the study are that a single research discovery would earn a net present value of $200 million, assuming peak year sales of $1 billion and a 5 percent royalty. As the study mentions the 1:10,000 probability of deriving a useful compound it is possible to derive a *present value per untested species of $253* from the Harvard study (see Box 5).

As with Ruitenbeek (1989), this study focuses on the expected net present value of a research discovery. As such it avoids all the machinations associated with the efforts of Farnsworth and Soejarto (1985) and Principe (1989b), and generates forward-looking information that is of more use for decision-making purposes. Unlike Ruitenbeek (1989), the Harvard study uses values for the marketable end product. The use of a royalty figure is the novel factor in the analysis. It obviates the need to consider research failures. However, as the implications of the likelihood of a research discovery is discussed only in passing, the analysis is not taken to its logical conclusion of an effective per unit value. In addition, the analysis of present value does not take into account the cost of capital over the long lead time needed to develop a marketable product. Nevertheless, it is possible to extrapolate to a present value per untested species and, again, it is substantially lower than previous estimates - which were annual values!

Pearce and Puroshothaman (1992) use data from Principe (1989b; 1991) and Farnsworth and Soejarto (1985) to generate additional annual estimates of the financial and economic value of losses due to plant extinctions. Again - as with the studies from which Pearce and Puroshothaman derive their figures - the market values are annual figures that rely on pre-1973 estimates of the composition of US prescriptions. The economic values are based on a figure for the UK of $4 million per statistical life saved, instead of the $8 million employed by Principe (1989b). Pearce and Puroshothaman follow Ruitenbeek (1989) in suggesting that

Box 6 Pharmaceutical Value and Value of Lives Saved - Plant-Derived Drugs

		Pharmaceutical Value	Value of a Life Saved
1.	Annual value of a plant-derived drug (US)	$390 million	$7 billion
2.	Royalty percentage	5%	5%
3.	Rent capture coefficient	.1	1
4.	Annual value per successful species	$1.95 million	$350 million
5.	Probability of success	1 in 10,000	1 in 1,000
6.	Annual value per untested species (US)	$195.00	$350,000
7.	Multiplier extending US data to OECD	3	3
8.	Annual value per untested species (OECD)	*$585.00*	*$1.05 million*
9.	Multiplier extending OECD data to World	1.4	1.4
10.	Annual global value per untested species	$819.00	$1.5 million

Notes: Pharmaceutical values based on market figures from Principe (1991) and value of a life saved based on UK estimate of $4 million. All figures in 1990 dollars.

Source: Derived from Pearce and Puroshothaman (1992)

such analyses should consider not just the total economic value, but the value that can be actually be captured by developing countries. The authors incorporate the idea of rent capture by using both the proportion of value that a country could gain through royalties (5 percent) and a coefficient of rent capture (0.1-1.0 percent) which is drawn from Ruitenbeek's idea of an "institutional factor."

The study takes a different tack from earlier studies by expressing value estimates in per hectare terms. Using an estimate of 60,000 plant species at risk and one billion hectares as the approximate area of remaining tropical forest, they arrive at a range of values from $0.01 to $21.00 per hectare of tropical forest. The market-based pharmaceutical value - $0.39 billion - and the value based on the value of lives saved - $7.0 billion - employed by the authors appear to be based only on US values. If the authors had used their OECD multiplier the resulting figures would be $0.04 to $88.00 per hectare.

Box 6 indicates the calculations necessary to arrive at the value of an untested species implied by the analysis in Pearce and Puroshothaman (1992). Using the value estimates for OECD countries the *annual value of an untested species ranges from $585 to $1.5 million.* For the purposes of guiding private or public investment such a wide range is of little practical use. Unfortunately, the authors confuse the rent appropriation issue by including a coefficient of rent capture on top of the royalty and using this in conjunction with both market and economic values. In fact, the royalty rate *is* essentially a measure of rent capture. For the purposes of such an analysis it would be sufficient to apply a royalty figure to market values and a coefficient of rent capture to the economic values.

Box 7 Value of a Pharmaceutical Prospecting Royalty Arrangement #2

		Base Case	Blockbuster Drug and Multiple Screens
1.	Net annual revenues	$10 million	
2.	Gross annual revenues		$1 billion
3.	Royalty Rate	3%	3%
4.	Probability (sample to lead)	1 in 10,000	1 in 1,000
5.	Number of screens	1	30
6.	Net present value (NPV)	$52,500	$46 million
7.	NPV per untested species	$52.50	$46,000

Notes: The authors assume a 10 year wait before marketing, 15 years of patent protection, 1,000 samples evaluated, a 1 in 4 chance of a lead making it to market and a 5% discount rate. All figures assumed to be in 1990 dollars.

Source: Derived from Reid *et al.* (1993)

Reid *et al.* (1993) carry out some quick calculations on the value of royalty arrangements in a similar vein to the Harvard Business School (1992) study. Two improvements are made in the Reid *et al.* study. First, the probability of making a research discovery is made explicit. The authors suggest a 1 in 10,000 chance of deriving a lead compound from a biotic sample and a 1 in 4 chance of a lead compound making it through to the marketplace. Second, the authors also incorporate the "renewability" aspect discussed in Section 2. They indicate that when screened against a company's battery of screens (up to 30) the chances of deriving a lead compound will rise to 1 in 1,000.

As shown in Box 7, Reid *et al.* (1993) conclude that the value a country can expect to receive from royalties will depend on the number of screens against which samples are tested and the level of revenues. Extrapolating from the base case and blockbuster scenario, *the net present value that may be garnered by a single untested species varies from $52.50 to $46,000.* Again, such a wide range is unlikely to assist decision-makers or private firms in their appraisal of investment opportunities in pharmaceutical prospecting. The lower figure does, however, establish a lower bound estimate for royalty revenues.

The results of the studies reviewed above are summarized in Table 1 (all figures are converted to 1990 present values to aid in the comparison). An extremely wide range of estimated values for an untested species - from $52.50 to $255 million - is revealed by this review of the literature on pharmaceutical values. All things considered, the results from the Harvard Business School (1992) and Reid *et al.* (1993) studies provide the most realistic indications of the pharmaceutical value that can be garnered by a developing country. It is evident that the amount a country is likely to appropriate is considerably lower than the gross estimates of pharmaceutical value arrived at by the early studies of Farnsworth and Soejarto (1985) and Principe (1989b). While the estimates of the value of lives saved by plant-derived drugs provided by Principe (1989b) exaggerate the value of untested species, the effort does illustrate the possibility that significant social benefits for society may be generated by innovative therapeutic treatments derived from natural products.

TABLE 1 Summary of the Literature on the Pharmaceutical Value of Biodiversity

Reference	Farnsworth and Soejarto (1985)	Principe (1989b)	McAllister (1991)	Principe (1989b)	Ruitenbeek (1989)	Harvard Business School (1992)	Pearce and Puroshotharman (1992)	Reid *et al.* (1993)
Biodiversity valued	plants	plants	trees	plants	Cameroonian species	Costa Rican species	rainforest plants	biotic samples
Scope of values	US	OECD	global	OECD	not specified	not specified	OECD	not specified
Type of data	drug sales	drug sales	drug sales	value of a life saved	patent renewal costs	royalties on drug sales	drug sales and value of life saved	royalties on drug sales
Type of value	annual	annual	annual	annual	annual	net present value	annual	net present value
Value per item	$200m	$200m US $600m OECD	$250,000	$37.5b	$7,500	$253,000	$1.95m - $350m	not specified
Success rate for discovery of new drugs	1:125	1:2,000	3:100	1:5,000	not specified (10:500)	1:10,000	1:1,000 or 1:10,000	1:40,000
Annual value per untested species (1990 dollars)	$2.58m	$474,000	$7,500	$23.7m	$15.00 - $150.00	na	$585.00 - $1.05m	na
Net present value per untested species (1990 dollars)*	$27.8m	$5.11m	$80,800	$255m	$162.00 - $1,620	$253.00	$6,310 - $11.3m	$52.50 - $46,000

Notes: *Due to the different methods used in calculating values the figures are not, strictly speaking, comparable. Net present values for studies presenting only annual values are calculated over a 40 year term with a 10% discount rate.
na = not applicable, m = millions, b = billions

4. CAPTURING THE VALUE OF PHARMACEUTICAL PROSPECTING

Section 3 suggests that there exists considerable uncertainty regarding the value of biodiversity as an input into the pharmaceutical prospecting process. It also reveals that attention typically focusses on the value of biodiversity and not on the value of the species information that is developed during the prospecting process. In Sections 5 and 6 a detailed exploration of the value of biodiversity *and* species information in the prospecting process is undertaken in order to attempt to provide a more reliable indicator of the potential importance of prospecting activities in the biodiversity conservation process.

To prepare the ground for such a valuation exercise, this section examines the economic characteristics of biodiversity and species information (both taxonomic and biochemical). A discussion of the market failures in each of the three "markets" - the markets for pharmaceutical R&D, biotic samples and biodiversity - illustrates the full social costs of investing in pharmaceutical prospecting. The distribution of these costs and the ability to capture benefits across the different actors involved in prospecting points to important incentives problems that may impede society's ability to obtain an "optimal" level of investment in the production of biodiversity and species information. Existing, evolving and potential market and policy solutions to these *incentive* problems are then discussed. While the emphasis is on measures which would assist developing countries in capturing the value of pharmaceutical prospecting, some thought is also given to measures that would maximize investment in pharmaceutical prospecting as a whole.

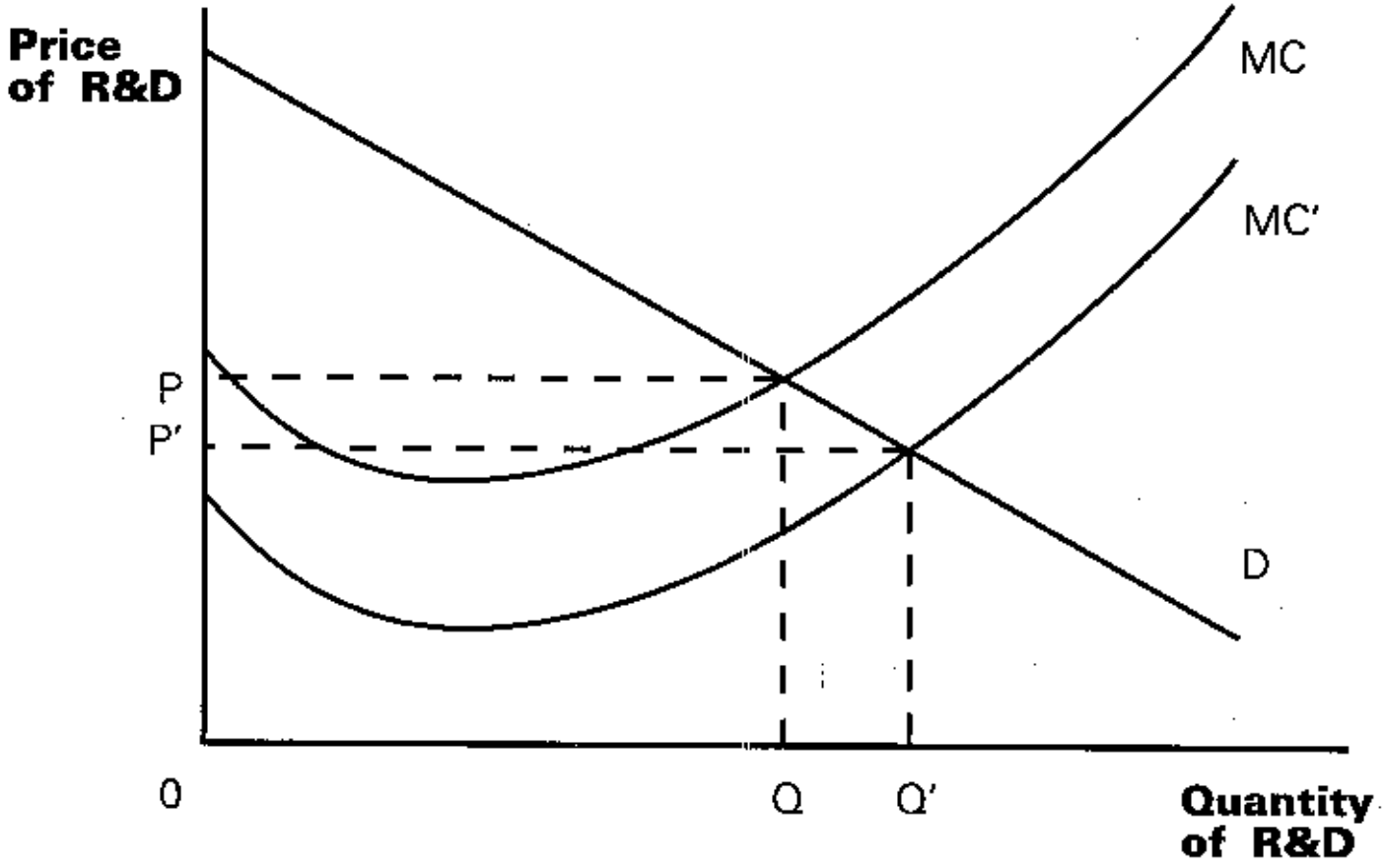
Species Information: Pharmaceutical R&D

Suffness and Douros (1979) indicate that the exploration of the pharmaceutical potential of biodiversity has three objectives:

- the discovery of active agents which can be developed as drugs
- the discovery of agents which can be modified through analog studies to yield useful drugs
- the discovery of agents with novel structures and mechanisms of action which can be used in the study of disease states

The generation of information about a species and its chemical constituents - i.e. the process of discovery - is the core activity of the pharmaceutical R&D component of pharmaceutical prospecting.

Figure 2 The Market for Pharmaceutical R&D



Information, or knowledge, of all kinds is "non-rival" - consumption of knowledge (learning) does not reduce the opportunity of the next consumer to learn the same information. Species information - whether chemical, taxonomic, ecological, ethnobotanical or otherwise - is no exception. However, the ability of a potential consumer to learn or acquire a particular set of information - and therefore the cost of learning - does depend on the "exclusivity" accorded to:

- the knowledge already gained by another consumer
- the raw material or raw data behind the knowledge and
- the finished product generated by the application of the knowledge.

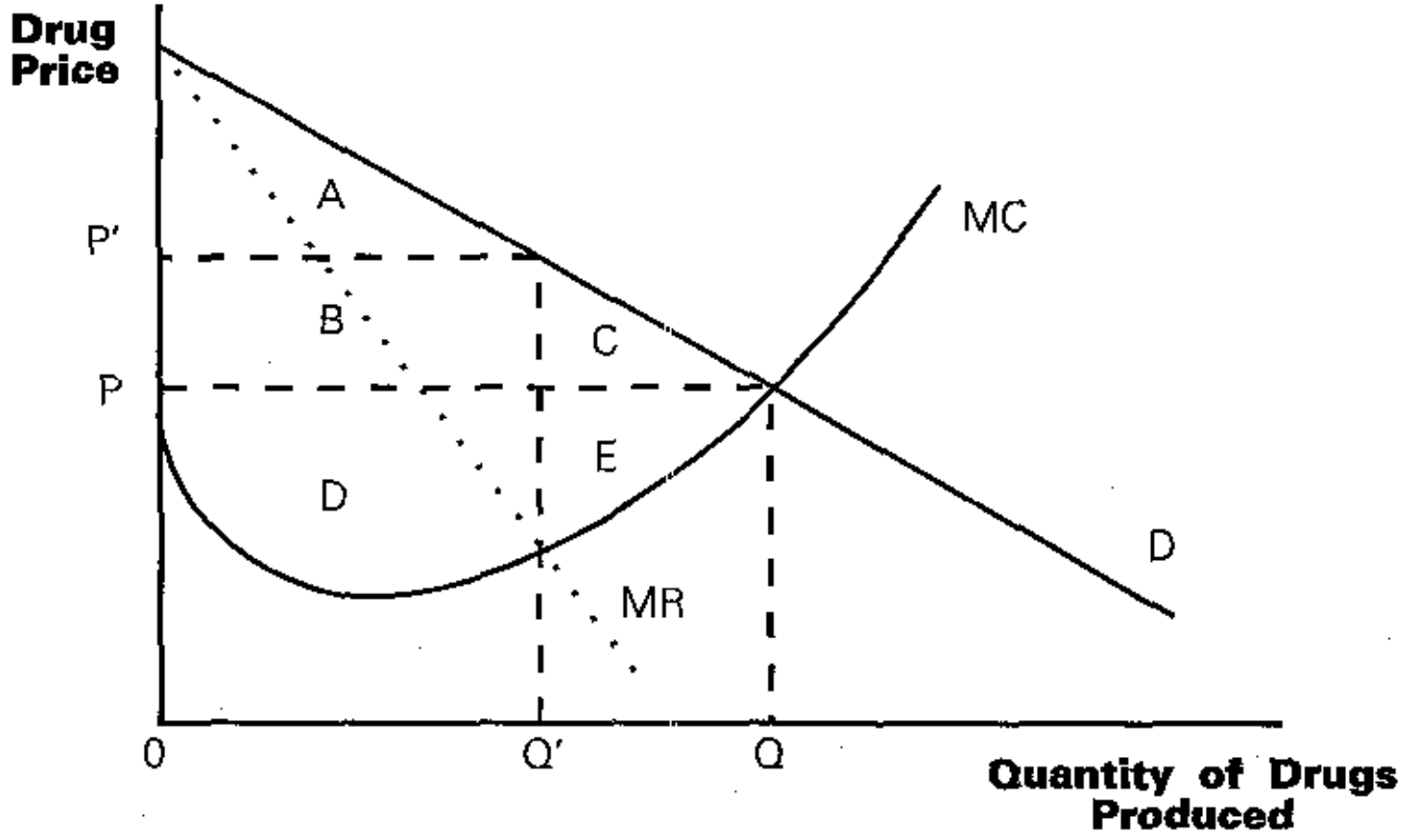
If the knowledge already gained by another consumer is made freely available, a second consumer can appropriate the information at little or no cost. If the finished product generated by the application of this knowledge is available, a second consumer may be able to "reverse engineer" the original knowledge (or simply the product) at a lower cost than that incurred by the original consumer. Finally, if the raw material or raw data that lies behind the knowledge is available the second consumer may reproduce the information or "reinvent the wheel." In this case any cost advantage obtained by the second consumer would be the result of being more efficient in the production of information than the original consumer.

In theory, the exclusivity problem posed by reverse engineering is the principal cause of market failure in the case of information produced during the pharmaceutical R&D process. In the pharmaceutical industry potential competitors are effectively excluded from the raw material, knowledge and intermediate products generated during the long process of R&D as information is deemed proprietary and many activities are kept in-house. Thus, there is likely to be little opportunity for competitors to reinvent the wheel. However, once the final product is brought to market, other potential consumers of this knowledge are capable of reverse engineering the information. Unlike the case of computer software there is no copy protection that can be inserted into a pharmaceutical product.

If it is likely that potential competitors in the pharmaceutical industry are able to obtain a substantial cost advantage in the R&D phase through reverse engineering, then "copy-cat" companies will be able to produce new drugs at a lower cost than that incurred by the original inventor. Figure 2 provides a graphic representation of the market for R&D with two representative competitors - an innovative company and a copy-cat company. The company making the initial discovery will have marginal costs, represented by MC, that exceed those of the copy-cat company, MC'. Given that both companies face the same demand for new pharmaceuticals, D, the copy-cat company will be able to meet market demand at a lower equilibrium price, P', and a higher quantity, Q', than will the innovative company at its equilibrium price and quantity, P and Q. If demand is elastic - i.e. a small fall in price leads to a large increase in the quantity purchased - the copy-cat company may greatly increase its revenues at the expense of the original inventor.

The copy-cat company - or the company that buys R&D products from the copy-cat and mass produces the final product - will gain the benefits of having lower R&D costs to recoup from its product sales. It could then, presumably, take the drug to market at a lower price than the innovative company, thereby cornering the market for the drug. In this fashion, prospective investors in pharmaceutical R&D are likely to consider that the non-rival nature

Figure 3 The Market for On-Patent Drugs



of the information embodied in the finished product and the difficulty of excluding others from access to the final product will reduce the ability of the inventor to capture the full returns of investments made in drug innovation. The expected outcome of such a situation would be a less than optimal rate of drug innovation and provision of pharmaceutical products.

Cooter and Ulen (1988) posit three differing underlying market situations that characterize the economics of information and that, in turn, lead to differing conclusions regarding the appropriate role of property law in generating optimal levels of information:

- The market allows the producer to capture enough revenue to cover the costs of generating information. No intervention is necessary.

- The market will under-produce R&D because of the non-rivalness of information. Intervention is thus justified in order to attain an economically optimal level of information, either through government provision, government subsidy or the granting of monopoly rights

- Competitive markets for information generate over-production of information as investors duplicate efforts. Intervention should attempt to assign monopoly rights early in the production process so as to limit competition (and over-production) in the latter stages.

As discussed above, in the case of pharmaceutical R&D it is unlikely that the market will either over-produce information or provide an optimal amount of information. Intervention is therefore required. By and large public policy in this area has relied on the granting of monopoly rights to the products of applied research and government support for basic research.

Most developed countries have intellectual property rights systems that provide some combination of patent protection for novel compounds, processes of production or uses for compounds.[13] In obtaining a patent, a company gives up its *exclusivity* over the information it has generated in return for a legal guarantee of *exclusive* rights (over a set time period) to sell the product itself. Thus a company will reap monopoly profits from its investment in R&D should any of its new compounds prove to be of commercial value. With the limited (in duration) monopoly provided by a patent the company is expected to recover - and indeed generate a return on - its investment in generating non-rival information.

In a well-functioning market the forces of supply and demand lead producers to produce an equilibrium quantity at market-clearing prices. In a monopoly - such as is shown in Figure 3 - there is no invisible hand of competition, only the self-interest of the monopolist. In planning output, monopolists produce at price, P', and quantity, Q', where the marginal costs, MC, of production equal marginal revenues, MR. If the revenue from the next additional unit is exceeded by the marginal costs of its production, there is no reason for the

[13]Patents are a form of intellectual property which Phillips and Firth (1992) define as "the legal rights which may be exerted in respect of the product of the human intellect."

monopolist to continue producing products. As the price the monopolist charges, P', reflects what the market can bear at a given quantity, considerable producer surplus is generated by the monopolist, equal to Areas B and D. As a consequence, the monopolists will stop production short of the quantity, Q, that would have been reached if the competitive forces of supply and demand had been allowed to play out.

In the case of the pharmaceutical industry, it is likely that large monopoly profits are captured only by drugs that represent a major advance over previous treatments, or that open up new areas of therapy. Such blockbuster drugs are rare. However, they appear to be an important component in maintaining the overall profitability of major pharmaceutical companies. Despite the existence of patent protection on particular compounds, companies competing in particular therapeutic areas quickly invent around the patent or develop parallel treatments. The combination of long lead times between patenting and regulatory approval, and the development of drugs that mimic the effects of novel compounds - "me-too" drugs - imply that true monopoly profits within individual therapeutic areas are of limited duration in the pharmaceutical industry.

Nevertheless, returning to Figure 3, it is possible to conclude that due to the existence of a monopoly, society appears to suffer a deadweight loss of Areas C and E due to the failure to attain the free-market equilibrium production level, Q. However, it is misleading to compare the economic benefits gained under monopoly with those generated by an undistorted market. The rationale behind the institution of patent rights is that the market fails to generate this level of benefits due to the non-rival nature of information. Thus, a strict interpretation of Areas C and E as efficiency losses is somewhat irrelevant as in the absence of patent protection the quantity produced would likely be far less than at the monopoly equilibrium point, Q'.

In the case of patents - which are designed to combat market failure by offering a monopoly of only limited duration - it is more instructive to consider efficiency concerns from a dynamic perspective. Cooter and Ulen (1988) suggest that the optimal patent life will depend on the social costs and benefits of granting a monopoly. When the marginal social benefits no longer exceed the marginal social costs the patent becomes a net drain on society. Normally, the marginal social costs reflect the efficiency losses incurred by monopoly production and the extraordinary costs incurred by users of the invention or the competitors of the inventor in "inventing around" the patent. Cooter and Ulen (1988) suggest that these costs will tend to rise over time. The marginal social benefits of patent protection decrease over time as the extension of patent longevity increases investment in information generation but at a decreasing rate. Given these trends it is possible, at least in theory, to specify the optimal length of a patent.

Application of these ideas in practice is difficult. The marginal social costs and benefits of patents will vary between - and perhaps within - different industries. There is little reason *a priori* to expect that patents for new widget designs and new drugs need to be of the same longevity. In addition, conditions within an industry may change over time. In recent decades, the increasing lead time required for the development and regulatory approval of new drugs has shortened the effective life of patents on compounds. Yet, the length of patent life in most countries is fixed by legislation at a single, seemingly arbitrary figure that applies across all types of inventions. It is highly unlikely that incentives for the provision of

optimal levels of information will be present in any industry. Patents as currently applied are a very blunt economic policy instrument.

This raises the issue of whether patent provisions are effective incentives for investment in pharmaceutical prospecting. In particular, since patenting applies to all pharmaceutical products it is important to consider if there is a level playing field for natural products-based as versus synthetics-based R&D.

Compounds isolated from natural sources are often difficult to synthesize and scale-up of programs aimed at mass production of synthetic compounds is often uneconomic compared with the cost of supply from natural sources. If commercial synthesis of natural product drugs were impossible, then - in the absence of patent protection - reverse engineering would require a company to work backward from a known chemical compound to the original and "unknown" species. The ability to exclude others from the taxonomic and collection information generated earlier in the prospecting process would make such reverse engineering a difficult feat - akin to looking for a needle in a haystack.

The need to intervene by guaranteeing patent protection, therefore, might be construed as less important for natural products research than for research into synthetic compounds. Nevertheless, the potential for synthesis of natural compounds is likely to lead pharmaceutical companies to perceive a reliance on a proprietary hold over species information as a risky means of ensuring the ability to capture the returns to R&D. In any case, it is unlikely that this situation would justify a separate policy approach for natural product derived pharmaceuticals - particularly as advances in basic science and technology may eventually render natural product compounds more amenable to commercial synthesis.

As discussed at the outset of this section, reinventing the wheel is unlikely to generate a cost advantage in pharmaceutical R&D. However, the existence of provisions for a limited period of exclusivity in collection contracts indicates that most pharmaceutical companies are concerned that access to the same raw material may allow another firm to discover promising compounds first. Given the existence of pantropical species, a "patent race" scenario - in which competing producers duplicate each others' work in an effort to be the first to patent - may be a legitimate concern both for society and potential investors in pharmaceutical prospecting. The prevalence of this problem will depend on the extent to which competitors screening programs are likely to be assessing the same chemical characteristics of biotic material.

If the problem of over-production of information is significant, Cooter and Ulen (1988) suggest the extension of monopoly rights to earlier stages of the R&D process. In the case of pharmaceutical prospecting, this would involve some form of exclusive rights over the exploration of particular species (or even particular genera as secondary metabolites are often common to a genus). A global register granting a limited exclusivity for evaluation of species would be one possible mechanism. The practical difficulties and costs involved in setting up and administering such a system would probably be considerable. Whether the potential complications presented of pantropical species would warrant such action would need careful consideration. Given that a large number of major pharmaceutical companies have recently agreed to share information in the search for AIDS, a collaborative effort by

companies - not external regulators - to prevent duplication of effort in exploring the pharmaceutical potential of biodiversity might be an interesting model.

In considering the relative incentives to invest in natural products R&D versus incentives for research into synthetic compounds, there are two factors to consider. If the length of time required to develop leads from natural compounds is significantly longer than in the case of synthetic compounds, the incentive to invest may be skewed towards synthetic compounds.[14] Secondly, if natural products are on average likely to generate significantly more in the way of uncapturable economic benefits - that is, they produce extremely novel compounds leading to breakthrough treatments - then the same argument may apply.

Evidence on relative lead times is anecdotal at best. For example, taxol first showed signs of bioactivity in the National Cancer Institute screening program in 1964, but did not complete clinical trials and receive regulatory approval until 1992. The difficulty in obtaining sufficient resupply of active material for pre-clinical development and clinical trials is a rate-limiting factor often experienced in R&D based on plants and marine organisms. How significant this factor may be is unknown. Collection of data on patent applications and drug approvals over the past two decades - as proposed in Appendix A - would provide material for an empirical assessment of this hypothesis.

If society gains proportionally more from the introduction of natural product-based pharmaceuticals than from the development of new synthetic drugs, action to ensure the production of such extra marginal benefits may be warranted. One critique of synthetic drugs argues that natural products are less likely to prove dangerous to society than synthetic compounds in ways that are unforeseen at the time of clinical trials and regulatory approval. This argument could be tested empirically by examining past cases of negative social and economic impacts resulting from unforeseen side-effects of drugs.

Another argument supporting the notion that natural products provide major positive externalities is based on the idea that synthetic drugs provide only incremental therapeutic advances, while new compounds derived from natural products often represent major advances - as is the case with the vinca drugs and taxol.[15] Unfortunately, it is difficult to assess whether natural products - in particular plants and marine organisms - are likely to be a "better" source of breakthrough therapies. The number of success stories from these species over recent decades is quite limited. In addition, reliance on relative success rates alone would be misleading, the cost-effectiveness of investments in different drug development methodologies would be a better indicator in this regard. However, it should also be recognized - as stated at the outset - that the derivation of pure or analog compounds that are marketable is not the only objective of pharmaceutical R&D. Miller and Brewer (1992) suggest that natural products chemistry has often played a leading role in the development of other synthetic products and the state of knowledge regarding disease itself.

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[14]This requires that the costs per unit time remain the same in each instance.

[15]Note that this argument has its analog in the area of crop breeding. Duvick (1990) suggests that incorporation of wild material into breeding stocks is far more likely to make major advances in crop characteristics than the cross-breeding of well-known cultivars.

This argument may also derive momentum from critics of the pharmaceutical industry who contend that too much attention (and investment) is devoted to developing "me-too" drugs and not enough to finding truly novel therapies. Green critics contend that instead of expending vast sums of money synthesizing "me-too" drugs, society would be better off if companies spent this money on developing more innovative treatments based on natural products. The economic implication of this argument is that the ability to capture returns from major advances in drug therapy is undercut by other companies efforts to "invent around" the breakthrough product, thus reducing incentives to invest in new product development - including natural products. However, at the same time critics of the drug industry often complain that novel treatments - such as AZT for treatment of AIDS - are often prohibitively expensive. Clearly, the argument cannot work both ways. It is not possible to criticize the industry for charging high prices on new drugs and at the same time criticize efforts to develop new - and cheaper - substitutes. Also, this argument does not explain why this scenario would lead to discrimination against research into natural products as opposed to synthetics - except for the likelihood that "me-too" drugs would be synthesized based on the patent data supplied by the originating company.

If either of these two differences between research into natural products and synthetics are significant, it is possible to argue that some additional incentive may be necessary in the case of pharmaceutical prospecting. It is worth emphasizing that patents and other forms of intellectual property protection such as copyrights and trademarks are not the only economic instrument available to governments seeking to intervene in the pharmaceutical marketplace.

For example, the US Orphan Drug Act (passed in 1983) stipulates that drugs developed for treating rare diseases receive a number of post-approval benefits. Most important amongst these concessions is seven years of market exclusivity. The US Pharmaceutical Manufacturers Association (1992b) reports that the US Food and Drug Administration had granted 488 orphan drug designations by March 1992 and that 189 orphan drugs are in the development stages. Rare diseases listed for the purposes of orphan drug research include most forms of cancer, AIDS and AIDS related conditions, and a host of childhood diseases, diseases of women, genetic disorders and neuromuscular disorders. The beneficial impact of this policy can be seen be the continued investment by Bristol-Myers Squibb in the development of taxol (in cooperation with the National Cancer Institute). As any patent once held on taxol was likely to have expired long ago, the orphan drug designation for ovarian cancer provided the needed incentive for the private sector to incur the costs of entering taxol in clinical trials.

Thus, there may be alternative forms of intervention that can be used to overcome the bluntness of current systems of patent protection. Tyler (1979) points out that current system of intellectual property rights maintained in countries such as the US and the UK actually provides disincentives for investment in establishing research programs into potentially useful areas of natural products such as compound-based drugs with a long history of use, as well as multi-source or herbal drugs. In addition, it can be argued that the development of new drugs from biodiversity is often constrained by uncertainty over supply and resupply issues, the lack of data on the chances of success, and lack of familiarity with the disciplines involved. One potential solution to this situation would be to provide a system of market incentives for drugs generated from natural products that is separate from patent protection, but that guarantees market exclusivity for a period of limited duration. If pharmaceutical

prospecting using plants, marine organisms and insects is in fact a higher risk, higher pay-off drug development strategy with longer and more costly lead times than conventional R&D based on development by design (or by laboratory manipulation of microorganisms) such a policy approach might be warranted.

Species Information: Collection and Identification of Biotic Samples

In producing biotic samples for use in pharmaceutical R&D, researchers may generate a number of different types of information about species:

- collection information - date, location, site conditions, etc.
- taxonomic classification of the organism
- ecological observations in the field that indicate biochemical activity
- ethnobotanical information about traditional medicinal uses of plants
- published reports of biochemical activity for a given species, genus or family[16]

This paper focuses on the research activities involved in generating *collection and taxonomic classification* information undertaken by collectors of biotic samples. This information is an essential input in the production of biotic samples for pharmaceutical prospecting.

As discussed in the previous sub-section information is a non-rival good. Information generated during the collection and classification of species is no exception. As in the case with species information developed in the R&D stage of prospecting, the ability of subsequent consumers to learn or to acquire species information depends on the *exclusivity* accorded to:

- the raw material - i.e. the biodiversity specimen
- the information itself
- the final product - i.e. the biotic sample

Generally speaking, a collector cannot exclude other collectors from access to the raw material - species in the wild. Thus, collectors are free to *reinvent the wheel* by collecting biotic samples. If a given collector has a cost advantage and can gain an increased share of the market this must be a result of being more efficient in production - i.e the collector has a competitive advantage over rival collectors. This is not a case of market failure, but of market competition.[17]

Access to species information - the taxonomic classification and details regarding the collecting - and the physical specimen itself is typically kept confidential by the collector and the buyer of biotic samples. Collectors of biotic materials are competing for "market share" and are unlikely to share species information with other collectors. In addition, pharmaceutical companies may request or require that collectors keep descriptions of

[16] These information sources often guide the selection of species for screening.

[17] However, if it leads to economies of scale, then a natural monopoly can develop.

collected species confidential. Collectors of biotic samples are, therefore, certain to exert exclusivity over the species information and physical specimens they collect. In addition, pharmaceutical companies are likely to restrict access to biotic samples and their associated information whilst they are under investigation. It thus becomes practically impossible for competing collectors to *reverse engineer* taxonomic information or biotic samples.

In sum, market failure is not an inescapable result of the non-rivalness of collection and taxonomic information. Because of the exclusivity exerted over both the information and the associated biotic samples, competitors do not necessarily generate a cost advantage by reinventing the wheel and reverse engineering becomes biotic samples impossible. Commercial collectors operate in a competitive end use market and are able to appropriate the profit, or producer surplus, generated by their investment in species information.

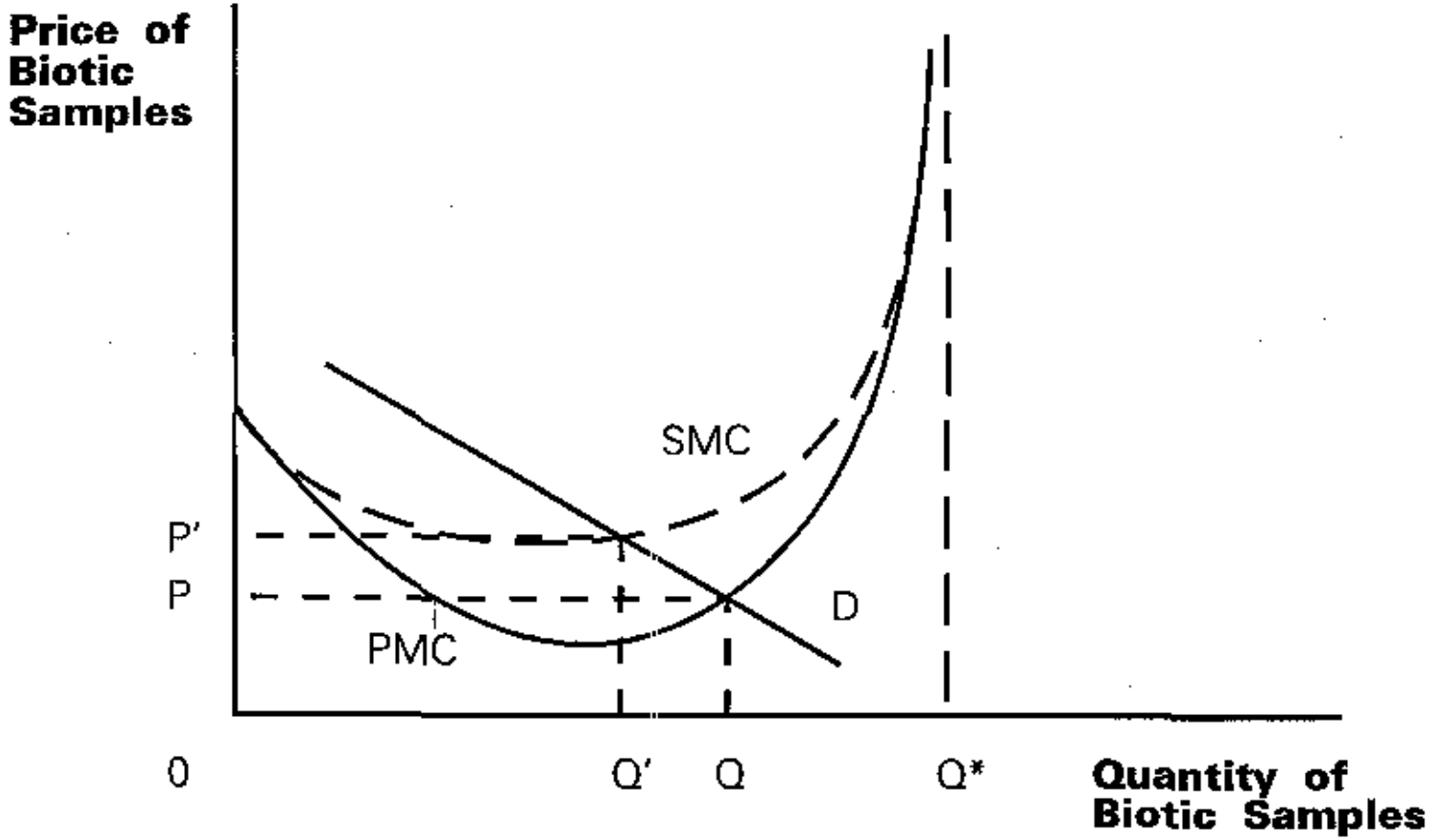
The implicit assumption of the preceding discussion is that collectors are generating species information on their own. However, collectors often rely on existing natural history museums or botanic gardens for a number of services - services often received free of charge. These taxonomic inputs are often an important element in the production of biotic samples. Market failure in this input, or factor, market may lead to a reduced incentive to invest in the broader base of taxonomic knowledge itself.

In the case of known species, commercial collectors may utilize existing reference collections in order to gather data on collection sites or to confirmation the identification of a specimen already collected. In the case of species that are not held in local collections or are outside the area of expertise of a collector, the collector may actually submit a sample to one of the large public institutions in the North (or South) that has the taxonomic expertise necessary to make an identification.

It is the investment of such institutions in developing the expertise of their staff, the physical collections and the information contained in collections and databases that goes unrewarded by pharmaceutical prospecting. These inputs make an important contribution to the commercial endeavor of producing biotic samples for sale to the pharmaceutical industry. Whether this unpaid social cost is interpreted as an external factor of production that does not enter the market calculus or as an implicit government subsidy (since most collection facilities are funded by public funds) is not important. The point is that carrying out such activities for free is a drain on already scarce taxonomic resources.

The market for biotic samples from a biodiversity-rich developing country is illustrated in Figure 4. For collections of small quantities of biotic samples the private marginal cost curve, PMC, of commercial collectors does not reflect the full social costs of collecting and identification as revealed by society's marginal cost curve, SMC. The gap between the private costs initially increases as the collector's own personal knowledge of the location and classification of species is exhausted and increasing resort to local herbaria and taxonomic support is necessary. However, as the quantity of samples collected approaches the limits of the expertise and reference collections on offer at local taxonomic institutions, Q*, both the private and social costs rise as it becomes increasingly difficult and costly to identify "new" samples. Typically, the burden of identification of further samples will shift primarily to taxonomic experts at Northern institutions that specialize in tropical biodiversity.

Figure 4 The Market for Biotic Samples



As a result of this market failure in the provision of taxonomic information collectors will produce and sell biotic samples at a price, P, that is lower than the true economic price of biotic samples (see Figure 4). Collectors will collect an equilibrium quantity, Q, that is larger than that dictated by the social equilibrium at Q'. Essentially, the public subsidy provided to collectors encourages them to collect in larger quantities and undercharge relative to the theoretical social optimum. The failure by taxonomic institutions to capture the value of their investments in information leads to overproduction of the complementary good - i.e. biotic samples.

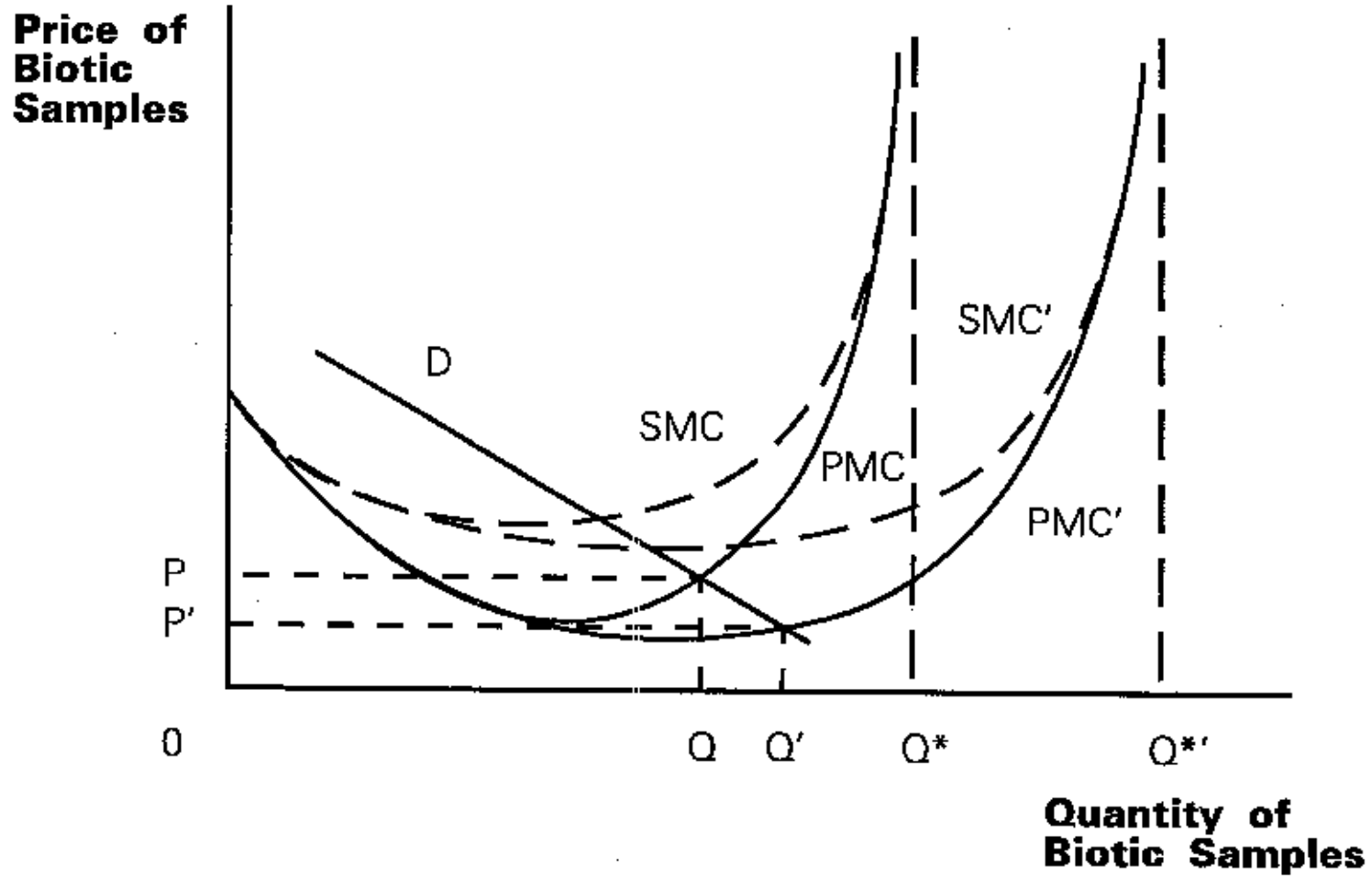
The recent upsurge in interest by pharmaceutical companies in evaluating biotic samples is considered to be a result of improvements in screening technology. Such technology is a also a complementary good, but on the demand side. Technical improvements in screening capacity are, therefore, likely to cause a demand shift out and up from the original curve leading to an increase in the quantity of samples screened.

Given that demand for biotic samples has risen in the past few years, Figure 5 explores the potential consequences of an increase in public investment in the development of in-country taxonomic expertise and knowledge. Increasing the supply of local knowledge will have the effect of shifting Q* out to Q*'. As the social marginal cost curve shifts out to SMC' the private marginal cost curve will also shift out to PMC'. The result is an increase in the quantity supplied, from Q to Q', and a fall in the market price from P to P'. Whether the change in net revenues will be positive or negative will depend on the elasticities of demand and supply - i.e. the responsiveness of the demand and private marginal cost curves to changes in price and quantity. The difference between the private and social marginal costs of generating biotic samples implies that an increase in investment in locally available taxonomic information is likely to increase the amount of biodiversity made available for biochemical evaluation.

Investment in taxonomic information may, therefore, be an important factor in the sustainability of pharmaceutical prospecting. Accompanying improvements in screening technology are continued technological and scientific improvements in the field of biotechnology and rational drug design. If these latter trends continue unabated, demand for natural products may be reduced in the future. Many of the new techniques for developing drugs are unlikely to make use of natural products. In addition, over the longer term - in this case 10-20 years - it is possible to suggest that improvements in new paradigms of therapy such as gene therapy may reduce the need for compound-based approaches to health care. As time progresses, then, improvements in taxonomic information that lower the private costs of providing biotic samples may assist in maintaining the market share of natural products in pharmaceutical R&D.

In sum, collectors may be able to capture the full value of their investment in information generation by competing in the market for biotic samples, but there is a hidden social cost that goes unpaid. The market in biotic samples, thus, fails to provide the requisite incentive to invest in the generation of the larger body of taxonomic knowledge that is essential to pharmaceutical prospecting. In addition - as indicated in the next section on biodiversity protection - collectors of biotic samples do not pay the social costs of biodiversity protection. The exchange of biotic samples between collectors and pharmaceutical companies does not,

Figure 5 Investments in Taxonomic Information



therefore, adequately compensate efforts to protect biodiversity or generate taxonomic information.

A solution to the incentives problem posed by the hidden social costs of the collectors use of staff knowledge, reference collections and databases of information at major taxonomic institutions is straightforward. Either public funds must render the necessary support for these commercial activities or fees should be charged by such institutions for services rendered. Given that public funding for pure taxonomic work is increasingly difficult to obtain it is recommended that user fees be instituted for services provided to commercial collectors. These fees should reflect not only the costs of generating biotic samples, but the costs of identification (Townes 1992). In addition, the cost of any classification work that is "farmed out" to specialists in other institutions who conduct the work for free, must be incorporated into any fees charged. Charging such fees should not hinder the circulation of the majority of taxonomic information; however, the generation of information for commercial purposes would be priced in an open and competitive market.

This solution is pertinent to both developed and developing country institutions that seek to advance the body of taxonomic knowledge. It is, however, particularly relevant in the developing country context where constraints and demands on public resources may mean that taxonomic research and inventories will have great difficulty in finding public funding. As a result, the development of such institutions in developing countries may require a much more pragmatic approach than their Northern counterparts which evolved with the support of the public purse. The need to charge commercial collectors of biotic samples for services rendered is likely to be only one of a number of areas where botanic gardens and other taxonomic institutions may commercialize the species information they produce. A research proposal aimed at examining the willingness to pay for taxonomic services is included in Appendix B.

The drawback to the initiation of charging systems for taxonomic information is that they may dramatically affect the demand for biotic samples by pharmaceutical companies. The internalization of the full social costs of producing biotic samples will lead to a rise in the market price of biotic samples and may cause a subsequent scaling back of the quantity demanded. Whether the impact would be large or small will depend on the elasticity of demand for biotic samples. A discussion of the potential impacts of raising the price of biotic samples is discussed below in reference to the additional need to internalize the costs of biodiversity protection in the prospecting process.

Biodiversity Protection

The protection, or maintenance, of biodiversity must be included in an economic analysis of pharmaceutical prospecting because the supply of this "raw material" input involves a significant social cost. Dixon and Sherman (1990) indicate that the social costs of protecting biodiversity are comprised of the direct and indirect costs of protection and the opportunity cost of allocating land to the production of biodiversity. As economically profitable, alternative land uses may exist for lands currently functioning as reservoirs of tropical biodiversity, it is important that the production of biodiversity be capable of generating real

economic benefits. Otherwise, there is little economic incentive for society to protect biodiversity.

The use of the "raw material" input in pharmaceutical prospecting may involve a number of interventions at the level of the biological resource itself. McChesney (1992) suggests that the following amounts of dried plant material are necessary for completion of the following stages of drug development and marketing:

- initial screening and isolation of lead compound - 5 kg of dried material
- confirmatory screens and initial development - 50 kg
- additional R&D through clinical testing - 200 tons
- "mass" collection or cultivation for production - as much as 200 thousand tons per year.[18]

However, recent improvements in the sensitivity of screening technology increasingly mean that secondary screening (and in some cases even isolation of the compound) can be accomplished with the amount of extract generated by just 1 kg of dried plant material (Thomas pers. comm. 1993).

The number of collections required vary with the type of natural product under investigation. Collection of microbial species in the form of a single environmental sample typically yields enough "starter" material for researchers to develop methods for culturing species that show promise in early screens. In the case of research into plants, marine organisms and insects a return to the source for additional material to complete the R&D process is the rule. If commercial synthesis of the compound is feasible the bulk production of the species is not required. Balandrin *et al.* (1985) suggest that since most natural product leads are secondary metabolites they will be difficult - and therefore costly - to synthesize. In the discussion that follows, the analysis is limited to the minimum initial collection required to confirm the classification of the biotic sample and to assess biochemical activity in an initial screen.

For the purposes of the initial collection, the raw material input of biodiversity is generally a *non-rival* resource. Collection by one individual rarely impedes the ability of another potential consumer to collect the same species. However, in the case of endangered species; species of limited size; or species making it through to further stages of testing, development and production; biodiversity may prove to be *rival* due to the effects of *congestion* on the resource. The intensity of collection activities relative to the prevalence of the species may cause the quantity or quality of the remaining stock to be degraded to the point where it impairs the ability of another collector to gather the same species. *Rivalness* in the later stages of pharmaceutical prospecting may imply absolute limits on the successful development of promising new compounds and raises concerns regarding the extinction of such species.

Non-intensive collection of biotic samples from public wildlands in developing countries is not subject to much in the way of government restriction or control. Collecting permits are required in some countries; fees payable to public authorities expressly for the privilege of

[18]McChesney's figures are based on a worst-case scenario regarding the concentration of the active material in the plant and will, therefore, represent the upper end of the range.

collection are typically insignificant if they exist at all. The difficulty and cost of asserting *exclusivity* to biological resources has left public authorities with little effective control over access to biodiversity. In this context, biodiversity is a non-exclusive, as well as non-rival resource, and fits the characteristic definition of a "public good." As a result, biodiversity is often left in a state of "open access" and is freely collected by all comers - biodiversity is treated as a "free good" by collectors.

Thus, there is no formal market for the raw material as it is collected from the wilds. However, the existence of social costs incurred in producing biodiversity allows the positing of an implicit market for biodiversity protection - e.g. the provision of biodiversity specimens. This market is illustrated in Figure 6. Activity in the market for biotic samples reveals that there is a demand, D, for the input of biodiversity specimens by collectors. Because society incurs the direct, indirect or opportunity costs of protecting biodiversity there is also a social marginal cost curve, SMC. The implicit equilibrium price, P, would clear the market for these specimens at a quantity, Q.

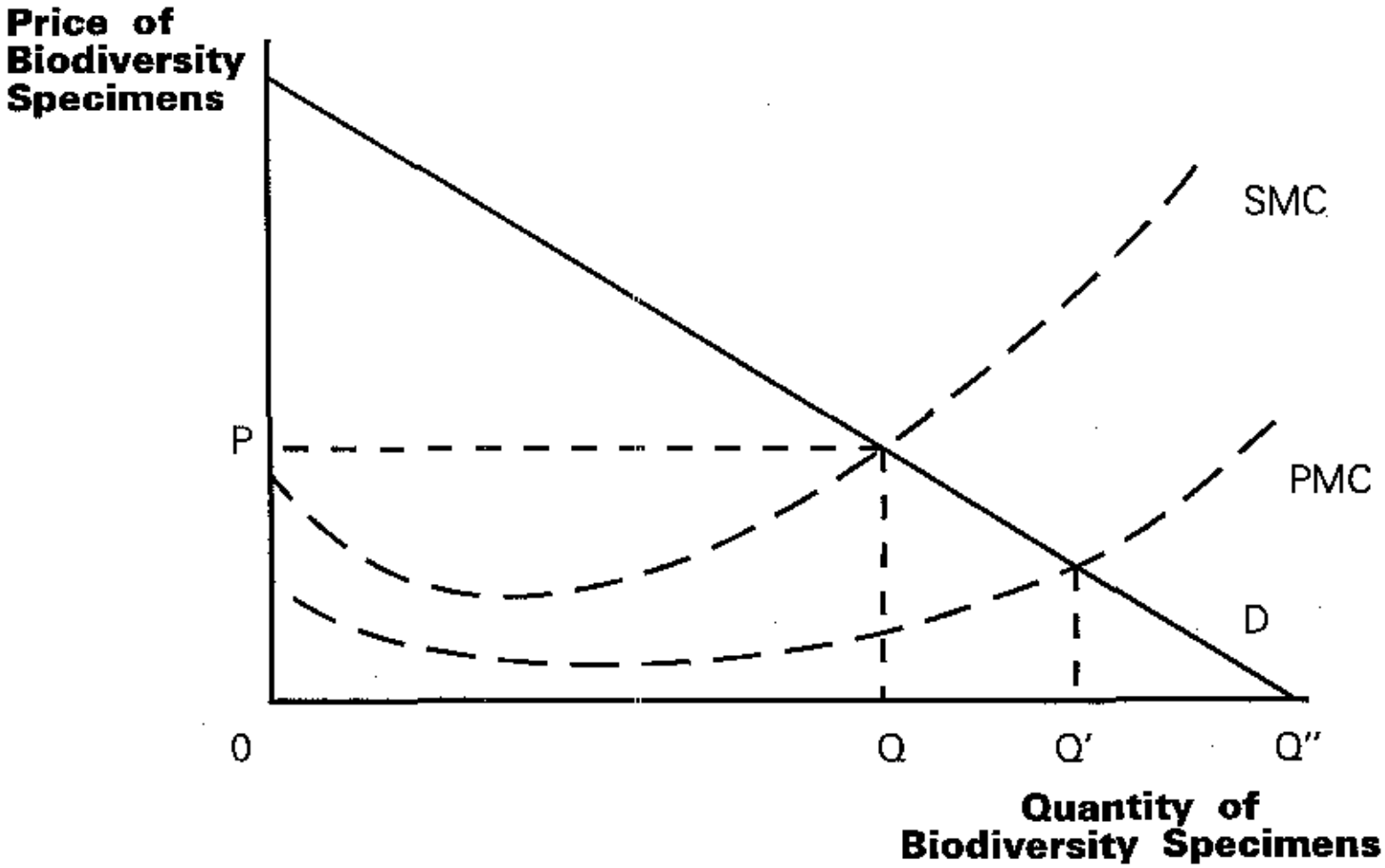
However, because of the open access problem, collectors are not required to pay anything for specimens and the market is unlikely to clear at the equilibrium quantity. Instead consumption is likely to exceed Q. The final level of extraction, Q', will depend on the private marginal costs of collecting, *PMC*.

This will be at a point in between the "pure" open access equilibrium at Q'' - i.e. where private costs are zero - and the optimal quantity Q. The result is that collectors gain the area below the demand curve from O to Q'. Meanwhile, producers of biodiversity not only lose the available economic rent they might otherwise have gained from protecting biodiversity, but fail to cover any of the social costs incurred in protecting biodiversity.

This market failure ensures that the actual returns to maintaining biodiversity are less than the social returns. In fact, under "pure" open access conditions the actual returns are negligible or even zero. Given these conditions, pharmaceutical prospecting does not provide a financial incentive for continued investment in the protection of biodiversity. If the economic value of biodiversity in the prospecting process is significant compared to its other economic values, then the incentives problem will lead to conservation land use options that compare poorly with alternative land uses in economic terms. Other things equal, this will lead to land being taken out of the production of biodiversity.

Solutions to the incentives problem posed by the *non-rival* and *non-exclusive* characteristics of biodiversity involve either government intervention to provide these public goods or the development of means to enable the "private" appropriation of their value. While public funding of biodiversity protection and the generation of species information has a long tradition, budgetary limitations mean that funding sources for biodiversity conservation are scarce in developing countries. In order to access public funds, the real costs incurred by conservation must be justified through demonstrating the economic value and social returns to biodiversity conservation. This may be difficult to do, particularly when competing uses of the land, such as conversion to agriculture, timber production and mining operations, can

Figure 6 The Market for Biodiversity Specimens



realize significant, immediate and visible financial gains.[19] The trend towards increasing commercialization of biodiversity indicates that one alternative to public funding is to commercialize biodiversity. Potential methods for capturing the value of biodiversity include the development of *property rights*, *contractual arrangements* and *vertical integration* of prospecting activities.[20]

In order to capture the value of biodiversity - the raw material in pharmaceutical prospecting - developing countries may develop their effective capacity to *exclude* potential collectors from public wildlands. Such exclusion might involve some combination of the legislation and enforcement of property rights over species found in public wildlands, or simply the imposition of effective managerial control over these wildlands. If it is possible to exclude potential consumers from access to biodiversity - or some subset of species - the benefits generated by the resource may be captured through the institution of a system for charging potential collectors for access to the resource. Unlike the case with information, *non-rivalness* of biodiversity specimens means little if access is not possible. Information may be recreated by reinventing the wheel or reverse engineering, but species cannot be regenerated if access is not permitted. The potential stumbling block to a property rights approach is the existence of pan-tropical species. Since many species are not endemic to a single country, it may prove difficult for a country to effectively exclude a collector from access to a particular species (known or unknown) that is found within its borders.

The difficulty with the property rights or access control approach is that it is unlikely to be sufficient to institute a fee system in simply one country. Foreign collectors would simply turn to alternative sources in countries where biodiversity remained a *free good*. Meanwhile, local collectors attempting to supply international markets would potentially be forced out of business due to the rise in their collecting costs. A variable fee system charging locals less than foreigners might ensure the continued production of local samples. Such a fee structure would amount to an export tax - and if high enough an export ban - on local production and export of samples by foreigners. Thus, the fee would discourage foreigners from collecting in the country.

However, it is not clear that the institution of a fee would meet its primary objective of raising revenues for biodiversity protection. As the local exporter would still face the going international price for biotic samples, the extent to which such a biodiversity user fee could raise significant revenues would depend in the first instance on the willingness of local collectors to absorb additional costs. This in turn depends quite heavily on whether buyers of biotic samples - be they intermediaries or pharmaceutical companies - are willing to pay more than they currently do for biotic samples. A crucial issues is whether the demand for biotic samples is elastic or inelastic. The impression received from industry and other observers is that the own-price elasticity of demand is elastic - i.e. the demand curve is flat.

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[19] For further discussion see Dixon and Sherman (1990) and Swanson and Barbier (1992).

[20] See Sedjo (1992) and Simpson (1992) for theoretical overviews of contracting and property rights issues. Both authors suggest that the seemingly gradual move towards property rights over wild genetic resources in the form of legal and administrative control is driven by technological change. Improvements in biotechnologies may make the benefits of biological resources more apparent, while growing ability to identify species might lower the costs of enforcing exclusivity.

A small change in the price of biotic samples would, therefore, lead to a large change in the quantity demanded by buyers.

If this is true, then a country that attempts to assert access control and charge significant user fees for collecting faces the possibility of seeing its collectors go out of business and pharmaceutical companies head elsewhere. This of course relies on the assumption that the quality of the biotic samples - both the information and the raw material component - are the same across different companies. This may not always be the case. As suggested in Aylward *et al.* (1993b), the quality of the product offered by the National Biodiversity Institute (INBio) of Costa Rica may have been instrumental in obtaining favorable contractual terms.

Over the longer term the cross-price elasticity of demand must also be taken into consideration. Other things being equal, a rise in the price of biotic samples is likely to shift demand in the market for substitute methods for generating new lead compounds for pharmaceutical R&D - such as random screening of synthetic molecules. The issue of the elasticity of demand is pertinent not just to biodiversity specimen user fees, but to efforts made by taxonomic institutions to charge for services rendered to commercial collectors. Drastic implementation of fee schedules for identifications and use of reference materials would be likely to have a similar effect on the market for biotic samples.

A second method for capturing the value of biodiversity protection is for protected area authorities, the relevant government ministries or local communities to establish *risk-sharing contracts* with pharmaceutical companies. These contracts will generally involve some combination of a payment for samples and a share of any future returns from marketable uses of a species' chemical compound (or semi-synthetic derivatives of the compound). The need for such arrangements is occasioned by the long odds of successfully deriving a marketable drug from a given species.[21] The balance between the size of the initial payment and the amount of royalty would reflect the relative risks borne by each party. Simpson (1992) suggests that the risk borne by a developing country in such an arrangement is the commitment to maintain its biodiversity in the face of the opportunity costs of converting the land to other uses. The company, in turn, bears the risk of actually developing valuable information about the species and its chemical constituents.

Laird (1993) provides a detailed description of a number of emerging contractual arrangements between pharmaceutical companies and the suppliers of biotic samples. In addition to initial payments and royalties these contracts may include provisions for the transfer of non-monetary benefits such as training and technology. However, Laird notes that contracts between collectors and companies have few explicit provisions for the conservation of biodiversity. As described above, the incentives problem facing efforts to conserve biodiversity is, therefore, not necessarily solved by the types of contractual arrangements that are currently in vogue. Either provisions for the use of the contractual sums must be included in these contracts, or additional contractual obligations must be struck between collectors and those entities in developing countries actively engaged in the protection of biodiversity.

[21] A success rate of one in ten thousand is often cited as an indicative "hit" rate for pharmaceutical screening.

A third option for a developing country wishing to capture the pharmaceutical value of biodiversity is for the country to establish local capacity in the initial stages of pharmaceutical R&D. If the country engages in protection activities, the collection and identification of biotic samples, and the initial screening and isolation of compounds it will be able to patent promising compounds and license them to pharmaceutical companies for further development. By undertaking all activities up through isolation of compounds the country achieves a degree of vertical integration and becomes able to capture the full returns to its investment in biodiversity protection.

Full vertical integration of activities from biodiversity protection, through to taxonomic identification, extraction of biotic samples, screening and isolation of promising compounds is highly unlikely even under favorable conditions. Such disparate activities are unlikely to ever be organized under one firm or government agency. Even in the case of INBio - where taxonomic work, collection and extraction are conducted in-house - the protection activity remains the responsibility of the park service. Organizations, whether private or public, often find it difficult to include too many businesses under one roof and tend to specialize in particular areas of expertise. The prospect of vertical integration of activities up through *isolation within a single country does, however, raise the interesting topic of how and to* what extent can biodiversity rich countries move into downstream activities whether through investment by the public sector, the private sector or external organizations.

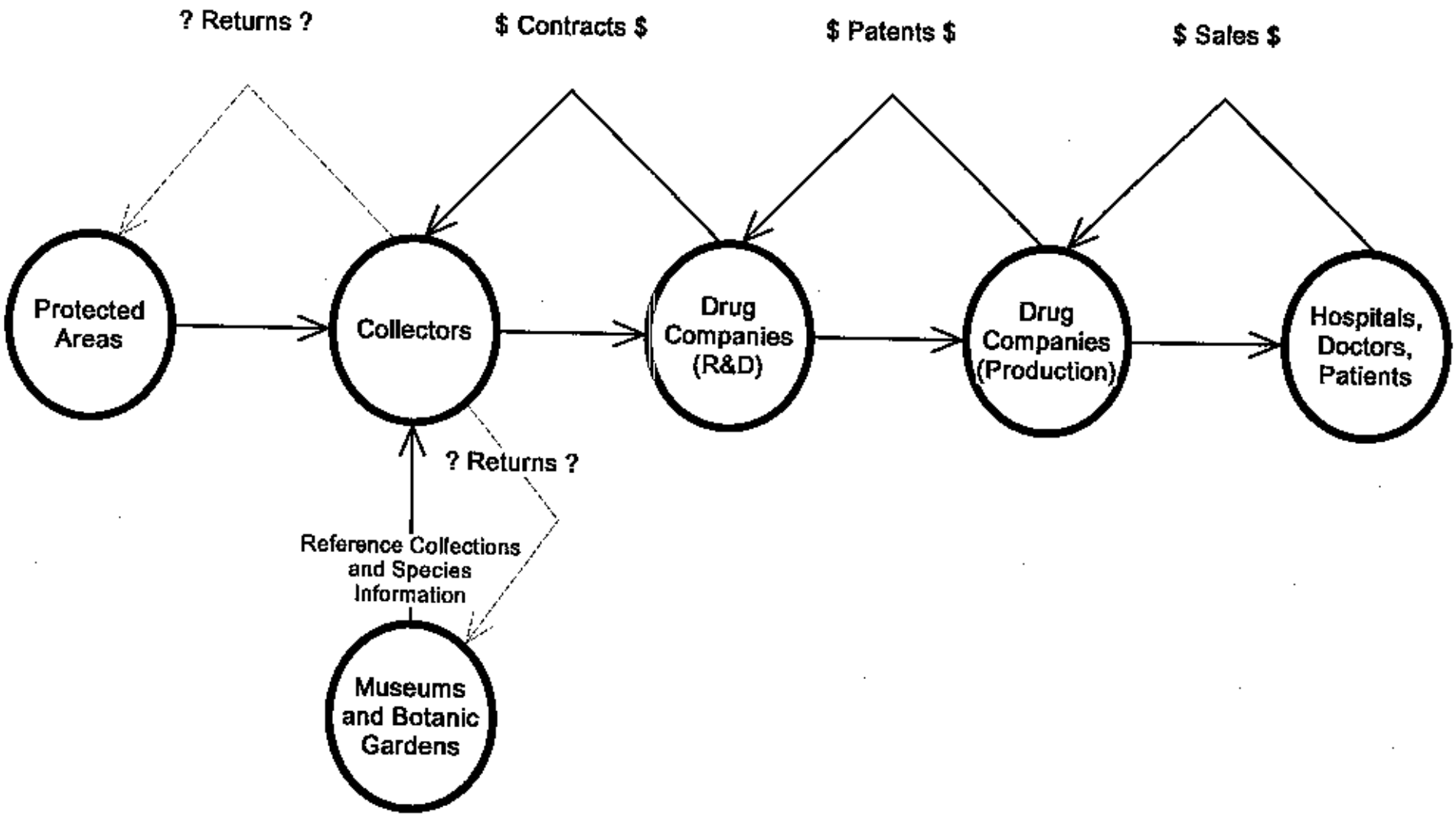
Before investing in the pharmaceutical value added process, a country (or external investor) must determine whether there is a potential economic return to be made from allocating resources to this process. It is not at all obvious that the returns from capturing the full pharmaceutical value of biodiversity is worth the costs of this enterprise for all countries. If a country can demonstrate a comparative advantage in value-added activities above and beyond biodiversity protection, they may be able to capture an increased share of the value generated by the production of species information in pharmaceutical prospecting.[22]

As cited earlier, Eisner (1990) maintains that the extraction and initial screening steps of the R&D process are technique-oriented and relatively labor-intensive. These activities could, therefore, be transferred to developing countries. Carrying out primary screening in biodiversity-rich countries offers certain advantages in addition to a lower cost labour force. A nearby source of supply lowers transport costs, as well as transaction costs involved in exporting and importing material across borders. These costs would only be incurred for those materials showing promise in initial or secondary screens. The movement of additional pre-clinical activities would clearly depend on the availability of capital and skilled human resources. Opportunities to move further downstream are limited. Regulatory agencies in OECD countries are very reluctant to accept clinical data from other OECD countries much less from developing countries.

However, discussion of transferring the initial stages of pharmaceutical R&D to biodiversity-rich developing countries may be premature, if the countries lack the necessary taxonomic expertise to supply biotic samples for screening programs. In presenting an analytic model

[22]*See* Aylward *et al.* (1993b) for an analysis of Costa Rica's National Biodiversity Institute, an institution that is succeeding in this endeavor.

Figure 7 Market Failure and Incentives Issues in Pharmaceutical Prospecting



that demonstrates that biodiversity protection and information generation are likely to be complementary activities, Aylward and Barbier (1992) implicitly assume that taxonomic expertise is available. Whether this is expertise held by the country or provided by outside institutions is not an efficiency question but a distribution question - to what extent is the value of this activity likely to be captured by the country as versus foreign nationals. However, if the expertise is not available to collect and identify biodiversity the whole process of pharmaceutical prospecting will come to a grinding halt. Thus, it is recommended that countries accurately assess their internal capabilities and access to external resources in the area of taxonomic expertise before proceeding further upstream.

In sum, the development of effective property rights, vertical integration or contractual arrangements are all potential mechanisms by which a developing country can capture the returns to biodiversity - and quite possibly taxonomic information as well. A user fee approach based on the assertion of exclusivity over biodiversity must be dealt with carefully due to the potential impact of substitution away from the use of a country's resources in prospecting activities. A less confrontational approach based on informed, contractual negotiation between parties - such as in the case of the INBio-Merck & Co. arrangement - may be more likely to extract larger payments for samples (Aylward *et al.* 1993b). Meanwhile, vertical integration across all activities in the pharmaceutical prospecting process appears unlikely. Nevertheless, vertical integration of a series of related activities may be an effective means of linking particular activities together - thereby reducing the need to establish a large number of contractual arrangements between different parties in the prospecting chain.

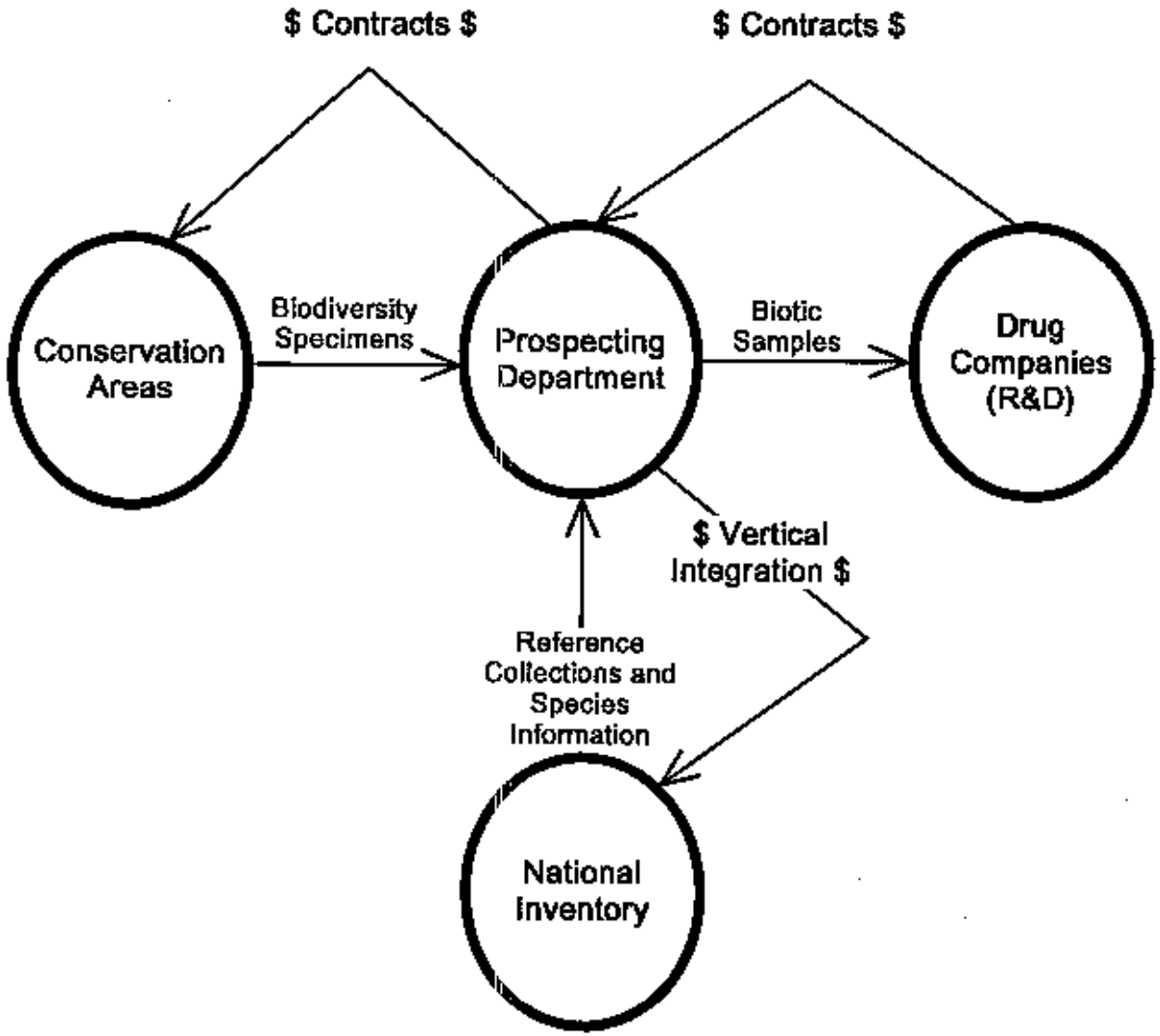
Distributional Implications of Institutional Approaches to Capturing the Value of Pharmaceutical Prospecting

Figure 7 summarizes the incentives problems discussed above. Quite simply, the ability of pharmaceutical companies to appropriate the returns from R&D and the ability of collectors of biotic samples to negotiate a share in these returns does not guarantee that investors in biodiversity protection and the generation of taxonomic information will be able to capture a share of these returns. As discussed above a variety of methods for capturing the value of biodiversity and species information exist. Whether such methods are actually employed is determined in large part by the type of institution or individual engaged in the production of biotic samples. Anecdotal evidence suggests that in the absence of firm regulation or access control individual collectors are unlikely to make a contribution to biodiversity protection or the larger body of taxonomic information. This is not necessarily the case with institutions that regularly engage in commercial collecting. Below a comparison is offered of the distribution of returns generated by three different types of such institutions:

- developing country research institutions - e.g. Costa Rica's National Biodiversity Institute[23]

[23]*See* Aylward *et al.* (1993b) and Sittenfeld and Gámex (1993) for more on INBio's pharmaceutical prospecting activities.

Figure 8 The INBio Solution to Market Failure and Incentives Issues



- purely commercial firms - e.g. Biotics, Ltd[24]
- Northern repositories of taxonomic expertise - e.g. the major botanic gardens[25]

The INBio solution to the problem of capturing the value of pharmaceutical prospecting is illustrated in Figure 8. As with other suppliers of biotic samples, INBio negotiates both an initial payment and a royalty arrangement on successful products resulting from collaboration with industry. A legal agreement with the government establishes a direct conduit whereby a portion of the initial payment (typically 10 percent) and any royalties (a 50-50 split) will return to fund biodiversity protection. As INBio conducts both the biotic samples collection activity and the development of taxonomic knowledge, the vertical integration of these two activities assures that the investment in taxonomic information is rewarded and sustained. The INBio example, therefore, is based on contractual arrangements regarding the supply of the raw material input and the vertical integration of information generating activities. Figure 9 indicates how this principle works in practice, by outlining the flows developed under the INBio-Merck & Co. agreement.

INBio's arrangement to split royalties with the national parks is novel in that it establish a contractual arrangement mandating the return of a set portion of royalties directly to the entity that funds biodiversity protection. Yet the royalty provision itself is not unique to INBio. Laird (1993) indicates that a host of institutions (collectors, brokers and companies) have either negotiated royalties arrangements, or have agreed to "letters of intent" ensuring that royalties will be negotiated upon derivation of a successful product. The royalties are expected to be shared equally between the broker and the collecting institution in the case of the Royal Botanic Garden, Kew; New York Botanical Gardens; and Biotics. On the other hand, the Missouri Botanical Garden and the University of Illinois suggest that the actual developing country collector negotiate royalties directly with companies. The National Cancer Institute's letter of intent provides for negotiation of royalties to benefit the in-country collector, but has no similar provision for rewarding intermediaries such as the Northern botanic gardens that manage the collection process.

Most of these contractual agreements do not dictate that royalties or a portion thereof must directly support biodiversity protection. Instead, the use of royalty payments is often left to the discretion of the collector or collecting organization. An alternative is for brokers to incorporate "third party" mechanisms in their contracts with collectors whereby returns from successful products can be reinvested in biodiversity protection and the development of biodiversity information. Biotics, Ltd insists that a portion of any eventual royalties received by its collecting partners be contributed to general development or, preferably biodiversity related projects in the country. This results in a 50-25-25 split of royalties between Biotics, the collector and biodiversity protection. Despite recent progress in improving awareness regarding contractual issues, INBio remains the sole example of an organization actually signing a contractual agreement providing for the return of royalties directly to an organization that is responsible for biodiversity protection.

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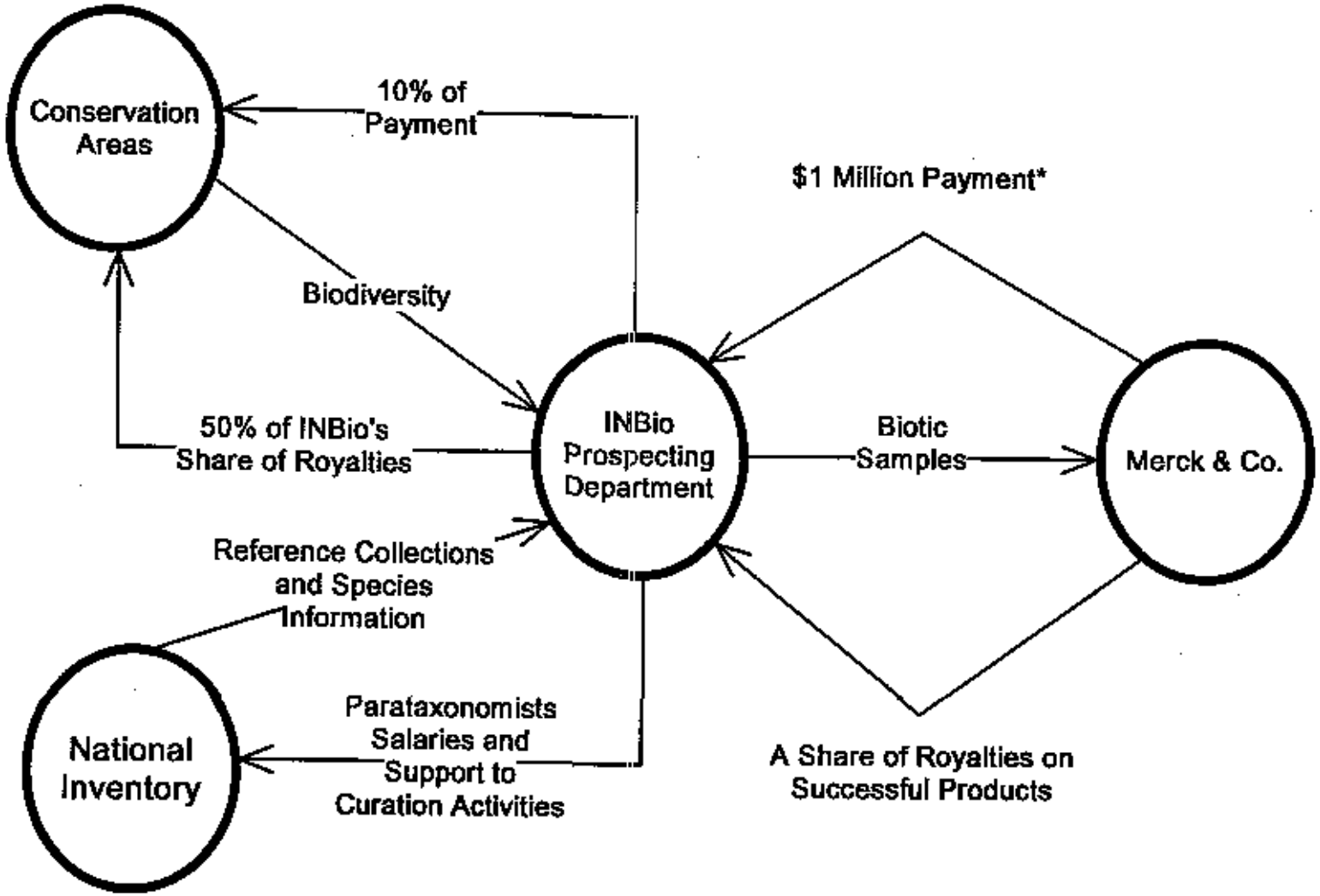
[24]An overview of activities undertaken by Biotics, Ltd. is provided in Appendix C.

[25]*See* Laird (1993) for more on the prospecting activities of the major botanical gardens.

Figure 9 The INBio - Merck Contract



*plus funding for establishing extraction facilities

In most cases, a fee is paid to the collector upon receipt of samples. Laird (1993) reports that most developing country collaborators receive more than simply a collecting fee from botanic gardens. Spin-off benefits of this form of scientific collaboration primarily include research and infrastructure assistance. This relationship is duplicated in the case of the INBio-Merck & Co. agreement. The difference is that INBio and Costa Rica receive not only direct support for taxonomic activities, but training and technical assistance in the initial stages of pharmaceutical R&D from Merck itself. In the case of Biotics, there is little in the way of spin-off benefits. As a commercial concern, there is little margin for funding scientific collaboration. However, Biotics' recent proposal to develop a network of fully independent extraction facilities in developing countries would support the transfer of useful technology to the South.

At the present time, all royalty agreements and distribution mechanisms remain untested. Which arrangements will prove effective in contributing to the conservation of biodiversity - defined widely as not only biodiversity protection but the development of biodiversity information - remains to be seen.

Other configurations are, of course, possible. For instance, a country's parks personnel might be directly involved in collection and identification of biotic samples. In this case, only one contractual arrangement - between the relevant ministry and the pharmaceutical company would be necessary. Vertical integration of the protection and collection functions would obviate the need for additional contracts. However, to the extent that biodiversity remained more or less an open access resource, uncompensated leakage of biotic samples from the country might continue. Development of an effective mechanism for controlling access to the country's wildlands might be required in such a case. Clearly, there are a range of solutions available and the choice of mechanisms will be determined by country-specific conditions.

There may also be synergies between efforts made at different stages in the pharmaceutical prospecting process. The ability on the part of a developing country to control access to its biodiversity might also serve to limit any problem posed by the *non-rivalness* of species information generated during collection and identification. Collectors that can guarantee companies exclusive access to particular species may be in a much better contractual negotiating position. It may also be the case - as with Costa Rica and INBio - that by investing in the generation of species information and striking contracts with pharmaceutical companies, a developing country may be able to develop a competitive advantage in biotic samples and capture the value attributable to its biodiversity without the need to engage in developing potentially costly mechanisms of exclusion.

To sum up, this section has suggested that patent protection on pharmaceutical products at least partially solves the difficult question of how to provide the pharmaceutical industry with incentives for investing in the generation of novel species biochemical information. Nevertheless, the unusual difficulties faced by prospecting activities may warrant further exploration of the potential for increasing the length of market exclusivity or other incentives measures.

Commercial collectors supplying biotic samples to industry operate in a competitive market environment and are also capable of capturing the value of their investment in species

information and the physical collection and processing of samples. However, the hidden subsidy provided by local and foreign taxonomic institutions does indicate a potential source of market failure. Largely funded by the public purse in the past, growing scarcity of funds for taxonomic research may imply the need for these institutions to initiate systems of fees for services rendered to commercial collectors.

Finally, biodiversity's nature as a *free good* implies that the large social costs of protecting biodiversity go unrewarded. A number of potential solutions to internalize these costs include the negotiation of contractual arrangements, the development of access restrictions and vertical integration of activities. Despite recent progress, examination of existing contractual solutions to this problem indicate that it remains a rare event for profits from pharmaceutical prospecting to be returned to protected area systems.

5. MODELS FOR VALUING PHARMACEUTICAL PROSPECTING

In Section 2 pharmaceutical prospecting is defined as a process that incorporates not only pharmaceutical R&D, but the development of species information and biodiversity protection. The literature review in Section 3 explored the limitations of previous efforts to estimate the pharmaceutical value of biodiversity. In Section 4 market failures that lead to suboptimal incentives to invest in biodiversity protection and species information (in the production of biotic samples and pharmaceutical R&D) are identified. In this section, two valuation models for estimating the net economic returns from investment in the protection of biodiversity and the generation of species information are developed. The models build on the analysis of the private and social costs of prospecting and the distribution of benefits presented in the preceding section. The data and results of the models are presented in Section 6.

Following a discussion of the markets and valuation techniques that may prove useful in valuing pharmaceutical prospecting, the two models for calculating the net returns to biodiversity and biotic samples are developed.

Markets and Techniques for Valuing Pharmaceutical Prospecting

As indicated in Section 4 there are at least four "markets" in the prospecting process that are useful vantage points in an examination of the incentives problems created by market failure. These markets also have potential for providing information about the value of the different inputs involved in prospecting. The four markets are:

- the implicit market for biodiversity specimens - the "raw material" for pharmaceutical prospecting
- the market for biotic samples - processed specimens plus species information
- the implicit market for pharmaceutical R&D
- the market for drugs

The term "implicit" is used to describe outputs that are rarely exchanged in formal markets. For each of these "markets" a number of techniques are available for valuing marketed and non-marketed outputs. These include price-based, surrogate market, constructed market or cost-based valuation techniques.[26]

In the case of biodiversity specimens there is no explicit market, no exchange between buyers and sellers. Nevertheless, as argued in Section 4, there is an implicit market for specimens that reflects both demand by prospectors and the social costs of biodiversity protection and specimen collection. In theory, a measure of the economic value of biodiversity in pharmaceutical prospecting could be derived using non-market valuation techniques, such as the contingent valuation method or the travel cost method.

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[26]*See* Barbier *et al.* (1992) for a discussion of these valuation techniques.

The existence of a strong strategic bias on the part of commercial collectors to understate their willingness to pay for collecting rights and the lack of information on the part of collectors as to the value of their own activities limit the potential for using the contingent valuation method. The travel cost method avoids these difficulties by relying on actual behavior revealed in related markets. However, the cost of meeting the data requirements of this method might prove difficult given the wide range of collectors and countries involved in this "market."

Unlike the case of biodiversity specimens, there is an active market in biotic samples. Laird (1993) states that commercial collectors receive from $50-$200 per kg per sample. Information gathered for this paper suggests that collectors receive from as low as $25 up through $200 for dried tropical plant samples - depending on whether the product is purchased from the actual collector in a developing country or obtained through a developed country intermediary such as a botanic garden. These payments for biotic samples do not appear to be linked in any way to the final value of the sample - i.e. as a promising candidate in the search for new drugs. Instead, these payments are designed to provide collectors with a sufficient incentive to engage in collection activities. In other words, these fees must provide a reasonable rate of return on the private costs of collection.

As described in Section 4, the evolution of contractual arrangements between buyers and sellers of biotic samples is increasingly resulting in the inclusion of royalty provisions in supply contracts. In these cases, suppliers obtain not only initial payments for samples, but a claim on the proceeds of successful products. Thus, the market value of the biodiversity and species information inputs that together form a biotic sample will depend on two factors:

- the value of initial payments made to obtain biotic samples for screening programs
- any eventual royalty payments on successful products

In this section, a model for valuing biotic samples is developed based on the use of royalties as an indicator of revealed preference for biotic samples. The model specifies the variables that are likely to determine the expected mean present value of royalty payments on biotic samples. The results from this model are then combined with estimates of the initial payments for samples and the costs of their production to indicate the expected net returns to biotic samples. This exercise improves on previous efforts (reviewed in Section 3) at valuing royalty arrangements by Harvard Business School (1992), Pearce and Puroshothaman (1992) and Reid *et al.* (1993).

As described in Section 3, Ruitenbeek (1989) pursued the intuition that a direct route to valuation of biodiversity benefits is to focus on the market for pharmaceutical R&D - the end product of pharmaceutical prospecting. A direct focus on the value of a research discovery would provide a concise estimate of the value of the prospecting process, eliminating the need to consider the value generated through the actual use of new pharmaceuticals. Unfortunately, the absence of a significant market for final outputs of pharmaceutical R&D - i.e. those making it past the regulatory approval stage - means that such an analysis must rely on surrogate markets. For example, the hedonic pricing technique might be utilized to examine the relationship between changes in equity values and confirmed research

discoveries. The theoretical difficulties of specifying other factors that affect share prices may, however, serve to limit the usefulness of such an approach.

The market for pharmaceuticals also provides information about both the prospecting and production components of pharmaceutical value.[27] A novel drug developed through the prospecting process is, after all, only an intermediate product along the way to the final mass-produced pharmaceutical. The economic value of biodiversity and species information is, therefore, linked to the benefits derived from the final medicinal product. This is the intuition which underpins the valuation exercises conducted by Farnsworth and Soejarto (1985), Principe (1989b), McAllister (1991) and Pearce and Puroshothaman (1992). As described in Section 3, these studies employ information on the market for pharmaceuticals to ascribe value to *in situ*, untested species.

Unfortunately, these analyses fail to generate reliable and useful estimates for a number of reasons. First, they fail to distinguish between the returns to prospecting and production activities. Second, they suffer from a number of methodological problems such as confusing the volume of trade with the value of trade. Third, the practical significance of these studies for policy or project decision-making purposes is reduced by the lack of information on the investment costs that are required to generate the benefits quoted. The studies produce estimates of total value, but do not investigate the net return on investment. Finally, little attention is given to the process of adding value to biodiversity by developing information about species. This difficulty arises in part because the gross value estimates are attributed solely to biodiversity instead of being spread across all prospecting activities.

In addition to the model based on royalties, a second valuation model is derived in this paper. The second model estimates the expected value of the net returns on investment in prospecting that is necessary to develop a single marketable drug with an average sales profile. These net returns are then allocated across the different inputs in the prospecting process based on the costs of pharmaceutical prospecting. Both a private and social cost version of the model is developed.

The model for estimating the net returns to prospecting based on the market for pharmaceuticals is developed first. Then, the royalty model based on the market for biotic samples is presented. At the outset, it is worth stressing that the general principles underlying these models should apply to the range of strategies that are employed in developing marketable compounds from natural products - e.g. ecological, ethnobotanical, random, etc. However, as the majority of current natural products screening programs are pursuing random screening strategies, the models and calculations that follow most closely conform to the requirements of a random approach to pharmaceutical prospecting.

The Net Economic Benefits of Pharmaceuticals and Pharmaceutical Prospecting

The end product of the pharmaceutical prospecting process is a new and marketable drug. Pharmaceutical companies then engage in production and marketing activities that deliver the

[27]In a sense the market for pharmaceuticals is a surrogate market for pharmaceutical R&D.

final pharmaceutical product to the marketplace. Pharmaceutical prospecting is simply an intermediary input in the process of generating the final product - the pill or tablet purchased by doctors, hospitals, patients, etc. For pharmaceuticals derived from natural products there are, then, two principal activities involved in generating the total economic value realized through the final consumption of pharmaceutical products:

- production and marketing of the drug (P&M)
- pharmaceutical prospecting (PP)

As stated earlier pharmaceutical prospecting itself can be construed as consisting of three principal activities

- research and development (R&D)
- production of biotic samples (BS)
- protection of biodiversity (BP)

As a result, society's willingness to pay for the final pharmaceutical product is related - but not identical - to the total economic value of prospecting activities. The total economic value of pharmaceutical prospecting will depend on the value of its marginal product relative to that of production and marketing activities.

However, the economic appraisal of investments is based not on total economic value, but rather a measure of the expected *net* economic value generated by the investment. Society's expected willingness to pay for the average drug, WTP, less the expected economic costs of all activities (R&D and P&M) necessary to deliver the drug to market, C, equals the expected net economic benefits generated by the new pharmaceutical:[28]

$$NEB = WTP - C \qquad (1)$$

Empirical estimation of this relationship is hampered by difficulties in obtaining comprehensive measures of both WTP and C. Torrance (1986) suggests that there are four types of benefits generated by new methods - such as new pharmaceuticals - of improving health. The ingredients of WTP are:

- direct benefits - reduced health care costs
- indirect (spin-off) benefits - improved earnings
- intangible benefits - alleviation of pain, grief and suffering
- the individual's willingness to pay for health improvement (net of any effect on earnings and health care expenditures)

The difficulty of estimating an expected average value of all four of these economic benefits for the average new pharmaceutical is considerable. In particular, Torrance (1986) suggests that the intangible benefits and the willingness to pay for health improvement are difficult to estimate.

[28]For simplicity sake, all variables in this sub-section are considered to be in present value terms.

Efforts to value pharmaceutical prospecting based on an examination of the market for drugs must, therefore, rely on estimates of expected market values for pharmaceuticals. Estimates based on market prices and volumes will tend to understate the level of economic benefits derived from a new pharmaceutical for a number of reasons. Market prices may not capture the full extent of individual's willingness to pay for health improvements (net of direct and indirect benefits). In addition, market prices may not fully reflect the direct, spin-off and intangible benefits generated by an improved course of treatment. However, the use of market prices does indicate the net returns gained by producers at the margin. It thereby provides important information on the economic incentives faced by firms and other producers faced with investment decisions.

Finally, the existence of the market and policy failures discussed in Section 4 indicates that the full social costs of pharmaceutical prospecting, C, are not necessarily taken into account by private actors in the investment decision-making process. Thus, a further difficulty in estimating the net social returns of new pharmaceuticals is determining the actual level of social investment required. Building on Section 4, the cost-based model of net returns presented below includes the full social costs of biodiversity protection and species information in order to obtain an indication of the net social returns to the three stages in the prospecting process.

The Net Returns to Pharmaceutical Prospecting

The first step in generating estimates of the net returns to individual stages of the pharmaceutical prospecting process is the development of a methodology for distinguishing the net returns to prospecting activities from information on the market value of the final pharmaceutical product. After establishing the level of gross returns to the pharmaceutical product itself, these returns can be allocated across investments in production and prospecting activities. The costs of prospecting can then be subtracted to yield net prospecting returns.

The present value of the gross revenues generated by sale of a new drug can be defined as:

$$GR = \sum_{t=0}^{t=n} S_t * e^{-rt} \qquad (2)$$

with $$S_t = S_0 * e^{\alpha t} \qquad (3)$$

where: S_t = the expected real value of sales of the drug in year t
n = the number of years in which the drug earns profits
r = the discount rate
α = the annual real rate of growth of the price of drugs

An important issue in determining the returns to pharmaceutical R&D (and therefore pharmaceutical prospecting) is determining the relevant time period in which to evaluate sales. Pharmaceutical companies operating in most OECD countries are guaranteed a limited period of monopoly on drugs they patent and develop. Monopoly profits that are derived

from patent rights are designed to enable companies to recoup product R&D costs. Thus, at first glance it would be fair to suggest that the relevant time period for evaluating rents attributable to R&D - the net returns to the intellectual property - should include only sales made prior to patent expiration. After all, once the monopoly has expired, theory would suggest that competition from other producers of the same drug would drive excess profits - above and beyond a reasonable margin on production and marketing activities - to zero.

A look at actual conditions in the marketplace, however, leads to the conclusion that monopoly profits do not fall to zero immediately. Competition to drugs going off patent comes from generic products. Generic products are generally produced by low-margin competitors that use patent information to manufacture the original chemical product and market it under a different name than the original patent drug (the name of which is typically registered as a trademark by the inventing company). In recent years generic competition has become increasingly vigorous, yet it still takes quite a few years for generic products to significantly erode the market share - and hence profits - of products going off-patent.

In the face of generic competition pharmaceutical companies generally maintain the price of their established trademark product. The gradual erosion of monopoly profits in the off-patent period is left to occur through the loss of market share.[29] Thus, it is possible to stipulate that monopoly profits attributable to the output of pharmaceutical R&D do not go to zero upon patent expiration, rather that they decrease gradually over time.

In addition to the distinction between the on- and off-patent periods, there is a further bifurcation of the on-patent period. Due to the length of time that it takes to complete prospecting activities and gain regulatory approval for the clinical use of a new drug, it is possible to split the patent period into pre- and post-regulatory approval periods. Thus, sales of most pharmaceuticals do not actually begin to gather steam until regulatory approval - a point well into the patent period.

Finally, in the case of R&D into natural products there is also bound to be a pre-patent period. Patenting cannot take place - at a minimum - until the initial steps from collection through to isolation of the active compound are completed. As this pre-patent period is part of the prospecting process it must be included in an economic analysis of prospecting returns.

As a result the representation of the sales profile presented in Equation (2) can be expanded to include four distinct periods: the pre-patent period, the on-patent period up to regulatory approval, the on-patent period from approval to patent expiration and the post-patent period.

[29]Merck & Co. has recently pioneered a new strategy - that of marketing the same drug at the same time under both the established trademark and as a generic product.

The expanded representation of the gross revenues first presented in (2) is:[30]

$$GR = \sum_{t=0}^{t=PT} S_t * e^{-rt} + \sum_{t=PT}^{t=RA} S_t * e^{-rt} + \sum_{t=RA}^{t=PE} S_t * e^{-rt} + \sum_{t=PE}^{t=N} S_t * e^{-rt} \quad (4)$$

where: PT = number of years until the natural product compound is patented
RA = number of years until the drug receives regulatory approval or length of the prospecting period
PE = number of years to patent expiration[31]

In order to reflect the decay of monopoly profits after patent expiration the year-on-year reduction (percentage change) in market share due to generic competition, μ, can be incorporated into the estimation of post-patent period revenues:

$$\sum_{t=PE}^{t=n} S_t = \sum_{t=PE}^{t=n} S_{PE} * e^{\mu(PE-t)} \quad \text{such that } 0 \leq \mu \leq 1 \quad (5)$$

For ease of notation, further references to the gross revenue of the final pharmaceutical product refer back to (2).

In order to arrive at the gross returns generated by prospecting activities, GR^{PP}, Equation (2) must be adjusted by subtracting the costs of drug production and marketing, $C^{P\&M}$, from sales in each year. In addition, normal net returns on P&M activities, $NR^{P\&M}$, must also be extracted from sales:

$$GR^{PP} = GR - \sum_{t=0}^{t=n} (NR_t^{P\&M} + C_t^{P\&M})e^{-rt} \quad (6)$$

Due to the difficulty of obtaining data on the costs of production and marketing that corresponds to the year-on-year sales profile, industry averages for P&M costs as a percentage of sales are employed as an approximation of the costs of P&M. As prices of off-patent drugs are kept at their monopoly price this assumption bears equally for the on- and off-patent period.

If patent protection did not exist, the production and marketing of drugs would be expected to be in a competitive equilibrium equivalent to that in a "mature" generic situation. All products would be priced at a competitive price for generic products - reflecting only the

[30]In the actual estimation of the model presented in the next section, the first two components of the sales profile in Equation (4) sum to zero as it is assumed that sales are minimal prior to regulatory approval.

[31]Note that as patenting does not occur until time PT, PE is not the same as patent life, rather it represents the sum of PT and patent life.

costs of drug production and marketing on the supply side - and earn a rate of return attributable only to these activities. The net returns attributable to the production and marketing stage are, therefore, likely to reflect normal returns (average margins) on generic products across the industry.

Thus, in order to estimate the gross returns generated by prospecting activities, (6) is respecified as follows:

$$GR^{PP} = GR\,(1 - (\beta\,(1 + \pi\,))) \qquad (7)$$

where: β = Drug P&M costs as a percent of gross sales
π = Normal rate of return on drug P&M

In order to obtain the net returns to pharmaceutical prospecting, NR^{PP}, the present value of average prospecting costs required to produce a single marketable drug, C^{PP}, must be subtracted from the gross returns to intellectual property:

$$NR^{PP} = GR^{PP} - C^{PP} \qquad (8)$$

Equation (8) completes the process of deriving expected net returns, or economic rent, attributable to pharmaceutical prospecting from the market for pharmaceutical products. In the next sub-section, two scenarios for estimating the costs of pharmaceutical prospecting are explored.

Allocation of Net Returns From Prospecting: Private and Social Cost Models

The second step in generating estimates of the net returns to the three stages in the prospecting process is the development of a practical methodology for allocating rents across pharmaceutical R&D, the production of biotic samples and biodiversity protection.

Theory suggests that, at the margin, each of these "factors of production" deserves an economic return proportional to the value of its marginal product. A production function approach to valuation would employ information on inputs and outputs in order to estimate the value marginal product of each stage, thereby indicating the relative contributions and returns made by each stage. For instance, each stage in the process uses some combination of available factor inputs - i.e. labor and capital (whether human, natural, technological or physical capital). In order to estimate a production function a series of observations of these inputs - and the relevant outputs - would be necessary. Given the difficulty of obtaining such data from proprietary industry sources a comprehensive effort to undertake such an analysis is beyond the scope of this paper.

A qualitative assessment of the case for allocating a share of net prospecting returns to each of the three stages (inputs) is an alternative to a quantitative analysis. Rents (in excess of normal returns) typically accrue to factors of production that are scarce relative to other factors and for which the quantity of demand is relatively unresponsive to changes in price - i.e. for which demand is inelastic.

Unfortunately, even a qualitative assessment is fraught with uncertainty. On the supply side, it is difficult to judge whether the supply of pharmaceutical R&D is relatively more scarce than that of biodiversity protection or taxonomic expertise. On the demand side, as indicated in Section 4, pharmaceutical companies are capable of switching from one geographic source of biodiversity to another and are typically investing heavily in the exploration of synthetic compounds - another substitute to biodiversity. This may indicate that demand for biodiversity and biotic samples is fairly responsive to changes in price - i.e. demand is elastic. How this compares with the elasticity of demand for pharmaceutical R&D is an open question. Demand for pharmaceutical products is typically considered to be inelastic. It is, therefore, possible to assume that demand for new products would be similarly inelastic. However, continued improvements in other areas of health care such as surgical techniques, prevention treatments and future applications of gene therapy, may mean that demand for compound based pharmaceuticals is not as inelastic as was previously thought.

Given the myriad difficulties involved in making even a qualitative case for a particular apportioning of rents across the three prospecting stages, a further simplifying assumption regarding the distribution of net returns is necessary in order to take the analysis forward. In the absence of evidence that one component of prospecting is more valuable than another, the assumption is made that the value of the marginal productivity of each activity is in proportion to its costs. That is, other things being equal - proportional increases in expenditures in each activity area would lead to proportional increases in the number and value of new drugs developed. By implication each prospecting activity should receive economic returns proportional to its share of total inputs - measured as the share of total costs.

Two models based on this hypothesis are developed below. The first model examines the allocation of net prospecting returns, assuming that only the explicit private costs of prospecting earn a share of the available rent. The second model incorporates the social costs of biodiversity protection and taxonomic information into a social cost scenario. Gross prospecting revenues are apportioned across investments in pharmaceutical R&D, biodiversity protection and the development of biotic samples.

A number of additional assumptions underpin the models that follow. These assumptions reflect the necessity of drawing on general parameters for pharmaceutical R&D as a whole. This is due to the lack of empirical studies demonstrating the similarity, or lack thereof, between R&D based on natural products and that based on synthetic chemicals. The models assume that the private financial costs of R&D do not differ between the development of natural product-based and synthetic drugs. The assumption is also made that the likelihood of generating a marketable compound from a single species is similar to the chances of doing so with synthetically derived compounds.

Private Costs Model. In this model the private costs of R&D, $PC^{R\&D}$, and the private costs of collection of biotic samples, PC^{BS}, make up the private costs of pharmaceutical prospecting:

$$PC^{PP} = PC^{R\&D} + PC^{BS} \qquad (9)$$

Equation (8) - which specifies the relationship between gross and net returns to pharmaceutical prospecting - is, therefore, reformulated to reflect net private returns:

$$NPR^{PP} = GR^{PP} - PC^{PP} \quad (10)$$

As it is assumed that these returns can be allocated to inputs on the basis of percentage share in total costs, the net private returns attributable to pharmaceutical R&D, $NPR^{R\&D}$, and the collection of biotic samples, NPR^{BS}, can be expressed as:

$$NPR^{R\&D} = (PC^{R\&D} / PC^{PP})NPR^{PP} \quad (11)$$

$$NPR^{BS} = (PC^{BS} / PC^{PP})NPR^{PP} \quad (12)$$

Social Costs Model. The private cost model of pharmaceutical prospecting omits the social costs incurred in the protection of biodiversity, SC^{BP}, and any social costs of developing taxonomic information, SC^{TI}. Thus a specification of the total social costs of pharmaceutical prospecting, SC^{PP}, should also include these costs:[32]

$$SC^{PP} = SC^{BP} + SC^{BS} + SC^{R\&D} \quad (13)$$

with: $$SC^{BS} = PC^{BS} + SC^{TI} \quad (14)$$

Equation (8) can then be modified to indicate the net social returns to pharmaceutical prospecting:

$$NSR^{PP} = GR^{PP} - SC^{PP} \quad (15)$$

The net social returns to pharmaceutical R&D, $NSR^{R\&D}$, the production of biotic samples, NSR^{BS}, and biodiversity protection, NSR^{BP}, can now be expressed as:

$$NSR^{R\&D} = (SC^{R\&D} / SC^{PP})NSR^{PP} \quad (16)$$

$$NSR^{BS} = (SC^{BS} / SC^{PP})NSR^{PP} \quad (17)$$

$$NSR^{BP} = (SC^{BP} / SC^{PP})NSR^{PP} \quad (18)$$

A comparison of equations (13)-(14) with (16)-(18) reveals that the internalization of these additional social costs into the equation will clearly reduce the net returns that are - at least in theory - attributable to pharmaceutical companies undertaking R&D and to collectors of biotic samples.

Having established the net returns to the different activities involved in pharmaceutical prospecting, it is possible to specify the expected net returns per species or per biotic sample. As the methodology is quite similar in the case of both private and social returns, the

[32]For the purposes of this model it is assumed that the private and social costs of pharmaceutical R&D do not differ.

explanation is presented only in the case of net social returns per species and per biotic sample.

The net returns per species reflect the share of the rent earned by investment in biodiversity protection that is attributable to those species evaluated in the production of the drug. The net returns must be equally divided across all species entering the screening process as there is little a priori information about the relative chances of success of a particular species in a random screening program. Equation (18) must, therefore, be adjusted by the expected success or hit rate of a given species, P(i), from collection through to regulatory approval and marketing. The hit rate reflects the expected number of species that a given company or research institute will need to test against their screening program in order to turn up a single marketable compound.[33] Thus, the net returns attributable to biodiversity protection of a given species, i, is:

$$NSR_i^{BP} = P(i) * NSR^{BP} \quad (19)$$

where $P(i)$ = the chances of a given species, i, becoming a marketable compound based on exposure to a single screening program - e.g. 1 in 10,000

In the case of attributing net returns per biotic sample it must also be kept in mind that a number of samples from a single species may enter the screening program. As the probability of success is calculated in terms of species - i.e. successes per species - an additional adjustment must account for the number of samples per species that are screened, η. Thus, the net social returns per biotic sample, k, is:[34]

$$NSR_k^{BS} = P(i) * NSR^{BS} / \eta \quad (20)$$

Finally, the importance of viewing biodiversity as a renewable resource in its use in pharmaceutical prospecting must be reiterated. The net social returns attributed to biodiversity in Equation (19) are assumed to pertain only to the use of a species (or sample) in a particular screening program. The species may well be tested in the screening programs of other private or public research organizations. It is possible to extend (19) to reflect this dimension as well.[35] Thus, the total prospecting rent, NSR_i, that can be generated by a particular species will depend on the number of screening programs, ρ:

$$NSR_i^{BP} = \rho * P(i) * NSR^{BP} \quad (21)$$

As discussed in the next section, the current level of prospecting activity implies that the opportunity for even a single screening of most plant species is limited. Thus, (21) is not actually estimated in this paper. Nonetheless, the equation is presented to reinforce the

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[33] Reid *et al.* (1993) suggest that companies often put natural products through their entire screening program which may number up to 30 different screens.

[34] Equations (19) and (20) may be derived in a similar fashion for the private costs model.

[35] Equation (20) may also be adjusted to reflect the number of screening programs in which biotic samples are evaluated.

argument that biodiversity is a renewable resource for the purpose of pharmaceutical prospecting and to indicate how renewability can be introduced into the valuation exercise.

Net Returns from Prospecting Royalties: A Revealed Preference Model

The cost-based models outlined above apportion the net returns to pharmaceutical prospecting in equal proportion to investment costs. Nevertheless, the actual outputs of one stage or another are likely to be more *valuable* than another. Recent contractual arrangements for the exchange of biotic samples call for payment of royalties on successful products developed from the samples. By referring to such market behavior a model for estimating the revealed preference of consumers - in this case for biotic samples - can be developed. The results of this model can then be compared with the results of the cost-based models in order to assess if market behavior - as revealed by the royalty model - indicates that biotic samples are a valuable element of the prospecting process (relative to the even-handed division of returns in the cost-based model).

As royalties are not likely to be paid on sales occurring after patent expiration, the calculation of gross revenues for royalty payment purposes, GR, will consist only of sales through to patent expiration:[36]

$$GR = \sum_{t=0}^{t=PE} S_t * e^{-rt} \qquad (22)$$

Industry sources suggest that product royalties are payable on net sales which typically involves some deductions from gross revenues for distribution costs from the point of production. Distribution costs, δ, are expressed as a percentage of gross sales. Thus, the formula for calculating net sales is:

$$NS = (1 - \delta)GR \qquad (23)$$

Total royalty payments on a successful drug as received by the producer of biotic samples, RY^{BS}, then depend on the expected rate of royalty, λ, and the level of net sales for a drug.

$$RY^{BS} = \lambda * NS \qquad (24)$$

Given expectations regarding the number of samples screened per species, η, and the success rate for species entering the screening process, P(i), the expected gross returns from royalties to each sample, k, is:

$$RY_k^{BS} = P(i) * \lambda * NS / \eta \qquad (25)$$

[36]As indicated earlier the actual estimation of the models assumes no sales in the period prior to regulatory approval.

In order to arrive at a measure of total net returns from the royalty model which can be compared with the results from the cost model it is necessary to include all the relevant costs and benefits of developing a single marketable drug, not just the royalty returns. On the benefit side, the initial fees received by the collector for biotic samples, F, must be incorporated. On the cost side the relevant costs (private or social) include the costs of protecting sufficient biodiversity and generating the required amount of samples to reach a single marketable drug.[37] In deriving the net private returns, NPR^{BS}, the relevant costs are simply the private costs of collecting biotic samples. For comparison of net social returns, the social costs of generating biotic samples and biodiversity protection must be included. Thus the net private and social returns resulting from the royalty model are:[38]

$$NPR^{BS} = RY^{BS} + F - PC^{BS} \tag{26}$$

$$NSR^{BS} = RY^{BS} + F - PC^{BS} - SC^{TI} - SC^{BP} \tag{27}$$

In the next section the cost-based models and royalty models are estimated and compared.

[37]All costs are in present value terms.

[38]Equations (26) and (27) can easily be adapted to indicate per sample net returns by inserting the relevant *per sample* costs and benefits on the right-hand side of the equations.

6. THE VALUE OF PHARMACEUTICAL PROSPECTING

Biodiversity's pharmaceutical potential has long been recognized. However, in the past few years, arguments for the conservation of biodiversity have increasingly emphasized this particular aspect of the sustainable use of biodiversity. Implicitly, such claims suggest that the benefits generated by pharmaceutical prospecting justify "saving" biodiversity. In particular the negotiating process leading up to the signing of the Convention on Biological Diversity appears to have been largely driven by expectations regarding the economic importance of biodiversity in the development of new pharmaceuticals and crop varieties (Jarvis 1993).

The claim that biodiversity's pharmaceutical potential serves as a rationale for conserving biodiversity supports two, related hypotheses, each of which supports a corresponding direction for international policy-making on biodiversity. The first hypothesis is that the rich OECD countries derive enormous social benefits from pharmaceutical prospecting based on tropical biodiversity - prospecting for which tropical countries are not compensated. The second hypothesis is that evolving contractual arrangements and property rights may enable developing countries to capture a substantial share of pharmaceutical revenues which would be capable of funding conservation activities in the South. The first contention leads to the argument that the North should devise mechanisms for transferring resources to the South so that tropical biodiversity may be saved for future prospecting activities - in recognition of its unappropriable "global" value. The second contention, implies that developing countries are in a position to help themselves on this front, albeit perhaps with the assistance of intergovernmental regulation provided by the Biodiversity Convention. In both cases the large values attributed to biodiversity in a number of the valuation studies reviewed in Section 3 have clearly contributed to these arguments gaining credence as the way forward for the preservation of tropical forests and other biodiverse areas.

In this section the cost-based and revealed preference models for valuing biodiversity and species information that were developed in Section 5 are used to explore these hypotheses. In order to do so, the assumption is made that the principal rationale behind efforts to protect biodiversity is to provide material for pharmaceutical screening programs. Additional benefits generated by biodiversity are, therefore, considered to be "spin-off" benefits. While this is very much an over-simplification it provides the means for investigating the importance of potential prospecting returns relative to the expected costs of conservation. In the first instance, the models provide an indication of the expected net returns to prospecting given two assumptions: (1) that enough species are screened in the first year to eventually yield a single profitable drug and (2) that prospectors must bear only the social costs of the biodiversity that is actually screened. A further elaboration of the results from the two models relaxes these assumptions to provide for an estimation of the actual capturable returns to various actors in the prospecting process and a comparison with the distribution of social costs incurred. First, however, the data used in the models are presented.

Data

In estimating the models presented in the previous section an attempt is made to derive reasonable estimates of the parameters involved. Data for the models come from a diverse

range of activities including protected area management, taxonomic classification, collection of biotic samples and the pharmaceutical industry. However, the foundations of both models draw extensively on information from the market for pharmaceutical products. This is fortunate, as economic data on the pharmaceutical industry are more widely available and reliable than data from the other activity areas.

The models are based on the results of a number of economic studies of the pharmaceutical industry, as well as a number of other publications and interviews conducted for this study. In particular, Grabowski and Vernon (1990) and DiMasi *et al.* (1991) provide important baseline data on pharmaceutical sales and R&D costs respectively. In addition, a recent United Nations Industrial Development Organization (UNIDO) study by Ballance, Pogány and Forstner (1992) provides important information and benchmarks on the global pharmaceutical industry. Data on the collection of biotic samples are provided on the basis of interviews with various organizations involved in commercial collecting. Figures on the social costs of developing taxonomic information in developing countries are drawn from Aylward *et al.* (1993b) who report on a rough, preliminary study of these costs at Costa Rica's National Biodiversity Institute. Information on the biotic samples market comes from interviews with various market participants. Finally, data on protected area management are derived from various estimates on the direct and opportunity costs of protection in Costa Rica.

With the time and resources available for data collection - and the lack of established data on a number of the parameters - any claim to precision is impossible. The data employed in the model are divided according to whether they are considered fixed or sensitivity parameters. The sensitivity parameters enable an exploration of the responsiveness of the results to variation in the initial parameters for a number of key variables.

The *discount rate, r,* used in the analysis is 10 percent. Not only does the rate chosen closely reflect the nine percent cost of capital in the pharmaceutical industry identified by Grabowski and Vernon (1990), but it ensures comparability with traditional donor agency estimates of discount rates used in appraisal of developing country investments. Sensitivity analysis of the results is conducted with discount rates of 5 and 15 percent.

A figure of 5 percent is used to reflect the *real price trend of pharmaceuticals, α,* over the past decade. The figure is obtained by adjusting nominal price rises in US pharmaceuticals over the period 1980-91 by the US consumer price index (The Economist 1992a). As pressure to contain health care costs rises, continued real increases in the price of pharmaceuticals are less certain than they have been for the last decade. For instance, Merck & Co. has indicated that it will voluntarily tie any price increases to the consumer price index. Sensitivity analysis is undertaken with a "no growth" scenario for the real price of pharmaceuticals.

According to the UNIDO study, *patent life, PE,* in OECD countries varies between 15 and 20 years (Ballance, Pogány and Forstner 1992). Most countries set their limit at twenty years, however the US provides only seventeen years and in Japan patent life varies from 15-20 years. A midpoint of eighteen is chosen to reflect this variation. Due to the long lead time involved in drug development (see below) pressure is building in the US to raise the

length of patent life. The effect of a twenty year patent life is explored in the sensitivity analysis.

The *decay rate of post-patent sales,* μ, reflects the extent of generic competition. Grabowski and Vernon (1990) suggest a cumulative loss of 60 percent in sales over a five-year period, or roughly a rate of 11 percent per year. However, increasing competition has led to falls in sales of up to 50 percent in sales as products go off patent (The Economist 1992b). The effect of such an increase in decay rates is examined in the sensitivity analysis.

The success rate per species or *species hit rate, P(i),* is a point of some contention, reflecting as it does the risk and uncertainty that surrounds pharmaceutical prospecting. Section 3 revealed that previous studies have used figures ranging from 1 in 125 to 1 in 40,000. In this study, 1 in 10,000 is used as a mid-point. Estimates of 1 in 1,000 and 1 in 100,000 are examined in the sensitivity analysis.

Two cost-based scenarios for apportioning the returns from prospecting activities are explored in this paper. The private cost model is based on the private costs of R&D and the *private costs of producing biotic samples,* PC^{BS}. The private cost of producing a biotic sample is set at $50 per sample based on interviews with collectors involved in commercial collection in developing countries. For the purposes of the analysis of net returns, this is deemed to be the actual cost of production - i.e. before any normal returns on factor inputs. In the sensitivity analysis high and low estimates of $75 and $25 are used. The per sample cost is grossed up - using the hit rate and number of biotic samples per species (see below) - in order to obtain the total costs of the number of biotic samples required to arrive at a single marketable drug.

In the social cost model, the social costs of biodiversity protection and the generation of taxonomic information are included into the analysis. The full social costs of generating two plant samples from the same species will include the private costs of producing two biotic samples and the social costs of developing taxonomic information for one species. The cost of a "new" identification - or the *social costs of taxonomic information,* SC^{TI} - is taken to be roughly $100 (Aylward *et al.* 1993).[39] Consultations with plant taxonomists reveal that in general the costs of an identification will have a wide range. A range of $50-$150 for the costs of taxonomic information is explored in the sensitivity analysis.

As prospecting is assumed to be the motivation for biodiversity protection, the *social costs of biodiversity protection,* SC^{BP}, should reflect the direct, indirect and opportunity costs of preservation. These costs will clearly vary from one protected area to the next and from one country to the next. They will depend on the area protected, the species richness of these areas and the costs incurred. Little empirical work has focussed on the costs of protected areas. As noted above, the numbers used in this analysis are based on rough estimates regarding the costs of protection in Costa Rica. A number of assumptions are necessary to provide these estimates, so further research into this area would assist in improving the

[39] In this context the costs of a "new" identification implies the investment required to collect, curate and positively identify a specimen of a species that is not already held by the local reference collection.

reliability of the figures developed below. Nevertheless, an effort is made to keep the estimates conservative, so as not to grossly overstate the costs of protection.

It is assumed that collecting is carried out in wildland areas that are fully protected. Collecting in such areas provides buyers the best assurance available that future supplies will be available upon demand. In Costa Rica, this definition applies to national parks, biological reserves and national monuments - a total area of 600,000 hectares. The direct costs are represented by expectations regarding the annual operating budget of the park system. Based on a variety of sources, a range of from $5-15 million is used with a midpoint of $10 million.

Measurement of opportunity costs is more complex. Lewin *et al.* (1992) point out that the opportunity costs of park land is reflected by the discounted net returns gained from neighboring agricultural land - $200 per hectare in the case of Guanacaste National Park. Another alternative is to use estimated prices from recent and projected buy-outs of private land to reflect the alternative use value of wildlands. A range of $100-$300 with a midpoint of $200 is used in deriving the annual opportunity costs of protection. Indirect costs are assumed to be minimal in comparison to the direct and opportunity costs of protection.

Assuming that most of the 500,000 species projected to reside in Costa Rica are represented in these areas of full protection, the annual costs of maintaining the protected area system are apportioned across the expected number of Costa Rican species. This yields an *annual per species cost of biodiversity protection* of $50 for use in the model. In the sensitivity analysis a range of from $25-$75 per species is examined.

The royalty payment scenario is modeled using a *royalty rate,* λ, of 2 percent. Industry sources suggest a 1-3 percent range depending on whether the products developed from biodiversity are pure compounds, or are semi-synthetic analogues. Analogues, typically, would receive a smaller share of royalties than a pure natural product drug. The 1-3 percent range is explored in the sensitivity analysis.

The fixed parameters are based on average figures for the pharmaceutical industry. *Annual drug sales,* S_t, during the patent period are derived from Grabowski and Vernon (1990) and adjusted to 1990 dollars using the nominal rate of growth in drug prices. Note that, although a blockbuster drug may earn $1-2 billion per year, market supremacy of such success stories is often limited to a few years as other companies produce "me-too" drugs - patentable drugs that mimic the original blockbuster and capture an important share of the market. In fact, the average drug is unlikely to break $100 million. Even a successful company such as Merck & Co has only ten products currently grossing over this figure (Merck & Co 1992). Grabowski and Vernon (1990) indicate the skewed nature of the distribution of pharmaceutical sales by observing that only 3 of 10 drugs is likely to cover its R&D costs. In order to give some insight into the range of values, two sales profiles - the mean and the top decile, or "big seller" - are explored for each of the valuation models presented in Table 2.

The *length of the R&D period, RA,* is taken from DiMasi *et al.* (1991) and the US Pharmaceutical Manufactures Association (1991a). These sources suggest that of the 12 years required for drug development roughly 4 years is taken up by preclinical development.

In order to derive the effective patent life of new drugs the assumption is made that promising natural compounds are patented 2 years into this process - the *time to patenting, PT*. This leads to an effective patent life of 10 years in the model.

This figure may overstate the brevity of effective patent life for pharmaceuticals. In the US, regulatory approval alone takes 3 years. Similar delays are occasioned in other OECD countries. According to industry sources, loss of patent life due to regulatory delay is often compensated by extending patent life by 3-5 years depending on the extent of the delay. This effect is not explicitly included in the model. However, the sensitivity analysis of the effect of extending the length of patent life to 20 years implicitly models the likely impact of such an extension of patent rights due to regulatory delay.

The *costs of production and marketing (P&M), β,* reflects the percentage of total sales incurred by all non-R&D expenses by pharmaceutical companies (The Economist 1992c; Merck & Co 1992). The *pre-tax rate of return on production and marketing, π,* is assumed to be much lower than the rate of return on pharmaceutical R&D due to the presence of an increasingly active market in generic products. Ballance, Pogány and Forstner (1992) suggest that the gross returns to the production of generic products is in the vicinity of from 5-10 percent. A figure of 10 percent is used in the analysis. According to industry sources, deductions from gross sales are typically made in obtaining the figure for net sales used in deriving royalty payments. This deduction reflects distribution costs - or roughly 5 percent of gross sales.

The *per sample collecting fee, F,* paid to producers of biotic samples is based on the assumption that on top of actual collecting costs of $50 per sample, collectors receive a generous 25 percent return on their investment. While a $63 fee may appear high given actual costs, it must be reiterated that this fee must be sufficient to entice botanical gardens, individual taxonomists or businessmen into this activity.

The final fixed parameter is the *number of biotic samples collected per sample, η*. In the case of plants, most collectors will supply at least two different samples from the same species. These may be leaves, bark, heartwood, twigs, etc. This figure is used in obtaining the actual number of biotic samples necessary to generate a hit. In other words, the costs cited for biotic samples assume that two samples of every species are collected. The hit rate remains based on the number of species, not samples, as there is no empirical evidence available regarding the improvement in hit rates occasioned by the collection of multiple samples.

The initial set of calculations in Table 2 covers sales and net returns to R&D. The gross return on pharmaceutical prospecting of $131 million provides the starting point for calculating the results of the cost-based models. The *private costs of pharmaceutical R&D, $PC^{R\&D}$*, are as calculated by DiMasi *et al.* (1991). The costs of R&D are not included as a fixed parameter because they are in present value terms and vary with the discount rate applied.

The mean sales profile indicates that the net of costs pre-tax return to R&D of $40 million equals a 44 percent return on investment. Ballance, Pogány and Forstner (1992) suggest that 40-50 percent is a reasonable rate of return for on-patent drugs. Thus, the model is well

Table 2 Net Returns from Pharmaceutical Prospecting

All monetary figures in 1990 dollars	Units	Sales Profiles: Mean	Sales Profiles: "Big Seller"
Sensitivity Parameters			
Discount Rate	% / yr	10%	10%
Real Price Trend of Pharmaceuticals	% / yr	5.0%	5.0%
Length of Patent Life	years	18	18
Annual Sales Decay Rate - Post Patent	% of sales	11%	11%
Species Hit Rate		0.00010	0.00010
Cost Scenario #1: Private Costs			
Per Sample Cost of a Biotic Sample	$	50	50
Cost Scenario #2: Social Costs			
Per Species Cost of Taxonomic Information	$	100	100
Annual Per Species Cost of Biodiversity Protection	$	50	50
Royalty Scenario			
Royalty rate (on gross sales)	% of sales	2.0%	2.0%
Fixed parameters			
Annual Sales - Patent Period Average	$m	69	289
Length of Prospecting Period	years	12	12
Time to Patenting	years	2	2
Costs of P&M	% of sales	60%	60%
Pre-Tax Rate of Return on P&M	% of P&M	10.0%	10.0%
Distribution Costs (adjustment to Gross Sales)	% of sales	5%	5%
Per Sample Collecting Fee	$	83	83
Number of Biotic Samples per Species		2	2
Results - Cost Model			
Sales and Net Returns (Check of Model Calibration)			
Gross Sales (including post-patent sales)	$m	388	1617
Gross Return on Pharmaceutical Prospecting	$m	131	550
Costs of R&D	$m	91	91
Net Return on R&D	$m	40	459
Pre-Tax Net Rate of Return on R&D		44%	503%
Cost Scenario #1: Private Costs			
Costs of Pharmaceutical Prospecting	$m	92.15	92.15
Costs of R&D	$m	91.15	91.15
Costs of Biotic Samples	$m	1.00	1.00
Net Returns			
Total Net Return on Pharmaceutical Prospecting	$m	39.13	457.71
Total Net Return To R&D	$m	38.71	452.74
Total Net Return to Biotic Samples	$m	0.42	4.97
Net Return per Biotic Sample	$	21.23	248.35
Cost Scenario #2: Social Costs			
Costs of Pharmaceutical Prospecting	$m	98.04	98.04
Costs of R&D	$m	91.15	91.15
Costs of Biotic Samples	$m	2.00	2.00
Costs of Biodiversity Protection	$m	4.89	4.89
Net Returns			
Total Net Return on Pharmaceutical Prospecting	$m	33.24	451.82
Total Net Return To R&D	$m	30.91	420.07
Total Net Return to Biotic Samples	$m	0.66	9.22
Net Return per Biotic Sample	$	33.91	460.86
Total Net Return to Biodiversity Protection	$m	1.66	22.53
Net Return per Tested Species	$	165.79	2253.38
Results - Royalty Model			
Gross Sales (during patent period)	$m	245.39	1027.80
Gross Return to Biotic Samples	$m	4.66	19.53
Royalty per Biotic Sample	$	233.12	976.41
Total Net Private Return to Biotic Samples	$m	4.91	19.78
Total Net Social Return to Biotic Samples a\	$m	-0.98	13.89

Notes: Assumes enough samples are screened in the first year to yield one new drug
a\ Including returns attributable to biodiversity protection.

calibrated in the sense that it provides a reasonable balance between the mean estimates of R&D costs and product sales used in the model.

Estimation of the Models and Comparison of Results

The basic objective of estimating the cost-based and royalty models is to establish the expected mean net returns to the inputs involved in pharmaceutical prospecting. The results of the cost model are presented first, followed by the results of the royalty model. It is worth reiterating that the calculations are based on the assumption that enough species - 10,000 in this case - enter the prospecting process in the first year to eventually generate one successful drug. In addition, the social costs of biodiversity protection are assumed to be only those protection costs incurred by the species actually tested. Thus, the estimation approximates the present value of net returns that would be generated by selecting a single protected area containing 10,000 species and immediately submitting them all to a single screening program.

The results of the two cost-based models are fairly straightforward. The mean net return to the commercial collector in the private costs model is $21 per sample, for a total of over $420,000 per successful product. Incorporating the full social costs of information generation and biodiversity protection, gives a return per biotic sample of $34 and a return per tested species of $166. Total net returns in the social cost model for both the production of biotic samples ($0.7 million) and biodiversity protection ($1.7 million) is $2.3 million The larger share attributable to biodiversity protection reflects its proportionately greater share in total costs - $4.9 million as opposed to $2.0 million for the biotic samples.

In the royalty model, the expected gross returns from royalties are $233 per tested sample or a total of $4.7 million per successful product. In order to arrive at a figure comparable with that from the private cost model, fees and costs of collecting samples must be included. Total net private returns are substantial at $4.9 million. Incorporating the hidden social costs of taxonomic information and biodiversity protection leads to a negative net social return of $1 million.

Comparing the net private returns yielded by the two models demonstrates that biodiversity and the species information embodied in a biotic sample are valuable inputs to the pharmaceutical R&D process. The private cost scenario reflects current market realities in which the social costs of protection and information generation are not made explicit. The results indicates that royalties generate net returns to biotic samples that are more than 12 times larger than net returns in the private cost model. The implicit suggestion is that the pharmaceutical industry - by negotiating royalty rates in the realm of 2 percent - reveals that biotic samples are an extremely important input in the prospecting process. Private collectors gain a total rate of return of 500 percent on their $1 million investment in generating biotic samples. The rather high rate of return to private collecting effort may lead to the conclusion that the expected level of royalties for which collectors have negotiated rights reflects more than just the value of the incremental effort expended by private collectors.

A comparison of the net social returns of the royalty and cost models indicates that royalties do not generate quite the same level of net benefits as indicated by a cost-based allocation

of returns. In fact, taking into account the social costs of biodiversity protection and the full social costs of developing biotic samples, royalties do not provide a positive net return to the information generation and biodiversity protection components of a biotic sample. In other words, the social costs entailed in preserving an area containing 10,000 species outweigh the royalties collected on an initial screening of all 10,000 species.

Nevertheless, it is remarkable that royalty returns could even come close - within $1 million on a $5.9 million investment - to covering the social costs of these activities. This would not necessarily be expected given that these social costs are not actually "visible" in the market place. The tentative conclusion is, then, that the value of biotic samples in the prospecting process - as measured by actual market behavior - comes close to providing a sufficient return to cover the one-off social costs of generating a local reference collection of these species and the full costs of protecting those species in perpetuity. The potential implication is that pharmaceutical prospecting may be an avenue for funding these activities in developing countries. This hypothesis is explored further in the next section.

Moving on to the "big seller" sales profile, the relative allocation of net returns indicated by the two models changes when sales are very large. The total net private returns from the royalty model are approximately $20 million. These returns still exceed those expected in the private cost model - $5 million - but only by a factor of four. In the case of a "big seller" the net returns to biotic samples and biodiversity under the social costs scenario - $32 million - are more than twice those of the royalty model - $14 million. As sales rise, the royalty obtained will remain a constant percentage of gross sales. Under the same circumstances, the cost-based models indicate that prospecting activities earn a rising percentage of gross sales. In the cost models, once production and marketing costs are covered revenues from additional sales are distributed across the prospecting activities. The rationale behind this effect is that by acquiring rights to royalties, collectors do not share in the downside risk associated with pharmaceutical R&D. As sales rise, pharmaceutical companies retain an increasing share of returns in order to cover their losses on other products. Meanwhile, royalties garnered by collectors fall off in percentage terms as their share of profits on blockbuster drugs is linked to sales - not the level of excess profits.

Table 3 presents the results of the sensitivity analysis indicating the low and high sensitivity parameters and the results under each of the models. Due to the nature of the cost models a number of the low range parameters produce negative numbers. This is a result of their effect on the balance between the costs of drug development and production and figures for gross sales. Technically, the implication is that the change in the parameter makes the generation of new drugs unprofitable. A discussion of the implications of these changes for the drug industry is beyond the scope of this paper. As indicated above, royalty payments limit the downside risk of collectors - royalty returns are always positive in the model.

In the case of the two cost models, the discount rate and real price trend for drugs have the largest impacts on the outcomes. The costs of drug development occur in the first twelve years with sales coming along afterwards. As a result, such a large sensitivity to the discount rate is not unusual. Most of the other changes tend to be confined within a fairly narrow range. The effect of lengthening the patent life to 20 years changes the net returns by 20-30 percent in the cost-based models. The effect of an increase in the species hit rate

Table 3 Sensitivity Analysis of Returns to Pharmaceutical Prospecting (Using the Mean Sales Profile)

All monetary figures in 1990 dollars	Parameters		Cost Scenario #1		Cost Scenario #2				Royalties	
			Biotic Samples		Biotic Samples		Tested Species		Biotic Samples	
	Low Range	High Range	Low	High	Low	High	Low	High	Low	High
Original Estimates (from Table 2)			21.00		34.00		166.00		233.00	
Sensitivity Parameters										
Discount Rate	15%	5%	-15.00	107.00	-34.00	188.00	-112.00	1610.00	114.00	499.00
Real Price Trend of Pharmaceuticals	0.0%	-	-21.00	-	-44.00	-	-217.00	-	111.00	-
Length of Patent Life	-	20	-	27.50	-	46.00	-	223.00	-	279.00
Annual Sales Decay Rate - Post Patent	50%	-	-0.36	-	-7.00	-	-33.00	-	-	-
Species Hit Rate	0.00001	0.001	15.00	22.00	-34.00	64.00	-111.00	209.00	23.00	2330.00
Cost Scenario #1										
Per Sample Cost of a Biotic Sample	25	75	11.00	31.00	26.00	42.00	169.00	162.00	-	-
Cost Scenario #2										
Per Species Cost of Taxonomic Information	50	150	-	-	26.00	42.00	169.00	162.00	-	-
Per Species Cost of Biodiversity Protection	250	750	-	-	37.00	31.00	91.00	225.00		
Royalty Scenario										
Royalty rate (on gross sales)	1.0%	3.0%	-	-	-	-	-	-	117.00	350.00

to 1 in 1,000 raises returns roughly by one-third. The cost-based parameters for costs of biotic samples and biodiversity protection produce variations of from 40-50 percent.

Sensitivity analysis of the royalty model demonstrates that royalties are far less sensitive to the discount rate. This arises because royalties do not depend on the costs of R&D. Swings in discount rates have less of an effect on sales which occur further into the future. Adding two years to patent life changes royalty returns by 16 percent. This indicates that - as suggested in Section 4 - changes to the market exclusivity accorded to natural product-derived pharmaceuticals might have a significant impact on returns and hence the incentives for exploring the pharmaceutical potential of biodiversity.

However, the greatest variance in the royalty model is in response to the species hit rate. Changes from 1 in 1,000 to 1 in 100,000 leads to a range in per sample returns of from $23 to $2330. Changes to the royalty rate lead to swings in per sample returns of 50 percent in either direction. The hit rate is not a policy parameter that can be manipulated to direct investment flows as with the length of market exclusivity. Nevertheless, the extreme sensitivity of results from both models to the hit rate do indicate the potential importance of perceptions regarding the hit rate. Demonstrable evidence of a rate in the realm of 1 in 1,000 would likely have a galvanizing impact on investment in all phases of natural products research.

Finally, in comparison with a number of other studies that have explored the potential range in their valuation methods (as previously summarized in Table 1) the results from this model are relatively robust. Actual mean returns - from the royalty model - are expected to vary at the most between $20 and $2,000 with a reasonable average in the low hundreds of dollars per sample.

Thus, the preliminary conclusion emerging from this analysis is that the per species financial returns that could be captured by collectors are at the lower end of the scale of previous estimates of per species values - and far lower than figures commonly cited by the media and conservationists.[40] Nevertheless, the analysis has shown that industry's willingness to pay for biotic samples, as reflected in royalty arrangements, does indicate the substantial value of biotic samples as an input to the prospecting process. It would, therefore, be incorrect to disparage fledgling efforts to develop contractual arrangements for having negotiated "meagre" royalty rates (Kloppenburg and Rodriguez 1992). These conclusions also indicate that current efforts to encourage the development of contractual arrangements need perhaps to focus less on the establishment of royalty provisions. Thomas (pers. comm. 1993), for one, insists that there are few if any examples of industry refusing to pay royalties once asked to do so. Instead efforts might be directed towards ensuring that contractual arrangements will reward not only the investments made by collectors, but the investment made by society in biodiversity protection and the development of taxonomic knowledge - and that these benefits are appropriable in the short-run rather than in 10-20 years time. The importance of these issues is explored below.

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[40]For instance, it is frequently stated in the popular media that the drug industry earns $200 billion each year from the developing world"s biodiversity (Vidal 1993). This paper demonstrates that such claims are at odds with reality.

The Economic Role of Prospecting Returns: A Distributional Analysis of Royalties

Given the potential for concluding that gross returns from royalties may cover the cost of biodiversity protection and the development of species information, it is instructive to explore the likely distribution of returns from payments and royalties across the actors involved in prospecting. This is possible based on a number of the institutional arrangements for distributing royalties discussed in Section 4 of this paper. The objective of this exercise is to evaluate the hypothesis that these contractual arrangements are likely to provide a significant incentive for developing countries to generate taxonomic information and protect biodiversity.

The cost figures developed for the cost-based model and the measure of expected mean royalty returns provide a starting point for such an analysis. However, the calculations presented in Table 2 were based on two important assumptions. The total net returns generated by both valuation models assume that enough species are screened in the first year to generate a marketable drug. In addition, only the protection costs of those species directly used in the screening process are charged in the estimation of the social costs of biodiversity protection. These assumptions must be reassessed in order to provide a realistic appraisal of the economic choices faced by a biodiversity-rich developing country that is contemplating investments in taxonomic information and biodiversity protection for the sake of pharmaceutical prospecting.

Activity in the market for biotic samples is determined first by the interest and screening capacity of organizations engaged in R&D and second by the capacity of collecting institutions to meet this demand. Estimates of annual sample turnover from past and current screening efforts gives an indication of the likely depth of the market for biotic samples.

The first phase of the US National Cancer Institute's plant screening program began in earnest in 1960 with the initiation of a supply contract with the US Department of Agriculture. Cragg *et al.* (1993a) reveal that from 1960-1982 approximately 114,000 extracts from roughly 35,000 different plant species were screened for anti-cancer activity by NCI. Suffness and Douros (1979) suggest that on average NCI obtained 2 plant samples per species and made 2 extracts from each sample. This puts the total number of plant samples screened during the period between 57,000 and 70,000. Over the life of the program that comes to an annual throughput of between 2600 and 3200 samples.

In 1986 the NCI natural products program was revitalized. Cragg *et al.* (1993b) state that NCI's current total annual screening capacity is 20,000 screens for cancer and 30-40,000 for AIDS. This includes the screening of fractionations and synthetic compounds as well as crude natural product extracts. In the case of plants, approximately 30,000 samples have been received by NCI since contracts were first issued in 1986. To date, 20,000 samples have been processed yielding 40,000 extracts of which 18,000 have been tested in the anti-cancer screens and 16,000 in the anti-HIV program. Working back to annual totals for activity since 1986, gives roughly 5,000 plant samples obtained per year with 1,500 and 1,300 actually tested in the anti-cancer and anti-HIV screening programs respectively.

Mallinckrodt and Laird (1992) and Reid *et al.* (1993) provide a list of nineteen biotechnological and pharmaceutical companies active in screening natural products. Annual

screening capacity for plant, marine, microbes and other natural products ranges from a few hundred samples to 15,000. Of the major pharmaceutical companies Syntex Laboratories (10,000) and Monsanto (9,000) have the highest annual turnover with Smith-Kline Beecham (2-3,000) and CIBA-GEIGY (4,000) not far behind. Abbot Laboratories, Bristol-Myers Squibb, Glaxo Group Research, Merck & Co., Pfizer and Upjohn all indicated that they have a natural products research focus, but declined to indicate yearly turnover figures. Unfortunately, the figures are not disaggregated according to the allocation of screening capacity amongst marine, plant, microbial and other natural products. Nevertheless, in the case of the major pharmaceutical companies it is fair to assume that a majority of natural products research involves the screening of microbial sources - rather than plants or marine sources.[41]

While the evidence is far from complete it would appear that current demand by pharmaceutical companies for screening plant samples is not out of line with past figures for NCI's operations. A figure in the low thousands might be indicative of annual demand from companies involved in plant screening.

As detailed in Section 4, there are a range of organizations and individuals involved in collection of samples for screening programs. NCI has a number of different contractors supplying natural products. Three 5-year agreements are currently in place with the major US botanical gardens - each of which is responsible for assembling over 1,000 samples a year. Actual collection is often undertaken by collaborators in the developing world. As a result, NCI's supply of plant material comes from approximately 25 different countries (NCI 1992). In addition to supplying NCI, these botanic gardens also manage additional contracts with major pharmaceutical companies. In the private sector, another intermediary supplier, Biotics, Ltd, provides a similar service. In the past few years Biotics has provided over 3,000 samples from more than 8 countries to a number of industry screening programs.

This overview of recent activity in the market for biotic samples demonstrates that it is extremely unlikely that a single contract for supply of biotic samples from a given developing country will involve the collection and processing of 20,000 samples in a single year. Levels of demand from screening organizations and data on the quantity of samples supplied by collecting organizations make this an unrealistic assumption. A more realistic expectation regarding the annual number of samples that a single biodiversity-rich country is likely to produce for screening purposes would be in the realm of 1,000 species or 2,000 samples per year. While this figure may be on the high side for a number of countries, it is chosen as a representative figure to reflect the annual output that a well-funded and well-organized institution might be capable of providing and selling to interested pharmaceutical concerns.

The second limitation to the original analysis of net returns to prospecting activities concerns the assumption that the benefits of pharmaceutical prospecting need only cover the costs of those species actually destined for testing under a contract. Fully protected wildlands in biodiversity-rich countries will contain many times the number of species that can actually

[41] As indicated earlier, pharmaceutical companies have exploited microbial species since the Second World War for their potential in developing powerful antibiotics. One exception would be Syntex - all 10,000 extracts currently screened each year are plants received from China.

be tested on an annual basis. If options are to be kept open for pharmaceutical prospecting, all the biodiversity in these areas must be maintained in perpetuity. For example, it is not possible to save just the plants that are in demand by pharmaceutical companies. In order to evaluate the hypothesis that the net returns generated by pharmaceutical prospecting justify - and provide funds for - conservation, the full costs of protecting all of biodiversity need to be charged to the larger endeavor of pharmaceutical prospecting.

Thus, two changes are necessary in order to estimate the likely returns a developing country can capture by investing in biodiversity protection and the development of in-country taxonomic and biotic samples processing capabilities. First, the gross returns indicated by the royalty model must be adjusted to accommodate a realistic measure of annual throughput of biotic samples destined for screening programs. By using a figure of 2,000 samples, the expected present value of gross returns in the first year will be far less than the amount of $4.7 million indicated in Table 2. However, the amount of royalties gained on the 2,000 samples then becomes a revenue figure received each and every year. Second, the full costs of protecting all biodiversity must be included as the social costs incurred by prospecting. As the per species costs of protection used in the original models are based on total species (not just those popular with pharmaceutical companies) the impact of this change is likely to be a significant one.

Based on these changes to the original royalty model, the net returns to effort invested in biodiversity protection, taxonomic information and the collection of biotic samples are recalculated in Table 4. The benefits and costs are evaluated over a forty year period using the variables from Table 2. Due to the low turnover in species actually screened, it is assumed that every species tested is a "new" species and incurs the social costs of generating a taxonomic classification. Country level data is again based on Costa Rica although the model can easily be adapted to the situation in other countries.

Including the social costs of biodiversity protection for all 500,000 species raises the total costs of protection from $4.9 million to close to $250 million. The expected royalty returns from screening 2,000 samples every year for forty years come to $4.6 million. The private costs of generating biotic samples are $1 million and the value of fees paid for samples is $1.2 million. The social costs of investing in developing taxonomic knowledge for the species screened comes to $1 million. The outcome is a net private return of $4.8 million and a net social return of -$240 million.

The large negative figure for net social returns demonstrates that current demand for biotic samples is simply not sufficient to generate enough value to cover the full social costs of biodiversity protection. Even if royalty and payments for samples understate the full economic value of the contribution made by biodiversity to the development of new drugs it is unlikely that a $240 million deficit could be covered. In other words, the worth of biodiversity in the prospecting prospect does not - in and of itself - justify incurring the costs of "saving" biodiversity. Even if OECD countries developed a fund to adequately compensate developing countries for the "global value" appropriated by realized from drugs based on tropical biodiversity it would not make an appreciable dent in Southern conservation budgets - or compensate countries for the opportunity costs of protecting wildlands. Keeping "options" open for biodiversity and pharmaceutical prospecting activities simply on the basis of potential returns from royalties and sample payments on pharmaceutical prospecting

Table 4 Distributional Analysis of Royalty Returns

	Units	Amounts		
General Parameters				
Expected Mean Royalties a\	$ / sample	233		
Number of Samples per Species a\		2		
Private Costs of Collection a\	$ / sample	50		
Costs of Taxonomic Information a\	$ / species	100		
Per Sample Collecting Fee a\	$ / sample	63		
Discount Rate		10%		
Number of Prospecting Years		40		
Country Parameters (Costa Rica)				
Annual Cost of Biodiversity Protection a\	$ / species	50		
Fully Protected Area	ha	600,000		
Number of Species		500,000		
Annual Supply of Samples for Screening		2000		
Total Benefits and Costs (in present value terms)				
Royalty Payments	$m	4.56		
Sample Fees	$m	1.23		
Costs of Collection	$m	0.98		
Costs of Taxonomic Information	$m	0.98		
Costs of Biodiversity Protection	$m	244.48		
Net Returns				
Net Private Return	$m	4.81		
Net Social Return	$m	-240.64		
Distributional Arrangements (of royalties)		**b\ 100-0-0**	**b\ 50-25-25**	**c\ 25-25-50**
Developed Country				
Collector/Broker	$m	4.81	2.28	
Taxonomic Institutions	$m	-0.98		
Developing Country				
Collector/Broker	$m		1.39	1.27
Taxonomic Institutions	$m		-0.98	0.16
Biodiversity Protection	$m	-244.48	-243.34	-242.07

Notes a\ Figures from Table 2

b\ First split goes to the developed country collector/broker, second split to the developing country collector/broker and the third split to biodiversity protection.

c\ First split goes to developing country collector/broker, second split to the local taxonomic institution and the third split to biodiversity protection. In addtion, 10 percent of the sample payment goes to biodiversity protection.

activities would be a risky and high-cost strategy for a country with many pressing development needs.

Table 4 also indicates how these benefits and costs will be allocated across different actors involved in the prospecting process. Three distributional arrangements - mirroring those discussed at the end of Section 4 - are explored. The first distributional arrangement describes the case of a private collector from a developed country who incurs all collecting and taxonomic costs and appropriates all royalty returns. The second arrangement considers the case of a developed country institution - such as a botanic garden or private company - that acts as a broker for a developing country collector. The local collector is, in turn, assumed to rely on a local institution as a source of taxonomic information. Under this arrangement the broker captures 50 percent of the royalties, returning half of these to the local collector who then apportions half again (25 percent of total royalties) to biodiversity protection activities. The local collector receives the initial fees for samples. The third distributional arrangement models the case of a developing country broker institution (such as Costa Rica's National Biodiversity Institute). This broker pays a 10 percent fee to biodiversity protection out of fees received for sample and returns 50 percent and 25 percent of total royalties, respectively, to biodiversity protection and the local taxonomic institution.

The results portrayed in Table 4 indicate the net returns from the perspective of the various individuals or institutions involved. Under the first two arrangements a majority of the benefits go to collectors or brokers in developed countries. The costs are largely incurred by developing countries - except for the first arrangement in which the investment in taxonomic information is undertaken by a developed country institution. In the second distributional arrangement the local collector receives a hefty share of the profits - a rate of return on investment of around 140%. In this instance, note that a positive rate of return (though only 20 percent) is generated if the collecting and taxonomic work are vertically integrated. Finally, in the third arrangement all returns go to the developing country, providing a 125 percent rate of return on collecting efforts and a 15 percent rate of return on taxonomic efforts. Allocation of 50 percent of royalties makes only a minor contribution to biodiversity protection.

The interesting conclusion emerging from the distributional analysis is that although these contractual forms for returning benefits to developing countries make little contribution to biodiversity protection, they can have an important impact on the incentives for generating taxonomic information. This is an important observation, given the lack of attention received by the taxonomic sector in developing countries from local governments facing funding constraints and international conservation organizations more interested in funding land purchases. In addition, it is clear that even under the best scenario biodiversity protection receives only 50 percent of total royalties. With operating costs forming one-half of the total bill for biodiversity protection, capturable prospecting revenues will obviously fail to make a measurable contribution in covering even the direct costs of protection. In order for royalty revenues over the period to cover the full costs of biodiversity protection - $250 million - a sensitivity analysis indicates that it is necessary to screen 110,000 species per year. However, even then only $125 million - half of that required by the developing country - is captured by biodiversity protection activities.

Two additional appropriation problems serve to further discredit the contention that developing countries can fund biodiversity protection from prospecting revenues. The first regards the distribution of the costs and revenues over time. Although, the present value of gross returns to taxonomic information and pharmaceutical prospecting may be enticing, the difficulty is that the actual cash flows from royalties on current prospecting projects will not materialize for ten years or more. Second, it must be emphasized that these figures are expected values. If a country has a low annual turnover of samples - or is simply unlucky - it may never actually record a "hit" and be in a position to capture a financial return. Thus, a large degree of risk is assumed by a country that enters into prospecting with the aim of generating future revenues, given that the costs of taxonomic information must be paid up front and the costs of biodiversity protection are incurred from year one.

A potential solution to these problems would be to develop the means for countries or organizations holding such royalty agreements to cash in on their expected present value. As a contract for royalties is an economic asset it may be possible to develop a market for these contracts. A competitive market would price the royalty component of a contract at its expected present value (minus some risk premium), thereby generating current funds for investment in taxonomic information and biodiversity protection. An alternative to the development of a formal market would be for the development of a fund that would pool the risks of individual contracts by purchasing all contracts. This role might be filled by an intergovernmental body - such as the Biodiversity Convention Secretariat - or by independent, non-governmental organizations already involved in financing conservation activities. In order to enable such an approach, future efforts to improve contractual forms for pharmaceutical prospecting would need to explore the possibility of ensuring that the rights to royalties established by such contracts are tradeable.

In sum, as long as demand for biotic samples remains at current levels, the returns from pharmaceutical prospecting cannot be expected to generate a "market" solution to the biodiversity crisis. Nor is it likely that financial transfers from OECD countries sufficient to fund biodiversity conservation are justified on the basis of biodiversity's pharmaceutical potential. Nevertheless, pharmaceutical prospecting offers a significant rate of return on investment for those able to secure a share of the market. Ongoing efforts to ensure that the returns from prospecting activities reward investments made in species information and biodiversity protection are currently matched by a renewed interest on the part of public and private prospecting institutions in the biochemical potential of biodiversity. If the opportunity can be seized, perhaps pharmaceutical prospecting may play a larger role in arguments for the protection of biodiversity in the future.

In the meantime, however, efforts to base biodiversity conservation on economic grounds need to consider the role of other more tangible benefits generated by protected areas such as ecotourism, ecological functions and the intangible benefits of existence values. These values are likely to be much more than incidental, "spin-off" benefits of conservation. Opportunities for commercializing biodiversity and developing global financial transfer mechanisms in these instances need to be explored if sources of sustained funding for conservation activities are to be found.

7. CONCLUSIONS

This paper has explored the valuation, incentives and distributional issues associated with pharmaceutical prospecting in biodiversity-rich developing countries. For the purposes of pharmaceutical prospecting, biodiversity is essentially a renewable resource capable of generating a continuing stream of benefits. However, previous analysis of these benefits have largely overstated the magnitude of their benefits. This study has shown that while prospecting for new drugs using biodiversity can be a profitable activity for developing countries, it is unlikely to make a major contribution to the costs of protecting biodiversity.

In particular, an important issue that needs to be addressed before investing in prospecting activities is the ability of a developing country to find solutions to the incentives problem posed by the *non-rival* and *non-exclusive* characteristics of biodiversity and species information. While the establishment of contracts is a solution currently in vogue, control over access or vertical integration of activities are also potential measures for capturing the returns from prospecting. While Costa Rica's National Biodiversity Institute provides an initial example of how returns to biodiversity protection and species information may be fully captured by a developing country through the use of contracts and vertical integration, other countries may need to develop their own solutions. A key, but often forgotten element in developing in-country capacity aimed at capturing prospecting values is the investment in the development of a local base of taxonomic knowledge and species reference collections. The analysis developed in this paper indicates that prospecting activities may generate sufficient returns to finance these investments in species information.

It may be unreasonable to expect that pharmaceutical prospecting should bear the full burden of funding biodiversity protection in developing countries. Biodiversity provides a wide range of goods and services to society. Nevertheless, the considerable public interest in prospecting, and the devotion of considerable political effort towards developing an agenda based in part on pharmaceutical prospecting during intergovernmental negotiations surrounding the Biodiversity Convention, warrants the critical reappraisal presented in this study. Despite every indication that prospecting cannot sustain biodiversity protection by itself, prospecting activities remain a potentially profitable activity for developing countries. As demonstrated in this paper, prospecting can provide funds for the development of taxonomic information which may yield many other economic benefits to society. In addition, investments in higher value-added activities such as chemical extraction, primary screening, and chemical fractionation and isolation may be important stepping-stones along a development path based on scientific and technological capacity.

The paper also puts forward a number of policy options for improving the incentives that determine the level of investment in pharmaceutical prospecting. The study suggests that because drug development using plants, marine organisms and insects is a high-risk, high-payoff strategy it may be useful to offer increased incentives to the private sector. For example, development of an extended period of market exclusivity for drugs derived from these organisms may increase demand for the exploration of the pharmaceutical potential of natural products. On the supply side, an alternative to anticipating that prospecting will fund the development of taxonomic information and value-added activities is for governments and donors to go ahead and invest public funds in the development of local centers of taxonomic and biochemical expertise in developing countries.

Finally, the study acknowledges that the lack of current information on the status of pharmaceutical prospecting represents a major drawback to economic research aimed at developing investment strategies and policy approaches in this field. Two proposals for further research in this area are presented in the Appendices to this paper. Appendix A presents a proposal to improve and develop a database of information on the past and present status of natural product pharmaceuticals, emphasizing patent, regulatory and market data. The second proposal - in Appendix B - suggests a study to build on the brief examination in this paper of the valuation and incentives issues surrounding the development of taxonomic information and its linkages to pharmaceutical prospecting.

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APPENDIX A Research Proposal - Development of a Database on Success and Failure in Pharmaceutical Prospecting

Early research into the composition of US community pharmacy prescriptions by Farnsworth and Morris (1976) indicated that 25 percent of prescriptions contained one or more active constituents from higher plants and that almost 50 percent of prescriptions contained material from natural products. These figures are based on data from 1959-1973. As indicated in this paper, there are good reasons for believing the relative importance of natural products - in particular plants - in the composition of drug prescriptions and sales has changed since 1973. However, no published work on the importance of plants or natural products in industry R&D programs over the past two decades is currently available.

A solution to this information deficit is to build a database made up of three principle components

- patent information on natural products - from patent data databases
- regulatory agency data on progress of natural products towards regulatory approval
- post approval data on efficacy and sales from industry sources

The following budget would enable LEEC - in cooperation with other interested parties - to design such a database, investigate the extent of the data available from the sources listed above, find an institutional home for the database and develop a full project proposal for implementation. The eventual objective is to provide the international community with a comprehensive information source on natural products that is updated on a continual basis.

For further details contact Bruce Aylward at the London Environmental Economics Centre, c/o IIED, 3 Endsleigh St., London WC1H 0DD, United Kingdom. Tel (44) 71 388 2117, fax (44) 71 388 2826, Email: leecuk@gn.apc.org.

Appendix B Research Proposal - The Willingness to Pay for Taxonomic Information and Services

The evolution of large taxonomic institutions in the North occurred largely based on the support of the public purse. The provision of taxonomic information was regarded as a public good worth of considerable government support. However, over the past few decades public interest in funding such basic taxonomic research has waned as interest in other areas of scientific research - such as microbiology and economic botany - has grown. Nonetheless, biological research begins with taxonomy. Unfortunately, recently renewed interest in assessing and evaluating tropical biodiversity has revealed that practicing taxonomists are in short supply and training opportunities few.

Meanwhile, the 'commercialization' of biodiversity proceeds apace and increasing use of taxonomic information is made by commercial collectors. This paper covers this phenomenon in detail in the case of pharmaceutical prospecting. While some institutions have taken initial steps to begin recouping the costs of services rendered to commercial users, the potential for 'privatizing' taxonomic services remains largely unexplored. To counter this lack of data, the proposed research project would survey the different types of users of taxonomic information and evaluate their willingness to pay for access to taxonomic services, reference collections and other taxonomic information sources.

This research would build on the research and contacts developed in the course of the current study with institutions such as the Royal Botanic Gardens, Kew; the Natural History Museum; the New York Botanical Gardens; the Smithsonian Institution, etc. Kew Gardens has already been informally approached and has indicated an interest in assisting with this research project.

For further details contact Bruce Aylward at the London Environmental Economics Centre, c/o IIED, 3 Endsleigh St., London WC1H 0DD, United Kingdom. Tel (44) 71 388 2117, fax (44) 71 388 2826, Email: leecuk@gn.apc.org.

APPENDIX C Background on Biotics, Ltd.

Overview

Biotics is a private company founded in 1983. Its efforts to supply the pharmaceutical industry with biotic samples began in 1986 as a result of a European Community initiative on biotechnology which provided funding for Biotics' initial activities in this area. The phytochemical programme at Biotics has developed largely over the past four years. In November 1990 Biotics launched BioEx, a commercial extraction facility based at the School of Chemistry and Molecular Science at the University of Sussex. Biotics is currently promoting an investment proposal to develop BioEx Associates - a number of privately held extraction facilities that will be located in developing countries. The company ran at a loss in the 1990/91 financial year, but reported a respectable gross profit margin in 1991/92 and in 1992/93

Biotics plays an intermediary/processing role between pharmaceutical companies and developing country suppliers of plant samples. Biotics negotiates and implements contracts for the delivery of plant samples with interested sellers and buyers. At their laboratory in Sussex, Biotics carries out the chemical extraction of plant material, stores surplus material and maintains a database recording collection, extraction and storage details of the plant material. The company currently has a staff of five people.

Supply of Plant Material

Since the inception of its phytochemical programme Biotics has established contracts for receiving plant material from eight different countries including:

- Ghana
- Malaysia
- China
- Costa Rica
- Nepal
- Guyana
- New Zealand
- Sierra Leone

Contracts have also been established with Cameroon, Mali and Uganda.

Biotics accepts dried plant material, preferably milled. The standard amount of material delivered by suppliers is 1 kg. Collectors supply leaves, stems and bark. Heartwood, roots, flowers and fruits are also supplied at times. Biotics requires samples to be identified to species level and accompanied by a voucher specimen. If there is reason to suspect that a sample is a new species (i.e.- it is considered sufficiently distinct from other samples) Biotics will accept it.

Material may be collected at random or be selected based on ethnobotanical information. Choice of selection criteria is left to the collector. All botanic information - including date,

time and location of collection - is shipped along with the sample material and voucher specimens to Biotics' offices in Sussex.

A fairly standard contract is used for suppliers of material. They receive an initial fee for samples and 50% of any eventual royalties obtained by Biotics. Biotics attempts to include in the contract terms requiring a share of the royalties gained by the collector to be contributed to infrastructure development or biodiversity related projects in the country.

The supplier agrees to provide additional material upon request and to refrain from collecting similar material for other buyers without prior notification to Biotics. Suppliers are not normally notified of who is screening their material, although they may inquire if interested. When possible Biotics endeavors to provide suppliers with non-confidential information on the results of screening.

Buyers

As of early 1993 Biotics has sold over 3,000 plant samples and extracts to pharmaceutical and agrochemical companies. Biotics has entered into supply contracts with a number of companies including:

- Rothamsted Experimental Station - under an agreement with British Technology Group, UK
- Glaxo, UK
- Sphinx, NC, USA
- Immunex, WA, USA
- SmithKline Beecham, NJ, USA

Biotics routinely delivers extracts from 25 grams of dried plant material to the buyer. Plant species are selected at random unless otherwise requested. Information about the origin of plant samples is conveyed to companies along with the sample. Contractual arrangements generally provide buyers with an initial period of exclusivity of around 6 months for screening samples. This can be extended to one year ore more upon request by the buyer. Once the initial period of exclusivity has expired, Biotics may use its remaining supply of the plant material in fulfilling contracts with other companies.

If the sample proves of interest, then the buyer may request additional material for secondary screening to confirm activity. Biotics' standard contract requires that such resupply be obtained through Biotics. If the material required is less than 0.5 kg dry weight of plant material Biotics will supply this second batch of material from their stock in Sussex. Additional requirements mean that Biotics must request the original collector to return to the source for recollection.

Within a year of testing positive in primary screens companies are likely to be in a position to patent promising compounds. Under the contractual arrangements between Biotics and both sellers and buyers of plant samples the right of the screening company to patent any such compounds is recognized. Biotics has two of its samples yield patentable compounds. None, of course, have yet been taken as far as clinical testing.

The financial terms of individual contracts are confidential. Income from dried plants naturally differs from that for extracts - information on this may be made on application. Royalty payments will vary depending on whether the plant sample yields a marketable compound, the starting material for the derivation of a semi-synthetic analogue or a product used in a composite drug.

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BOOKS

Edward B. Barbier
Economics, Natural-Resource Scarcity and Development: Conventional and Alternative Views, Earthscan, London, 1989 (paperback £17.50)

The history of environmental and resource economics is reviewed; then using insights from environmentalism, ecology and thermodynamics, Barbier begins the construction of a new economic approach to the use of natural resources, particularly to the problem of environmental degradation. With examples from the global greenhouse effect, Amazonian deforestation and upland degradation on Java, Barbier develops a major theoretical advance and shows how it can be applied. This book breaks new ground in the search for an economics of sustainable development.

David W. Pearce, Anil Markandya and Edward B. Barbier
Blueprint for a Green Economy, Earthscan, London, 1989 (paperback £8.95)

This book was initially prepared as a report to the Department of Environment, as part of the response by the government of the United Kingdom to the Brundtland Report, *Our Common Future*. The government stated that: '...the UK fully intends to continue building on this approach (environmental improvement) and further to develop policies consistent with the concept of sustainable development.' The book attempts to assist that process.

Edward B. Barbier, Joanne C. Burgess, Timothy M. Swanson and David W. Pearce
Elephants, Economics and Ivory, Earthscan, London, 1990 (paperback £10.95)

The dramatic decline in elephant numbers in most of Africa has been largely attributed to the illegal harvesting of ivory. The recent decision to ban all trade in ivory is intended to save the elephant. This book examines the ivory trade, its regulation and its implications for elephant management from an economic perspective. The authors' preferred option is for a very limited trade in ivory, designed to maintain the incentive for sustainable management in the southern African countries and to encourage other countries to follow suit.

Gordon R. Conway and Edward B. Barbier
After the Green Revolution: Sustainable Agriculture for Development, Earthscan Pub. Ltd., London, 1990 (paperback £10.95)

The Green Revolution has successfully improved agricultural productivity in many parts of the developing world. But these successes may be limited to specific favourable agro-ecological and economic conditions. This book discusses how more sustainable and equitable forms of agricultural development need to be promoted. The key is developing appropriate techniques and participatory approaches at the local level, advocating complementary policy reforms at the national level and working within the constraints imposed by the international economic system.

David W. Pearce, Edward B. Barbier and Anil Markandya
Sustainable Development: Economics and Environment in the Third World, London and Earthscan Pub. Ltd., London, 1990 (paperback £11.95)

The authors elaborate on the concept of sustainable development and illustrate how environmental economics can be applied to the developing world. Beginning with an overview of the concept of sustainable development, the authors indicate its implications for discounting and economic appraisal. Case studies on natural resource economics and management issues are drawn from Indonesia, Sudan, Botswana, Nepal and the Amazon.

David W. Pearce, Edward B. Barbier, Anil Markandya, Scott Barrett, R. Kerry Turner and Timothy M. Swanson
Blueprint 2: Greening the World Economy, Earthscan Pub. Ltd., London, 1991 (paperback £8.95)

Following the success of *Blueprint for a Green Economy*, LEEC has turned its attention to global environmental threats. The book reviews the role of economics in analyzing global resources such as climate, ozone and biodiversity, and considers economic policy options to address such problems as global climate change, ozone depletion and tropical deforestation.

E.B. Barbier and T.M Swanson (eds.)
Economics for the Wilds: Wildlife Wildlands, Diversity and Development, Earthscan Pub. Ltd., London, 1992 (paperback £12.95).

This collection of essays addresses the key issues of the economic role of natural habitat and wildlife utilization in development. The book argues that this role is significant, and composes such benefits as wildlife and wildland products, ecotourism, community-based wildlife development, environmental services and the conservation of biodiversity.

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