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THE COMMERCIAL USE OF BIODIVERSITY: AN UPDATE ON CURRENT TRENDS IN DEMAND FOR ACCESS TO GENETIC RESOURCES AND BENEFIT-SHARING, AND INDUSTRY PERSPECTIVES ON ABS POLICY AND IMPLEMENTATION

The Executive Secretary is pleased to circulate herewith, for the information of participants in the fourth meeting of the Ad Hoc Open-ended Working Group on Access and Benefit-sharing, a report entitled "The Commercial Use of Biodiversity: An Update on Current Trends in Demand for Access to Genetic Resources and Benefit-sharing, and Industry Perspectives on ABS Policy and Implementation" prepared by Sarah A. Laird and Rachel Wynberg. This paper was commissioned by the Secretariat of the Convention in response to decision VII/19E, paragraph 10 (f) of the Conference of the Parties.

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The Commercial Use of Biodiversity:

An Update on Current Trends in Demand for Access to Genetic Resources and Benefit-Sharing, and Industry Perspectives on ABS Policy and Implementation

December 2005

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Executive Summary

A wide range of sectors undertake research and develop commercial products from genetic resources. They include the pharmaceutical, biotechnology, seed, crop protection, horticulture, cosmetic and personal care, fragrance and flavor, botanicals, and food and beverage industries. Each sector is part of a unique market, undertakes research and development in distinct ways, and uses genetic resources and demands access to these resources very differently. Incorporation of these factors into ABS regulatory frameworks is essential.

This paper begins with a review of trends in markets, research and development, and demand for access to genetic resources in five sectors: pharmaceuticals, biotechnology, seed, crop protection, and horticulture. It then reviews broader trends in benefit-sharing across sectors and reports on the impact of the CBD, and national ABS policies and regulations, on industry demand for genetic resources. It concludes with recommendations for more effective ABS policy.

Demand for access to genetic resources

The industries of which bioprospecting is a part are research intensive, and driven by rapid advances in science and technology. While many of the sectors are dominated by large multi-national companies, a significant and growing portion of research and development – particularly in the earlier discovery stages – is done by smaller companies. Large companies then license-in promising products, or acquire smaller companies with interesting pipelines. Thus, there is a range and variety of companies and business models that demand access to genetic resources.

Demand for access to genetic resources in most sectors has changed in recent years in response to market demand and scientific and technological advances. For example, over the last 10 years, scientific and technological advances have resulted in a decline in demand for natural products on the part of the pharmaceutical industry, as other approaches looked more promising, efficient, and cost-effective. Today, however, new technologies and scientific understanding are once again making natural products of interest as sources of truly novel molecular diversity, particularly as the alternative approaches, such as combinatorial chemistry, have not lived up to their promise. The diversity found in microorganisms is of particular and increasing interest to pharmaceutical and biotechnology companies.

In the seed industry, there has been reduced demand for wild genetic resources and greater reliance on *ex-situ* and private collections but demand continues when inputs are needed on quality, to meet consumer demands for reduced use of chemicals, and to reduce vulnerability to pests and diseases. Demand for wild genetic resources for vegetables and flowers is also greater than that for commodity crops. The crop protection, cosmetic and personal care, and food and beverage industries continue to demand access to genetic resources to meet consumer demand for ‘natural’ products, and reduced use of chemicals and synthetic ingredients. The ornamental horticulture industry has a low dependence upon wild genetic resources, and instead largely relies on creative use of existing germplasm in collections. However some companies, usually smaller in size, continue to hunt for material to introduce new ornamental species, and some companies involved in breeding rely on wild germplasm to provide new variations of color and other character traits.

New scientific and technological developments have facilitated research on biodiversity, but have also made it possible to look with new eyes at what is found in companies’ ‘backyards’ and to generate more diversity in the laboratory, where existing genome sequences and databases can yield novel structures. The full impact of these developments on demand for access to genetic resources is still unfolding, but it is likely that nature will continue to be a source for original

novelty and complexity that will then be modified in the laboratory. The ways genetic resources are used, and thus the nature of demand for access, will evolve alongside science and technology, and it behooves providers to stay abreast of these rapid changes. The clarity and workability of ABS policies and laws is also considered to have a significant impact on future industry demand for genetic resources, with many reporting dampened interest in the face of regulatory uncertainty and difficulties.

Trends in benefit-sharing

Benefit sharing varies by sector, but since adoption of the CBD standards for best practice in benefit-sharing have become widely accepted. This has been a significant and positive achievement of the CBD and ABS policy dialogue. Larger or socially responsible companies today do not generally consider genetic resources freely available, or the 'common heritage of mankind'.

Groups with the most experience in benefit-sharing emphasize the importance of non-monetary benefits and 'front-loading' benefit-sharing packages to ensure that provider countries receive a stream of benefits through the discovery and development phases, given the small odds of any one partnership yielding a commercial product. While responsible users of genetic resources understand that providers must benefit, there remains debate about appropriate monetary benefits, in particular up front payments and royalties. At the heart of this debate are different concepts of the value of genetic resources to commercial product discovery and development. A regular feature in current industry commentary on the CBD and ABS measures is the need to match expectations of value with commercial realities, and to appropriately value genetic resources in negotiations with companies.

Many companies seek the benefits of better-developed and longer-term partnerships with source country institutions. Partnerships allow companies to access local expertise and resources in areas of interest, and in some cases companies build research capacity to undertake a greater share of discovery, more affordably, in provider countries. Partnerships also provide more insurance to companies that the resources they access are legally obtained. Partnerships also enhance the benefits accruing to provider countries and their institutions, particularly those that build the scientific and technological capacity of countries to undertake research on their own biological diversity. Because provider country scientists play a larger role in discovery when part of partnerships, it also means that financial benefits derived from any commercial product will be more significant. Better-established partnerships also help provider countries monitor the ways samples are collected and used; this is particularly important as scientific and technological advances mean that companies often do not need to go back to providers to re-collect promising species.

Industry perceptions of the CBD and ABS

Industry and researcher perceptions of the CBD, and ABS in particular, have become increasingly negative in the last decade. Some continue to cite the positive role the CBD can play in promoting equitable relationships, conservation and best practices in industry, but many more consider the negative impacts to far outweigh the positive. Rather than coming together over the last 13 years to create simple, workable legal and regulatory frameworks for access and benefit-sharing, providers and users of genetic resources are increasingly estranged, and the environment in which bioprospecting takes place is often characterized by misunderstanding, mistrust, and regulatory confusion. Researchers in both academia and industry also expressed significant concern about the negative impact ABS is having upon basic science and upon traditions of trust and collaboration among scientists.

Recommendations

During the course of this project, a range of recommendations were made by industry and researchers on ways to improve the ABS policy process. They include those to provider country governments on how to make ABS measures more effective; to user country governments on the need to provide ABS support and information to their industries; and to CBD Parties to undertake an on-going process of informing decision-makers about the nature of commercial use of biodiversity.

1. Introduction

This paper provides an overview of recent market and research trends that impact industry demand for genetic resources. It also identifies trends in benefit-sharing, and – 13 years after the CBD entered into force – the impact the CBD, and national ABS policies and regulations, have had on industry demand for and research on genetic resources. The paper also reports on industry and researcher perspectives on the strengths and weaknesses of the CBD, and ABS measures in particular.

As part of the research for this paper, approximately 40 interviews were undertaken in 2005 with a wide range of academic and industry researchers, as well as company executives, government officials, and individuals working on ABS issues for NGOs and other groups. The breakdown of interviews with researchers and industry representatives by sector is as follows: pharmaceuticals: 7; biotechnology: 4 ; seed and crop protection: 5; horticulture: 3; personal care and cosmetic (including fragrance): 4; botanicals: 4; food and beverage: 1.

This paper is an overview of the state of the field today, and in no way can be considered comprehensive. While it identifies the broad parameters of current trends that should impact the design, development, and implementation of effective ABS measures, a far more comprehensive study, or an on-going effort on behalf of the Parties to the CBD to track these developments and perspectives, is warranted.

The paper begins with a review of trends in markets, research and development, and demand for access to genetic resources in five sectors: pharmaceuticals, biotechnology, seed, crop protection, and horticulture. Drawing on perspectives from a broader range of industries - including the cosmetic and personal care, botanical, fragrance, and food and beverage - it then reviews trends in benefit-sharing across sectors and reports on the impact of the CBD, and national ABS policies and regulations, on industry demand for genetic resources. It concludes with recommendations for more effective ABS policy.

2. Industry Profiles

A wide range of sectors undertake research and develop commercial products from genetic resources. They include the pharmaceutical, biotechnology, seed, crop protection, horticulture, cosmetic and personal care, fragrance and flavor, botanicals, and food and beverage industries. Each sector is part of a unique market, undertakes research and development in distinct ways, and uses genetic resources and demands access to these resources very differently. Incorporation of these factors into ABS regulatory frameworks is essential.

Following is a brief overview of five sectors – pharmaceuticals, biotechnology, seed, crop protection and horticulture - that highlights some of the recent market and scientific and technological trends, and the ways they impact demand for access.

2.1 The Pharmaceutical Industry

Market Trends

Pharmaceutical industry global revenues in 2004 topped $500 billion, dominated by sales in North America, Europe and Japan (Table 1). The industry is also concentrated in the US and Europe (Table 3), followed by Japan. Despite poor research and development productivity, the loss of patent protection for some major products in recent years, and pressures for containment

of drug costs, the industry grew around 9% in 2004 (Class, 2004). Companies are adapting to changes in the market and regulatory environment in a number of ways, including moving away from the 'blockbuster' model to smaller niche markets with still significant sales, although 85 blockbusters are expected to account for 30% of global sales in 2005, up from 69 in 1993 (Lewis et al, 2005).

The top 10 companies in 2003 accounted for half of all worldwide sales, but their relative contribution to overall industry growth declined to 41% in 2003 from 53% in 2001. The greatest rates of growth were seen in generic and biotechnology companies (Class, 2004). Biotechnology products account for an increasing share of the market, with 17% growth in 2004. Eighty percent of the biotechnology market was held by just ten firms, with Amgen the leading player (Lewis et al, 2005). [1]

There is continued consolidation in the pharmaceutical industry, although the rate of mergers and acquisitions has slowed in the last few years. Recent 'megamergers' have produced mixed results, with many of the top companies having lower actual market shares in 2003 than the sum of their components in 1998 (Table 2). It has become evident that mergers can actually have a negative impact on R&D productivity, previously cited as a one of the main drivers of mergers and acquisitions. Many analysts now believe that the optimal number of scientists for a successful R&D program is 300-800, with any more being unmanageable. Large companies like Glaxo SmithKline and Lilly are breaking their research teams into therapy areas to promote an 'independent, entrepreneurial spirit' (Class, 2004).

Targeted acquisitions of small biotechnology firms to gain access to a specific product or technology are increasing in importance, as are licensing deals, to make up for unproductive R&D programs in large companies. In 2001, in-licensed products accounted for 16-20% of the top 20 companies' revenue; by 2007 this figure is expected to reach 40%. Some predict that the industry will divide into two, with small R&D boutiques providing candidates for large companies that focus on development, sales and marketing (Class, 2004). This means that smaller companies may be more likely than the largest to seek access to genetic resources for their discovery programs, and that promising compounds will then be licensed to the larger companies for development.

Trends in Research and Development

Pharmaceutical R&D falls into *discovery* – the process by which a lead is found, including the acquisition of materials for screening – and *development* – which includes chemical improvements to a drug molecule and animal and clinical studies. It takes roughly 10-15 years for a compound to make its way through discovery and development into commercialization, and roughly one in 10,000 compounds screened are commercialized (Table 4; see Laird and ten Kate, 1999 for a discussion of the components of R&D).

Despite continual increases in R&D expenditures, including the highest-ever investment in R&D in 2004[2], pharmaceutical industry productivity is significantly lower than in recent years. The number of new chemical entities (NCEs) launched worldwide in 2004 was the lowest for 10 years (Lewis et al, 2005). Of the New Drug Applications approved by the FDA in 2002, only 22% were for NCEs, with the majority being 'me-too' drugs that are new formulations or line extensions of

[1] In 2004 Amgen saw 30% growth and has five of the ten biotechnology blockbusters – Epogen (erythropoietin), Aranesp (darbepoietin alpha), Enbrel (etanercept), Neulasta (pegfilgrastim), and Neupogen (filgrastim) (Lewis et al, 2005).

[2] 2004 R&D investment was $49.3 billion for PhRMA member companies alone (www.PhRMA.org).

existing products. Biotechnology is making an increasing contribution to the industry's bottom line, and biotechnology research tools and techniques are central features of pharmaceutical discovery and development today. Eight of the thirty NCEs launched in 2003 were biotechnology-derived, and 27% of active compounds in industry's pipeline were biotechnology-based[3] (Class, 2004).

Advances in molecular biology, cellular biology and genomics in the 1990s deconstructed disease pathways and processes into their molecular and genetic components to identify the exact point of malfunction, and the point in need of therapeutic intervention. The result was an increase of molecular targets that may be applied to the discovery of novel tools for the diagnosis, prevention and treatment of human diseases from approximately 500 to more than 10,000 targets (Class, 2004; Newman et al, 2003; Bio, 2005).

The development of high-throughput screens based on molecular targets led to demand for large libraries of compounds that might inhibit or activate a specific biological target, such as a cell-surface receptor or enzyme. For much of the 1990s, scientists thought the best way to generate compounds for the screens was through mass-produced combinatorial libraries (Newman et al, 2003; Koehn and Carter, 2005). The importance of natural products as a source of molecular diversity for drug discovery and development was overshadowed by chemical approaches that use combinatorial chemistry and biological approaches such as the manipulation of biosynthetic pathways of microbial metabolites through combinatorial biosynthetic techniques (Cragg et al, 2005). Natural products were considered too slow, too costly, and too problematic from both a scientific perspective (for example, the additional steps needed to identify and isolate active components in mixtures), and for the legal and public relations uncertainties associated with gaining access to genetic resources as a result of the Convention on Biological Diversity. This latter point is dealt with in Section 4.

Box 1. Reasons for the decline in pharmaceutical industry natural products research in the last decade

(Koehn and Carter, 2005)

1. Introduction of high-throughput screening against defined molecular targets (and the move from natural products extract libraries to 'screen-friendly' synthetic libraries);
2. Development of combinatorial chemistry, which appeared to offer more drug-like screening libraries of wide chemical diversity;
3. Advances in molecular biology, cellular biology, and genomics, which increased the number of molecular targets and prompted shorter drug discovery timelines;
4. Declining emphasis among major pharmaceutical companies on infectious disease therapy, a traditional strength of natural products;
5. Possibly uncertainties with regard to collection of biomaterials as a result of the Convention on Biological Diversity.

[3] Biotechnology is transforming drug discovery and development, including high-throughput screening that has revolutionized the process of target identification, DNA sequencing machines that shaved years off the mapping of the human genome, and monoclonal antibodies that transformed the diagnostics industry and are now used in treatments (Ernst and Young, 2005). Biotechnology techniques used in drug discovery and development include: bioprocessing (using living cells to manufacture products such as human insulin); monoclonal antibody technology (using immune system cells that make antibodies to target treatments to specific cells); molecular cloning (creating genetically identical DNA molecules); and recombinant DNA technology (combining and modifying genes to create new therapies) (PhRMA, 2005).

Despite the contributions of natural products to industry's bottom line[4] (see Chart 1), particularly in categories like infectious disease and cancer[5], natural products experienced a slow decline over the past two decades due to both scientific and commercial considerations (Koehn and Carter, 2005; See box 1). Disease categories for which natural products are well suited – in particular infectious disease – lost ground within companies (Koehn and Carter, 2005; Handelsman, 2005). The US pharmaceutical industry essentially abandoned antibiotic discovery around 1990, even as resistance problems were emerging. Antibiotics have limited profitability (compared with those taken over long periods of time for chronic conditions) and there was a misplaced belief of having conquered infectious diseases. Wyeth's tigecy-cline released in 2005 is the first new class of antibiotics to be introduced to the market in 20 years (Handelsman, 2005).

After a multi-billion dollar investment in combinatorial chemistry since the late 1980s, however, large pharmaceutical companies have found very little in the way of new structurally diverse entities, and their pipelines are all but empty. The percentage of synthetics as new chemical entities (NCEs) has remained roughly the same (see Chart 2; Newman, 2005). It is now widely agreed that while combinatorial chemistry is a valuable development tool for optimization of leads, including those from natural products, it does not yield much in the way of new molecular diversity.

At the same time the limitations of combinatorial chemistry have become evident, breakthroughs in technologies (eg in separation and structure-determination) have made screening mixtures of structurally complex natural product molecules easier, and have expanded the potential role of natural chemical diversity in the drug discovery process (Koehn and Carter, 2005). Expanded understanding of the genes involved in secondary metabolite biosynthesis also mean that researchers can now discern the complex chemical structure of a secondary metabolite which will result from the enzymes produced following expression of a particular set of genomic sequences. This makes "genome mining" of even well-known natural products a potentially powerful new approach to natural product discovery (McAlpine et al, 2005). Advances in synthetic chemistry have revolutionized the process of material supply, making it possible to recreate almost any compound in the laboratory, and addressing one of the fundamental concerns in natural product discovery, the 'supply issue' (Koehn and Carter, 2005). The result of these developments is renewed interest in natural products as a source of chemical diversity and lead generation, and a view of natural products and combinatorial synthesis as complementary rather than stand-alone approaches (Koehn and Carter, 2005). [6]

Demand for Access to Genetic Resources

Despite renewed interest in natural products, most large companies are not at present expanding their in-house natural products programs, but they are licensing in, or forming partnerships, with small companies and universities that generate interesting leads from natural products discovery research. However, the same technological and scientific developments that make natural products more interesting again, also mean that a great deal of research can be done in

[4] See, for example, Newman et al, 2003; Newman, 2005; Newman and Laird, 1999.

[5] In addition to infectious diseases, cancer drugs draw heavily upon natural products, and companies with aggressive oncology programs, like Novartis and Bristol Myers Squibb, maintain natural products R&D programs in this area. Newman et al (2003) undertook a study of natural products as sources of new drugs from 1981-2002 and found drugs of natural origin predominate in certain disease categories like cancer and infectious disease, despite the expansion of combinatorial chemistry in the 1990s.

[6] Newman et al (2003) suggest the best solution to the current productivity crisis is "…a multidisciplinary approach to drug discovery that involves the generation of truly novel molecular diversity from natural product sources, combined with total and combinatorial synthetic methodologies, and including the manipulation of biosynthetic pathways (so-called combinatorial biosynthesis)." (p 1036).

laboratories or on a computer looking at the genomes of already known organisms. Analysis, using new scientific and technological tools, of the genome of the well-characterized microorganism *Streptomyces aizunensis*, for example, produced novel and highly defined structures (McAlpine et al, 2005). Demand for access to 'new' natural products is therefore different in approach and character to that of previous cycles of natural products research.

Microorganisms
While plants, insects, marine and other organisms are still of interest to natural products researchers, the trend over the last 5-10 years is towards microorganisms. Metagenomic technology allows researchers to extract DNA directly from microorganisms found in environmental samples, making available the 99% of microbial diversity previously inaccessible through traditional cultures, while at the same time discovering a far greater number of secondary metabolities in a given organism by 'genome mining' (Handelsman, 2005; McAlpine et al, 2005; see section 2.2 for a discussion of micororganisms). The genomes of micoroganisms can be more easily sequenced than those of plants or insects, and can be grown in culture, rather than collected (eg plants), which makes it easier for companies to deal with supply issues as research progresses (although synthetic chemistry is making it possible to produce most compounds in the laboratory).

Marine organisms
The last 10 years have also seen a surge of interest in marine organisms. Marine chemistry is new to natural products chemists, but already approximately 20 marine natural products are in clinical trials, and 34 of the 36 phyla of our planet's biodiversity is found in oceans (only 17 are found on land) (William Fenical, SCRIPPS, pers.comm.., 2005). The US National Cancer Institute has reduced its interest in plants and is now focusing its collections on marine organisms. Although plants can still provide invaluable leads for other disease categories, they have not been as promising for anti-cancer agents. Marine organisms live in extremely hostile environments, and in a perpetual state of 'chemical warfare' that produces potent toxins, and a number of novel compounds that work in a way similar to existing anti-cancer agents have been found (David Newman, NCI, pers comm., 2005).

Complex associations between organisms
It is also increasingly recognized that distinctions between organisms – plant, marine, invertebrate, microorganism – are not always clear-cut, and that promising compounds may in fact be produced by symbiotic microbial species (Cragg et al, 2005). For example, in 1972 researchers working with the US National Cancer Institute isolated maytansines from an extract of *Maytenus serrata* collected in Ethiopia, and subsequently found them in other *Maytenus* and *Putterlickia* species. However, recollections of the plants, cell cultures, and greenhouse-grown plants did not yield the active compounds. In recent years, it was found that microorganisms isolated from the rhizophere appear to be responsible for producing the active compounds, perhaps with plants playing a role in determining the final chemical structures (Yu and Floss, 2005). Toxins in birds feathers or secreted by reptiles have been found to originate in insects they eat; promising compounds from insects are traced back to the microorganisms living in their gut; and marine invertebrates have been found to undertake the bulk of the chemistry that produces an interesting compound, which is then modified by associated microorganisms, or vice-versa. Through co-evolution a spectrum of complex community associations, rather than single organisms, appear to be the source of many promising compounds.

Demand for diversity

These associations get to the heart of another on-going discussion within natural products research: the need for accessing 'new' biological diversity to fuel discovery. New research tools mean that diversity found in one's 'backyard', particularly that found in the previously inaccessible genomes of microorganisms, and even those of known microorganisms (eg McAlpine et al, 2005), can keep researchers busy. A number of researchers feel that for microorganisms "every species is everywhere" and that there is enough at home, or in a few provider countries, to fuel research for many years to come. But as Jo Handelsman of the University of Wisconsin-Madison put it (pers.comm., 2005): "Until very recently I used to think that 'everything is everywhere', and it is true that going into any backyard is like going to Mars. But even if every species is everywhere, members of the same species will produce different secondary metabolites in different places, and I think it is unlikely that all species are indeed everywhere. Insects, for example, have highly specific associations with microorganisms, with some microorganisms known only to exist inside one species of insect. No one would argue that insect diversity in the tropics is not unique, so if macrodiversity is unique, it is likely that the associated microdiversity is as well. We really don't know, and it is premature to make those judgements, because we are so far from having a complete census of the microbial world. It is very possible that most microorganism species are everywhere, but that the most interesting strains are not." The same advances in science and technology that currently make many research programs focus on existing collections or materials easily available at home, may very well lead to expanded interest once again in a broader range of biological diversity.

Supply issues

A decade ago, the unknown associations between organisms created issues with re-supply, and researchers at times faced difficulties re-locating individual plants or marine organisms that produced the active compounds. However, today DNA is isolated and expressed in an external host for mass production, so this circumvents that element of the supply issue. The technology is still developing, and all genes cannot be expressed in this way, so there is still some demand for re-supply along a continuum from full synthesis, to semi-synthesis from a precursor taken from the raw material produced in culture, and so on. However, the need for re-supply of material for research and development, and in some cases commercialization, was until recently an important component of the relationship between providers and users, and served as a useful incentive for users to establish solid partnerships with providers. While advances in technologies also make it easier to trace plant, marine and other compounds back to the source, it is much more difficult to do this with microorganisms. The need for providers and users to develop strong partnerships as a way of monitoring development of natural product compounds is far greater today than even a few years ago, and will continue to grow in importance.

Demand for traditional knowledge

The role of traditional knowledge in pharmaceutical discovery has been relatively small in recent decades (see Laird and ten Kate, 1999), but appears to be growing smaller. In part this is due to the emphasis of pharmaceutical drug development on disease categories that do not feature prominently in traditional medicine, but it is also due to the increasing role of microorganisms, and the diminished role of plants, in discovery. [7] It is also the case that new research approaches do not easily integrate the type of information available through traditional knowledge, however companies will still consult the literature and databases following a promising lead.

[7] However, many traditional healers collect from very precise locations and make distinctions between individual plants that do not correspond to taxonomic differences. Individual plants found in a particular location, for example, will have properties that are not found in other locations, quite possibly due to microorganism associations.

The CBD
Although scientific and technological developments, and commercial considerations, have resulted in increased interest in microorganisms, and marine organisms, it also appears that the CBD and concerns associated with gaining access and legal title to material, and re-supply of raw material for research, have played a role. We will discuss these issues further in Section 4, but it is important to note that many researchers include difficulties in gaining access to materials as a factor driving research away from the bioprospecting models of the 1980s and 1990s (see Koehn and Carter, 2005; Box 1).

2.2 The Biotechnology Industry

Biotechnology is the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods, and services (OECD,2005). It includes a diverse collection of technologies that manipulate cellular, sub-cellular, or molecular components in living things to make products or discover new knowledge about the molecular and genetic basis of life, or to modify plants, animals, and micro-organisms (US Department of Commerce, 2003).

The biotechnology industry spans a wide range of sectors, and can be broken down into industrial, agricultural, and healthcare biotechnology. Agricultural biotechnology (see section 2.3) comprises 7% of European and 5% of US biotechnology companies (EuropaBio, 2005). Health care biotechnology (see section 2.1) is the largest and most profitable sector, comprising 51% of European and 60% of US biotechnology companies, and accounting for a majority of industry revenues (EuropaBio, 2005). Following a discussion of market trends for all elements of the biotechnology industry, this section focuses on industrial biotechnology, which uses living cells like moulds, yeasts or bacteria, as well as enzymes, to produce goods and services. Industrial biotechnology applications may create more efficient and cost-effective industrial processes that produce less waste, and use less energy and water in such sectors as chemicals, pulp and paper, textiles, food, energy, and metals and minerals (Bio, 2005; EuropaBio, 2005). In some cases, environmental biotechnology products make it possible to clean up hazardous waste more efficiently by harnessing pollution-eating microbes without the use of caustic chemicals. (Bio, 2005).[8]

Market Trends
The global biotechnology industry had revenues of $54.6 billion in 2004, a 17% increase over 2003. The US dominates the industry, accounting for 78% of global public company revenues, followed by Europe at 14%, Canada at 4% and the Asia-Pacific region at 4% (Ernst and Young, 2005; Table 5). In 2005, the top 12 biotechnology countries, ranked by number of biotechnology companies (private and public), were: the US, Canada, Germany, UK, Australia, France, Sweden, Israel, China and Hong King, Switzerland, India and The Netherlands (Ernst and Young, 2005). The largest companies are primarily found in the US (see Table 6).

Biotechnology firms vary greatly in size and scope, ranging from small, dedicated biotechnology companies that are R&D-intensive to large, diversified companies that have greater in-house resources and well-established production and distribution systems. In a survey undertaken of the

[8] Industrial and specialty enzymes produced an estimated $3.6 billion in revenue in 2000 (www.Diversa.org, 2005).

US biotechnology industry, 90% of firms had 500 or fewer employees, and only 19 (2%) had more than 15,000 (US Department of Commerce, 2003).

The majority of biotechnology companies operate primarily on venture capital, grants, initial public offerings and collaborative agreements, and the state of this research-intensive industry depends heavily upon the availability of these forms of financing (US Department of Commerce, 2003). Biotechnology companies need external capital to act as a catalyst for growth in early years, fund R&D, and allow them to build on their intellectual property without the need to develop a separate infrastructure to generate revenues to fuel the business (EuropaBio, 2005).[9]

After the collapse of the boom market for biotechnology companies in 2001, the investment cycle entered a 'bust' phase and investors stayed away from the sector. Companies responded by restructuring, spinning off assets, reducing cash burn rates, refocusing their business models to place more emphasis on product development and commercialization and less on technology platforms, and forming alliances with other companies (EuropaBio, 2005; Ernst and Young, 2005).[10] By 2004, a surge of products in the late-stage pipeline and product approvals[11], as well as better-articulated company paths to products and profitability, had drawn investors back to what is now considered a more mature industry (Ernst and Young, 2005).[12] At the same time, partnerships between biotechnology companies, and between biotechnology and pharmaceutical companies, continue. Biotechnology companies need capital and pharmaceutical companies, concerned about the effect their innovation deficits will have on future earnings, need products (EuropaBio, 2005).

Trends in Research and Development

Biotechnology is one of the most research-intensive industries in the world. In the US, biotechnology-related R&D accounted for roughly 10% of all US industry R&D in 2001 (US Department of Commerce, 2003). New biotechnology research tools have enabled researchers to tease apart cellular and genetic processes, and to understand biological systems at the molecular level. Biotechnology research tools have changed the research questions scientists ask, the problems they tackle, and the methods they use to get answers (Bio, 2005). Biotechnology includes bioprocessing technology, monoclonal antibodies, cell culture, recombinant DNA technology, cloning, protein engineering, biosensors, nanobiotechnology, and microarrays. The need to integrate the pieces of data generated by biotechnology into an understanding of whole

[9] A study by EuropaBio found that the biggest barrier to development of the European biotechnology industry was the lack of a suitable financial infrastructure later in the business cycle. While US companies raised $2.4 billion in venture capital in 2004, sold an additional $3.3 billion worth of equity in 2004, and raised a further $3.3 billion in debt in 2004, European companies raised $771 million in venture capital, $1.3 billion through equity, and $820 million in debt financing in the same year (EuropaBio, 2005).

[10] Examples of biotechnology/biotechnology deals includes Idec Pharmaceuticals $4.2 billion all-share merger with Biogen, Amgen's $7.8 billion acquisition of Immunex, and the range of acquisitions made by Genzyme Corp in recent years. Pharmaceutical giants such as Novartis, Pfizer and Johnson & Johnson have also acquired biotechnology companies in recent years, but the most common relationship between pharmaceutical and biotechnology companies remains discreet biopartnerships (EuropaBio, 2005).

[11] In the US, 365 products were in Phase II clinical trials in December 2004, compared with 290 the previous year, and as of early 2005 there were 55 new drug application submissions under review at the FDA. European companies brought 9 products to market in 2004, compared with 6 in 2003 (Ernst and Young, 2005).

[12] The global biotechnology industry raised $21.2 billion in venture capital in 2004, a 15% increase over the capital raised in 2003, and IPOs raised $2 billion in the US, Europe, and Canada in 2004, compared with $450 million in 2003. Asia-Pacific companies raised about $500 million through Initial Public Offerings in 2004, led by offerings in Australia, Japan, and India (Ernst and Young, 2005).

systems and organisms has given rise to other new information technologies called the "omics" - genomics, proteomics, metabolomics, immunomics, and transcriptomics. At the same time, new bioinformatics technology uses computational tools provided by the information technology revolution - such as statistical software, graphics simulation, algorithms and database management – to consistently organize, access, process, and integrate data from different sources (Bio, 2005). [13]

These new technologies have changed new product discovery, and identified new uses for existing products, by helping researchers understand the basic biology of the processes they want to control or change, and manage vast quantities of data. They have also made product development quicker and often cheaper. For example, pharmaceutical companies can better identify molecular targets, pinpoint winning compounds far earlier in the discovery process, and use cell culture and microarray technology to test the safety and efficacy of drugs and observe adverse side effects early in the drug development process; agricultural biotechnology companies developing insect-resistant plants can measure the amount of protective protein that a plant cell produces and avoid having to raise the plants to maturity (Bio, 2005). Combined, these technologies are leading to synthesis of living organisms from scratch. Venter (2005) notes how science is moving from "reading the genetic code to writing it", predicting that within 2 years it will be possible to synthesize bacteria, and within 10 years single-cell eukaryotes. Increasingly, technological changes are enabling biological materials to exist in a 'virtual' as well as an actual state (Parry, 1999).

The Role of Genetic Resources in Biotechnology R&D

The ways biotechnology companies use genetic resources vary significantly by sector. Some companies develop specialty enzymes, enhanced genes, or small molecules for use in crop protection and drug development; others develop enzymes that act as biological catalysts in the production of polymers and specialty chemicals, or for use in industrial processing; and others might insert genes that impart desirable traits into crops. The pharmaceutical, crop protection, and seed industries are dealt with in other sections. The remaining biotechnology market is primarily focused on the use of enzymes, which we will review here.

Enzymes are proteins found in every living organism and are the 'tools of nature", ie they cut and paste products and speed up vital biological processes in cells. They have been used for more than 60 years by textile, detergent, food, feed and other industries, to make higher-quality products and make production processes more cost-effective and efficient, and therefore more environmentally-sound by minimizing the use of water, raw materials and energy. Since they are biodegradable, enzymes are also a more environmentally-sound substitute for synthetic chemicals (Novozymes.org, 2005).

Enzymes used by industry are usually found in microorganisms, in particular bacteria and fungi. Microorganisms are the world's most genetically diverse organisms, and include bacteria, archae, fungi, yeasts, and viruses. Through billions of years of natural selection in dissimilar environments, microbes have developed broader and more varied characteristics than those observed in plants or animals, while silently enabling and supporting life for larger plants and animals (Mathur et al, 2004).

Microorganisms called extremophiles are of particular interest to researchers today because they live in environments similar to those required by industrial processes, and reflect the necessary

[13] For a full description of these technologies and their applications, see: *Guide to Biotechnology*, Biotechnology Industry Association, www.bio.org, 2005.

range of conditions - for example, extreme hot or cold temperatures, or acidic or salty conditions. For example, starch and baking require high temperatures and low pH; textiles, pulp and paper, and detergents a high temperature and high pH; and dairy and food a low temperature and low pH (Lange, 2004). As technologies to collect and study extremophiles advance, commercialization of processes and products derived from extremophiles is likely to increase (Arice and Salpin, 2005).

Recent advances in bio- and information technologies allow target compounds from environmental samples to be identified much more rapidly. Microorganisms were traditionally isolated and cultured in laboratories, a process that requires scientists to recreate the environments in which the target microbe lives, and as a result less than 1% of the billion plus microbial species have been studied (Mathur et al, 2004). Today, using metagenomics – the culture-independent analysis of assemblages of uncultured microorganisms - DNA is extracted directly from a soil, water or other environmental sample, it is cut with restriction enzymes, and cloned into a culturable host such as *Escherichia coli* (Handelsman, 2005). The host organism will then produce the biochemicals from which commercially valuable enzymes and other biomolecules are developed. Using computer-assisted techniques such as massive parallelism and randomness, genome sequencing can now occur at a speed previously unheard of. In 1995, for example the first genome sequence was described (for *E. coli*) – a task that then took 15 years and today could be done in less than a day (Venter, 2005).

Demand for Access to Genetic Resources

A striking trend over the past five years has been the vigorous attention given to micro-organisms. The astounding numbers and diversity of microbes, combined with their all-pervasive existence – from thermal vents to the subglacial environments of Antarctica – and advances in technological development, have led to renewed interest in their use for energy saving, climate control, pollution control, biomaterials, and many other applications.

Biotechnology companies continue to demand access to genetic resources, which are either collected from nature or acquired through external collections. Microorganism samples needed for biotechnology research tend to be small – typically a few grams of soil or milliliters of water - and recollection is not usually necessary. The majority of companies and research institutes maintain in-house collections of genetic resources, including microorganisms, plants, insects, human genetic material, animals, fungi, bacteria, and derivatives of these resources such as enzymes, purified compounds, and extracts. Researchers access *ex situ* materials from the collections of companies, universities, national culture collections, and international collections (eg the International Mycological Institute) (ten Kate, 1999).

Most collections made by biotechnology companies outside of pharmaceuticals and agriculture are microorganisms. Insects, plants, animals, marine organisms and others continue to hold interest, although often for their associated microorganisms. Biotechnology companies do not incorporate traditional knowledge into their collecting programs, in part due to their emphasis on microorganisms, but also because their research approaches and technologies do not lend themselves to incorporation of this type of information (Lange, 2004; Mathur, 2004).

When collecting from nature, companies are interested in samples from diverse and extreme environments and ecological niches (eg salt lakes, deserts, caves, hyrothermal vents, cold seeps in the deep seabed), as well as areas with microbial diversity associated with endemic flora (eg epiphytes, endophytes and pathogens) and fauna (eg insects, pathogens and endosymbionts) (Lange, 2004; Arico and Salpin, 2005). The objective of micro-organism collection is *biochemical* diversity, which can be found not only by collecting in areas with high species diversity, but also in extreme environments or unique ecological niches (Lange, 2004). To access

regions high in microbial diversity, for example, Diversa, a publicly traded US biotechnology company whose business involves the discovery and evolution of novel genes and genetic pathways from unique environmental sources, has entered into 18 partnerships with groups providing access to genetic resources in 10 countries across six continents, and to all international waters around the world (Diversa, 2005).

The Venter Institute has likewise, through 'Sorcerer II', embarked upon a global expedition to sample microbial abundance and diversity in marine and coastal environments describing, in its initial findings a situation where 85% of data collected is unique to each site. Findings from the Sorcerer II's voyage will be used, among other things, to: design and engineer species to replace petro-chemicals; better understand reef health; analyze drinking water and air quality; track and avoid emerging viruses; and understand the effects of ballast water, where ships flush micro-organisms from one part of the world into the seas of another (Venter, 2005). The related 'Air Genome Project' of the Venter Institute aims to determine the numbers of new protein families from air-borne bacteria. Initiatives such as these throw up a host of new questions and challenges with regard to access and benefit-sharing, in particular relating to the sovereignty of microbes and the difficulties of ascribing ownership.

While initiatives such as these signify an accelerated increase in collecting microbes at a global scale, there are also companies that believe that new scientific and technological developments, coupled with the astounding diversity often found in their own 'backyards' or in existing collections, do not necessitate prospecting overseas.

Recent trends in science and technology have impacted demand for genetic resources from nature in both positive and negative ways. The poor showing of combinatorial chemistry and synthetic compounds over the last decade, limitations to protein engineering, and a realization that natural solutions to the pressures of evolution have come up with things that could not be engineered in the laboratory, have made genetic resources in nature more attractive candidates for discovery. The ability to isolate DNA directly from samples, without resorting to culturing, also means that the vast genetic diversity in microorganisms can be accessed. At the same time, however, new scientific and technological developments mean that more diversity can be generated in the laboratory through molecular biology, shuffling, and protein evolution, and tools like bioinformatics allow researchers to hunt, not in nature, but in existing genome sequences and databases, for novel proteins and enzymes. Bioinformatics and sophisticated molecular biology tools also mean that for each sample collected, a great deal more information is gleaned, and so only a few strains are needed to keep research programs busy in a given year.

Novozymes, the leader in biotechnology-based enzymes and microorganisms, with more than 700 different products, net turnover of DKK 6,024 million in 2004, and 4,000 employees, has long-standing partnerships in Thailand and other countries for sample collection (novozymes.org, 2005; Lange, 2004). Although patents have been filed on interesting developments, no new products have been developed from collections made since the CBD entered into force. The 5-6 new products that come out each year primarily derive from a handful of well-known strains that continue to yield valuable products (Lange, pers. comm., 2005).

Diversa, on the other hand, has developed a number of new products from its collections undertaken with partners overseas. For example, Luminase - which enhances the reactivity of pulp fiber to bleaching chemicals and reduces the need for chlorine dioxide and the cost of pulp processing - was developed from a microbe discovered in a thermal feature in Kamchatka, as part of a research partnership between the company and the Center for Ecological Research and BioResources Development (CERBRD) in Russia. Diversa estimates the potential market for

Luminase at $200 million. Another Diversa product, Cottonase, reduces the use of harsh chemicals, extreme temperatures and large volumes of water in cotton scouring (diversa.com, 2005). [14]

2.3 The Seed, Crop Protection and Plant Biotechnology Industries

The seed, crop protection and plant biotechnology industries all use wild genetic resources, although their dependence on these resources varies considerably across and within each sector. The seed sector in general is far more reliant on breeding material from its own private collections or from genebanks than from that collected from the wild, whereas the crop protection sector has a greater interest in wild genetic resources for chemical protection or plant improvement. All however share a focus on the 130 species responsible for feeding humankind and in many cases those crops cultivated on a large scale. This needs to be considered in the context of just nine crops – wheat, rice, maize, barley, sorghum/millet, potato, sweet potato/yam, sugarcane and soybean – accounting for over three quarters of the plant kingdom's contribution to human energy, with wheat, rice and maize providing more than half of this amount (Fowler & Mooney, 1990).

Industry Overview and Market Trends

The use of genetic resources in the breeding and sale of agricultural products involves a diverse group of players, including the private sector, universities and other research institutions, public and private genebanks, farmers and a variety of other organisations. A notable trend since the 1930s has been a shift towards increased involvement of the commercial sector, culminating in the 1990s with the integration of the seed industry into food and agrichemical companies and the formation of the so-called 'life science giants' (ten Kate, 1999).

The seed industry is characterized by three levels of companies: life science giants, large multinational firms, and small and medium-sized enterprises. The first two tiers play a central role in the seed trade, but small and medium-sized seed companies, of which there are several thousand, are also significant and occupy different market niches. For larger companies, the emphasis is on high value seed such as maize, soybean, cotton and canola, and vegetables such as tomatoes, peppers and melons (Smolders, 2005). Smaller companies in contrast focus on vegetables, grasses and more marginal crops. Most of the larger companies also have active interests in agrichemicals and pharmaceuticals.

An intensifying trend over the past decade has been the continued consolidation of the seed, crop protection and plant biotechnology industries, and consequent increase in the available genepool (Bijman, 2001; ten Kate, 1999). Currently, just ten companies control 49% of the global seed market, with an increased trend towards acquisitions and mergers (Table 7). There is a great deal of overlap between seed and agrichemical companies (See Tables 7 and 8).

Higher levels of concentration are evident at the level of crop, region or trait. For example, Monsanto alone – through licensing or direct sales - accounted for 88% of total genetically modified (GM) crop area worldwide: 91% of GM soybeans, 97% of GM maize; 64% of GM cotton; and 59% of GM canola (ETC, 2005).

[14] Cottonase grew from the companies' collaboration with the National Institute of Biodiversity (InBio) in Costa Rica (Leif Christofferson, pers. comm., 2005).

The crop protection industry likewise is concentrated in the hands of only a small number of multinational companies (Table 8). They pursue a range of approaches to crop protection, including chemical control – which uses chemical compounds to kill pests; biological control – which uses living organisms; and genetic modification of the crop plant itself – which introduces diseases and herbicide resistance into crops through GM and traditional crop breeding techniques. As ten Kate (1999) notes, all three approaches require access to genetic resources.

In 2004, global commercial seed sales were estimated at between $21 billion (ETC, 2005) and $30 billion (International Seed Federation, 2005a) (Table 7). GM seed – predominantly soya, maize, cotton and canola - comprises about 16% of this trade, based on a total trade figure of $30 billion (James, 2004). Major seed companies report a gross profit of about 50% or higher and aim to have a mid-term EBITDA (Earnings before Interest, Taxes, Depreciation and Amortization) of 25% on sales or higher. Table 9 gives a breakdown per crop of the value of exported seed of major crops, indicating the high relative value of maize, herbage crops, potato and beet.

In the crop protection sector, sales were US$27.7 billion in 2002, representing an overall decline of 12% over five years (Agrow, 2003). Herbicide sales constitute the bulk of sales, accounting for almost 50% of the total crop protection market in 2002, with insecticides comprising 25.3%, fungicides 21.6% and others about 3.4% (CropLife International, 2002). In 2003, genetically modified crops represented 15% of the global crop protection market (James, 2004).

The rapid uptake of GM crops has been one of the most profound industry trends over the past 5-10 years, escalating at a rate that surpasses than of any new technology ever embraced by the agricultural industry. From 1996 (the first year of commercial plantings) to 2004, the global area of GM crops increased more than 47 fold, from 1.7 million hectares in 1996 to 81 million hectares in 2004 (James, 2004). Leading growers of GM crops are dominated in the main by the United States (59% of the global total) and Argentina (20% of the global total) (Table 10). The most commonly planted GM crop is soya, and 55 per cent of the world's soya crop, covering 48.4 million hectares, is now genetically modified (James, 2004). GM maize was planted on 19.3 million hectares worldwide in 2004, an increase of a quarter over the previous year; GM cotton was grown on 9 million hectares; and GM canola occupied 4.3 million hectares.

In 2004, the global market value of genetically modified crops was $4.70 billion, calculated on the basis of the sale price of GM seed plus any technology fees that apply (James, 2004). The value of GM crops since they were first commercialized in 1996, is an estimated $24 billion (James,2004).

Trends in Research and Development

In common with other areas of the life sciences, there have been substantial scientific and technological changes in the seed and crop protection industries over the past 5-10 years, stimulated in the main by advances in genomics, combinatorial chemistry, information technology and DNA technology.

Traits that improve performance and farming efficiency for major crops have comprised a major focus area for large seed companies, with the development of high value commercial lines through advanced marker-assisted selection and breeding techniques (Smolders, 2005). For smaller seed companies, levels of technological investment have in contrast been much lower, with the development of DNA markers, for example, not being pursued for varieties where margins are low (eg grasses) (Noome, Advanta Seeds, pers. comm., 2005).

In the crop protection industry, chemical discovery has been aided significantly through the use of genomics to identify suitable product candidates, and combinatorial chemistry which has increased the number of products subject to biological screening. A key trend has a shift in expenditure from conventional agrichemical research to an expansion of in-house R&D efforts on transgenic crops (Phillips McDougall, 2005). Rising R&D costs in combination with a stagnant market for crop protection products have also led to a continued focus on major crops that are cultivated on a large scale, like cereals, oilseed crops, and cotton (Bijman, 2001)

Agronomic traits such as herbicide resistance – guaranteed to bring high returns when used – have dominated R&D efforts for GM crops, and in 2004 over 70% of all hectares planted to GM crops, including soybean, maize, canola and cotton included this trait. Insect resistance has also comprised a major focus, with 19% of GM crops in 2004 planted to insect resistant crops. An important trend is the continued development and introduction of second generation traits (plant varieties that have one or more output characteristic modified), as well as combined or stacked traits, intended to improve the performance of transgenic crops. Stacked genes for herbicide tolerance and insect resistance, used in both cotton and maize, now account for 9% of all GM crops (James, 2004).

Breeding efforts reflect an emerging division of labour between the public and private sector, with the former largely devoted to open-pollinated crops and the latter tending to work predominantly on hybrid crops (Rangnekar, 2005). However, this is not the case all over the world. For example, in Europe, much breeding work is done by the public sector on cereal seed, whereas almost all work on soybean and cotton is private (Le Buanec, International Seed Federation, pers. comm., 2005). A striking trend has been the escalation of private sector interest in agricultural research and associated decline in public sector research. In the US, for example, private sector spending on crop variety R&D increased 14-fold between 1960 and 1996, with research focused predominantly on marketable input and output traits of corn, soybeans, and cotton (Fernandez-Cornejo & Schimmelpfennig, 2004). In the public sector, this same period saw a change in research focus towards minor crops and public goods such as environmental protection and food safety, areas less attractive to the private sector because of lower profit potential (Fernandez-Cornejo & Schimmelpfennig, 2004).

Although there has been private sector interest in agricultural research for decades, its accelerated development has arisen in part because of the advent of genetic engineering, and also because many of the technologies used can receive patent protection. Companies are therefore able to earn higher returns from their agricultural research than they could from conventional plant breeding. However, IFPRI (2005) and others note that nearly all R&D done by the private sector has been based on crops and traits important to developed-country farmers, with little attention paid to crops important to poor farmers[15].

A growing trend towards increased public-private partnerships aims to address these divergences. One example is a partnership between Syngenta and various universities and public research institutions to develop *GoldenRice*™, a GM crop manipulated to deliver Vitamin A to its consumers (IFPRI, 2005).

Increased attention is also being given to improving old varieties, using the new tools of genomics and modern biotechnology. The improved flavouring of crops such as tomatoes, for

[15] An alternative viewpoint is that crops such as soybean, maize and cotton and traits such as herbicide and insect resistance are not exclusively tailored towards developed countries (Le Buanec, International Seed Federation, pers. comm., 2005).

example, has received renewed attention, and old varieties with a long history of research and development are now being considered anew.

Despite growth trends in GM crops, many European-based companies have reported a decline in biotechnology research, linked predominantly to consumer resistance and environmental concerns. One opinion voiced is that modern biotechnology may provide an advantage for specific crops with particular problem diseases, but that its application is limited and is often not cost-effective. However, opinions on this matter are widely conflicting.

Technological change and patents have been major drivers of the consolidation of the global seed and crop protection industries and, through achieving vertical and horizontal integration, companies have been enabled to consolidate research efforts and enhance control of distribution channels and agricultural inputs (CIPR, 2002; Rangnekar, 2005). In the 1980s, for example, the university and public sector accounted for 50% of US patents relating to genes encoding various forms of insect toxins from the bacteria *Bacillus thuringuensis* ("Bt"), now used widely in GM crops to confer insect resistance. By 1994, 77% of patents in this area were held by small biotechnology start-up companies. By 2004, consolidation in this sector and acquisition of small biotechnology start-ups, resulted in over 65% of patents relating to the insect-resistant trait incorporated into GM crops being held by the top five biotechnology companies (Rangnekar, 2005).

Some analysts suggest that due to reduced threats of competition, increased consolidation and increases in market concentration have reduced the incentives to invest in research, and have led to surviving firms devoting fewer resources to innovation. Others note that seed companies are increasingly doing less or no basic research and that exotic germplasm and landraces are perceived as having little practical value for a seed company, with their introgression into breeding lines being time-consuming and risky (Smolders, 2005). Currently R&D investments in leading seed companies stand at about 10 (+/- 2)% on sales, compared to 23.2% recorded in the "euphoric" period for biotechnology in 1988/89 (Smolders, 2005). R&D investment varies by crop and is typically higher for fruity vegetables and substantially lower for open-pollinated small grains, peas and beans.

Budget allocations for the exploration of wild genetic resources vary considerably depending on the crop. Sugar beet, for example, requires no wild collection whereas vegetables may have an allocation as high as 10%, especially for crops where traits such as insect resistance are paramount. Typically, about 1-3 % of the total research budget is applied to exploratory breeding, equalling about 0.1-0.3% of the overall turnover of the company.

Investments in new product discovery are substantially higher for the crop protection industry. A recent survey of R&D in ten leading crop protection companies indicates an overall R&D expenditure of $2250 million, equivalent to 7.5% of sales for these companies in 2004 (Phillips McDougall, 2005). About 54% - or 4% of sales - of the total industry R&D budget is devoted to the process of new product discovery and development, most of this due to expenditures in chemistry- and biology-based research programmes, with the discovery process alone accounting for 31% of the R&D budget. A growing trend is towards greater expenditures in environmental risk assessment and human health risk assessment, driven predominantly by consumer concerns and regulatory requirements (Short, 2005). However, several companies have only limited new product discovery programmes, and use methods such as product acquisition and licensing, joint ventures and generic product manufacture to enhance their product portfolios.

Demand for Access to Genetic Resources

Although a prevalent trend within the seed industry, and particularly for commodity crops, seems to be reduced dependence on wild genetic resources, this varies considerably depending on the size and nature of the company, and the type of resources under investigation. High levels of interest in wild genetic resources are still evident for example where new inputs are needed on quality, to meet consumer demands, and to reduce vulnerability to pests and diseases. Demand for wild genetic resources for vegetables and flowers (and for plant genetic resources not covered by the FAO International Treaty on Plant Genetic Resources for Food and Agriculture) is also greater than for commodity crops.

A central question is the extent to which the industry is dependent upon diversity. Crop varieties and animal breeds, for example, are often selected for domestication characteristics, which are typically contrary to those characteristics that enable their survival in the wild. Much of this diversity is now conserved ex situ in gene banks or breeders' materials although coverage of 'minor' crops such as root crops, fruits and vegetables remains incomplete (Rubenstein *et al*, 2005). As Stannard (2005) notes, in wild resources most value lies at the species level.but for agricultural resources, the value lies *within* crop and animal species, and in the complexity of their genepools that have been built up by farmers over thousands of years.

Several seed industry representatives have commented on the fact that DNA technology, genomics and other technologies have given greater insight as to what is available, leading to the in-depth use of genetic resources already existing in breeding programmes and genebanks, rather than requiring new collection: "We are looking at old material with new eyes; existing material has aspects that were not recognised before". However, as Rubenstein et al (2005) remark, agricultural production increasingly relies on 'temporal diversity', requiring varieties to be changed more frequently to maintain resistance to pests and diseases.

The crop protection industry in contrast has increasing interest in wild genetic resources to improve the plant or to produce chemical protection. This increased interest in natural compounds is predominantly driven by environmental concerns and consumer demand for reduced use of chemicals. "Because of the consequences of chemical use, we are looking at new options and ways to improve the product itself", commented a representative from a multinational crop protection industry.

A crucial factor determining the demand for genetic resources in the seed and crop protection industries is the effort required to turn them into usable resources. Genetic resources that widen a company's genepool but without identified properties of interest are typically considered to have little commercial value as they require considerable investment, and the return on the investment is often risky (Smolders, 2005). Although new technology can assist in the search for a specific trait, the expense of doing so is generally prohibitive for smaller companies.

Because of these factors, several industry commentators suggest there to be little pricing advantage for having genetic variability. Therefore diversity is not considered to add value. "The market is not asking for diversity to be made available to the farmer", stated one representative of a major seed company. Moreover, much material, including pre-bred material, is available free from the public sector, and payment if any for exotic and unadapted material, and even pre-bred materials, will normally not exceed a nominal fee, such as US$5-20 (Smolders, 2005). However, the value of material increases with characterisation and evaluation, if there is an indication of a trait or characteristic of potential commercialisation. Upfront payments in these circumstances may vary from US$5,000-50,000 (Smolders, 2005).

Although breeders royalties typically fall in the 5-10% range these vary considerably from case to case although are ultimately market-determined. The value of a trait will also vary depending upon whether the trait originates from plant genetic resources or from another source such as bacteria. Across the board, however, there would appear to be little data available regarding the local use and potential future values of genetic resources, and in the absence of this data, an assumption from genetic resource providers that the genes, gene sequences, and related material have maximum potential value.

2.4 The Horticultural Industry[16]

Industry Overview and Market Trends

All plants used in ornamental horticulture, and the diversity of cultivars derived through selection and breeding, originally came from wild plants, with first records of their use for ornament from the Xia dynasty in China in 2100BC (Heywood, 2003). However, like the seed sector, the modern-day horticultural industry has relatively low reliance on wild genetic resources, and many of the genetic resources it uses have been developed over decades and exist within industry collections. Presently, about 100-200 species are used intensively in commercial floriculture (eg carnations, chrysanthemums, gerbera, narcissus, orchids, tulips, lilies, roses, pansies etc) and up to 500 species as house plants, and these represent the mainstay of the industry. Several thousand species of herbs, shrubs and trees are also traded commercially by nurseries and garden centres as ornamentals, many introduced from the wild with little selection or breeding (Heywood, 2003).

Overall, ornamental horticulture is growing both in size and worth, and the sector is characterised by high levels of competition, dynamism and entrepreneurship (Hall, 2004). Statistics reported to the United Nations[17] from more than 100 countries show the world import trade value in horticulture (live trees, plants, bulbs, roots, cut flowers and foliage) in 2004 was US$12,425 million – an increase of 28% since 2001. Of this amount:

- US$5,417 million (43,6%) was attributed to fresh cut flowers,
- US$5,128 million (41,3%) to live plants,
- US$1,056 million (8,5%) to bulbs, tubers and corms; and
- US$880 million (7%) to fresh cut foliage (UN Comtrade, 2005).

A variety of different sized companies are engaged in breeding ornamental plant varieties. Ten Kate (1999) describes three main categories: (a) a small group of multinationals accounting for the majority of sales worldwide; (b) a larger group of mainly national companies; and (c) hundreds of small and medium-sized enterprises.

About 55% of the import value of the live plant trade is accounted for by five countries: Germany (20%), France (11%), the United Kingdom (8,8%) United States (8,5%), and the Netherlands (6,5%) (Table 11). The export trade of live plants is dominated by the Netherlands (41%), with Denmark, Belgium, Italy and Germany comprising 32% of exports, and other countries the balance of 27% (Table 12).

[16] The definition of 'horticulture' is notoriously ambiguous, embracing the large-scale commercial production of vegetables and fruit through to cut flowers and ornamental plants. For the purposes of this section, the focus is on herbaceous ornamental horticulture.

[17] Note that market data for horticulture is not definitive due *inter alia* to the differing definitions that are used, the fluidity of trade between importing and exporting countries, their frequent exclusion of developing country statistics, and the difficulties of distinguishing between different products (ten Kate, 1999).

Current growth trends are expected to persist, and these are pitched closely to projected income earnings of consumers in the North (European Commission, 2003). Heywood (2003) notes two antagonistic trends with regard to the products offered by ornamental horticulture. On the one hand, the streamlining of operations by commercial nurseries is leading to simplification and a reduction in the number of cultivars grown and offered for sale. On the other hand, market saturation by traditional materials is leading to increasing interest in cultivars or new introductions from the wild, and greater interest among countries in their native flora as a source of such introductions. This has clear implications both for industries wishing to access these genetic materials, and for countries of origin wishing to derive benefits from their use.

Trends in Research and Development

Technological developments over the past decade have impacted the horticultural industry significantly. The advent of tissue culture biotechnology and plug production has provided growers with uniform, consistent plantlets or cuttings that may offer disease resistance; slow-release and soluble fertilisation and irrigation technology has improved production; and automation technology and climate control systems have increased the efficiency of many commercial nurseries and greenhouses (Hall, 2004). The adoption of information technology has also led to fundamental changes in business practices. Some examples include the capability to improve supply chain management through 'just-in-time' delivery; the ability to develop targeted relationships with customers through practices such as Efficient Consumer Response; improved business-to-business ('B2B') collaborations through the Internet; and increased on-line transactions (Hall, 2004). An important trend appears to be greater institutional collaboration, and the initiation of long-term partnerships, rather than reliance on more ad hoc approaches to collaboration such as student internships (Kopse, Syngenta International, pers. comm., 2005).

Despite these technological advances, the fundamentals of horticultural science remain paramount: "Much of what we do today hasn't changed since Mendel", remarked one Chief Executive of a major horticulture company, referring to the industry's continued reliance on traditional breeding, yet acknowledging that major advancements had been made through enhanced ability to do broad crosses. Improved understanding of plants and their genetics is a major factor that has affected horticultural developments, enabling old cultivars and varieties to be looked at with new eyes. Commented one industry representative: " … we understand plants much better now and can discern specific traits more easily. Faster breeding is now possible and is more focused – even without using genetic modification".

Indeed, it would seem that there has not been a wholehearted adoption of genetic modification in ornamental horticulture, one respondent commenting that there is no need and that costs are out of proportion to the benefits gained, more especially in light of societal concerns: "We don't need Petunias or other flowers that are Round Up Ready". In contrast, other horticultural companies are focusing solely on genetic modification. Florigene, for example, an Australian-founded company which in 2003 became part of the Suntory group, does research exclusively on colour modification of important flower species using genes of the anthocyanin biosynthesis pathway. In 1997 this company marketed the first blue carnations, and in 2004 announced the world's first biotechnology-driven 'blue rose' (Florigene, 2005).

Demand for Access to Genetic Resources

For the bulk of plants traded, the ornamental horticultural industry has a low dependence on wild genetic resources, and is instead reliant on the creative use of existing germplasm, much of which already exists in collections. One example is the introduction of a new Begonia cultivar ('dragon fly'), which has been in collections for decades but is now being put together in new ways (Corr, Ball Horticulture, pers. comm., 2005). However, as ten Kate (1999) notes, while the search for

new materials is immaterial to some companies, for others especially those wishing to enter the market with new species, it comprises an important component of their work. For some smaller companies – particularly those who sell material on to firms for use in breeding programmes - the hunt for new material comprises the main focus of their work. And for some companies involved in breeding, the reliance on wild germplasm – and the associated variations of colour and other character traits - is paramount, because clonal germplasm from nurseries and collections has little of these critical variations. New germplasm is thus highly desired and much sought after by these companies.

There is also increased interest in new introductions and native plants, with a major advantage of wild genetic resources being their novelty. Where wild material is collected, however, it is seldom 'plucked' out of the wild and introduced but rather is accompanied by a long process of research and development – more especially where new products are involved. The time and cost of this process vary considerably - from a breeding programme that may use highly sophisticated technologies and cost several million dollars, through to the introduction of ornamentals that require little selection or breeding (ten Kate, 1999). Overall, however, it would seem that most of the larger companies allocate relatively low proportions (less than 10%) of their research budgets to investigating wild genetic resources.

It is envisaged that interest in wild genetic resources will peak once the market is saturated with existing material. There is thus a crucial need by the industry to ensure continued long-term access to wild germplasm. In some cases this is being done through benefit-sharing agreements with countries of origin (eg Ball Horticulture and the South African National Biodiversity Institute – see below). In other cases, collaborations have been struck between horticultural companies and those specialising in wild plant collections.And in other instances the illicit collection of material seems to be the norm.

Low reliance of the industry on wild material, combined with the difficulties of 'proving' the origin of germplasm[18], has led to the sector, with some exceptions, still having low levels of awareness about the CBD and its ABS requirements. Indeed, it appears that in many cases germplasm acquisition via the 'cowboy approach' is still prevalent with many plant collectors working outside of government approval systems to supply nurseries and horticultural firms. Commentators have mentioned the ease with which the horticultural industry can 'hide its tracks' with regard to the origin of these resources, especially in cases where freshly collected germplasm is incorporated into existing genetic resources. This is a key difference between the horticultural and, for example, the pharmaceutical industry.

3. Trends in benefit-sharing and partnerships

Benefit-sharing as standard practice in industry

Benefit sharing varies by sector, but since adoption of the CBD standards for best practice in benefit-sharing have become widely accepted. This is a significant and positive achievement of the CBD and ABS policy dialogue. Although unscrupulous and ill-informed companies continue to by-pass these standards, the larger or more socially responsible companies today would not consider genetic resources freely available, or the 'common heritage of mankind'. The package of

[18] Wolfson (South African National Botanical Institute, pers. comm., 2005) notes the possibility of exploring the potential of the 'Barcode of Life' project to deal with this issue, through a DNA-based system of species identification.

benefits typically includes a mix of monetary benefits like fees per sample, milestone payments, royalties on net sales, and licensing agreements, as well as non-monetary benefits like training, capacity-building, research exchanges, supply of equipment, technology transfer[19], and joint publications[20]. Groups with the most experience in benefit-sharing generally emphasize the importance of non-monetary benefits and 'front-loading' benefit-sharing packages. 'Front-loading' benefit-sharing packages ensures that provider countries receive a stream of benefits through the discovery and development phases, given the small odds of any one partnership yielding a commercial product and the fact that all products will not necessarily be billion-dollar 'blockbusters', generating large royalties, or that in most industries products rarely, if ever, achieve this status[21].

Concerns continue to be raised about the quality of prior informed consent and benefit-sharing arrangements in particular cases, and there are many companies and indeed some sectors (eg cosmetic, fragrance, botanical, horticulture) that have not fully grasped the new legal and ethical obligations that arise from the Convention on Biological Diversity. In general, however, companies now see benefit-sharing as a necessary business practice associated with accessing genetic resources. For example, the European biotechnology firm Novozymes has developed a partnership with BIOTEC, Bangkok. BIOTEC collects, isolates, identifies and screens samples, with Novozymes sponsoring the research and providing training at BIOTEC, while transferring enzyme technologies and libraries, bioinformatics, providing training, and royalties if products are commercialized (Lange, 2004). A three year access and benefit sharing partnership between Syngenta and the Hubei Biopesticide Engineering Research Centre in China aims to discover natural chemicals that can be used as starting points for the development of novel crop protection agents. Under the terms of this agreement, HBERC will collect micro-organisms from natural habitats in China, screen them for interesting biological activity and produce information on their chemical properties. Syngenta will provide technological and financial support and will pay HBERC royalties on any products derived from the research (Syngenta, 2005).

Horticulture is a sector characterized by ignorance of the CBD, but even here new access and benefit-sharing agreements have been developed. A Research and Licensing Agreement between the Chicago-based Ball Horticulture and the South African-based National Botanical Institute (now the South African National Biodiversity Institute), was entered into in 1999. The five-year agreement, which is the first North-South bioprospecting agreement in the horti- and flori-culture sector, involved the NBI using its expertise to select South African plants of horticultural interest for Ball, both from its living collections and from the wild. Thus far three varieties have been introduced, based on South African species, although royalties, despite being substantial, have yet to surpass costs of the project (Brian Corr, Ball Horticulture, pers. comm., 2005). While the agreement has raised concerns about the adequacy of benefits and the role of public institutions (Wynberg, 2003), the process of negotiation and revision in response to public concerns has

[19] The International Seed Federation (ISF), for example, reports that technology transfer as it relates to the maintenance of plant genetic resources for food and agriculture is common practice, with more than 40% of ISF members granting licenses free of charge to developing countries and some members also participating in programmes for technology transfer (International Seed Federation, 2005b).

[20] As part of their roughly 125 agreements since 1993, the ICBGS have provided formal training for 2,800 individuals from 12 countries, with 90% of these from developing countries. Associated with training and research efforts, a substantial amount of equipment and infrastructure enhancement for both US and developing country institutions is carried out, and capacity-building to undertake research. Other benefits address the direct needs of collaborating communities, and include water tanks, fencing for gardens, shade cloth, boats, and refrigerators (Rosenthal and Katz, 2004).

[21] As noted in Section 2.1, even within the pharmaceutical industry, companies are moving away from the 'blockbuster' model to smaller niche markets with still significant sales (Lewis et al, 2005).

helped to refine expectations and stimulate discussion about standards for benefit-sharing within South Africa, which will eventually be incorporated in a re-negotiated contract between the parties.

Benefit-sharing in sectors that consume large quantities of raw material

An important trend observed is that many companies in sectors reliant on bulk trading of raw material (rather than genetic resources) are becoming more socially and environmentally responsible and are considering benefit-sharing measures. The nature of benefits reflects the different research and business practices of particular industries. For example, in ornamental horticulture a vast amount of material is already in the public domain, but many developing countries do not have the funds to develop cultivars for IPR registration, the primary mechanism for benefit-sharing (Coetzee, 2002). An alternative approach proposed for generating benefits for local communities and rural producers is to promote fair trade certified horticultural products[22]. Socially–responsible personal care and cosmetic, and botanical companies, similarly emphasize a range of benefits associated with raw material sourcing following product development. Aveda, for example, seeks to develop sourcing partnerships with local groups that include long term agreements and fair prices, as well as contributions to community development funds, bringing in certifiers to broaden the market appeal of the products, and helping communities link with other buyers (Waddington and Laird, 1999; David Hircock, Aveda, pers.comm., 2005). But it takes a great deal of time and money to do this, including staff dedicated to following and monitoring these activities, so most companies do not invest in these activities.

Increasingly, non-governmental organizations are adopting the role of intermediary or facilitator in these deals. PhytoTrade Africa, for example, is a non-profit organization that links rural producers, industry and consumers, developing new products for the personal care and cosmetic, botanicals and other industries. PhytoTrade works to ensure that benefits result from the discovery and development of new commercial ingredients and products (see www.phytotradeafrica.com) through innovative applications of intellectual property and trust funds. However, they consider the most significant benefits for rural producers to be those associated with improving livelihoods through long-term sourcing partnerships for raw materials (Aldivia and Phytotrade, 2005; Cyril Lombard, 2004).

Questions remain about who should benefit

Difficulties remain about who should benefit, with many in industry feeling that scientific research institutions and partners, rather than governments, should receive the lion's share of benefits, as a way to build local capacity in this area. [23] Many acknowledge that indigenous peoples and local communities should clearly benefit from the use of their traditional knowledge, but this has presented challenges in a number of sectors, depending upon: how knowledge is accessed (eg field collections, literature, databases, botanic gardens, genebanks); how 'communities' are defined and represented, and knowledge is 'owned'; and levels of awareness within industry of their obligations to seek prior informed consent and share benefits with

[22] For example, Fair Trade certified cut flowers were launched in 2001, and are now sold widely in European supermarkets. Fair trade roses have since gained a market share of 8% of imported roses (Jorgensen, 2004; Lawrence, 2005).

[23] The seed industry presents particular problems with benefit-sharing because of the cumulative nature of plant breeding, because the entire chain of development leading to the final product may not take place within one company, and because intermediate products themselves are sometimes marketed (Stannard, 2005). As Stannard (2005) observes, this raises questions as to where the values are captured, and how the benefits are shared: on the first commercial product, on all marketed products throughout the development cycle, or only when a final product enters the market?

communities (eg numerous botanical and personal care and cosmetic products are developed without appropriate agreements with communities, and little or no return of benefits).

A case that reflects many of these difficulties concerns the development of the succulent plant *Hoodia* by Phytopharm and Unilever as an anti-obesity product. The plant has a long history of use by indigenous San communities in southern Africa and this, catalyzed by public pressure, led to their eventual inclusion in a benefit-sharing agreement with the South African-based patent holder, the Council for Scientific and Industrial Research. Initial reluctance to engage the San as partners was due to concern that expectations would be raised, that the genuine holders of traditional knowledge about *Hoodia* could not be identified, and that this would be challenged by other groups holding this knowledge. Ultimately, however, it was agreed by the San that a nit-picking exercise to link benefit-sharing to specific communities using *Hoodia* was divisive, and that benefits must be shared equally amongst all San peoples. Moreover, the agreement sets out mechanisms to resolve any 'third party' claims that may arise (Wynberg, 2004). The initiative has demonstrated the importance of moving forward, even in the absence of full certainty, and 'learning from doing' rather than waiting for complete resolution of often intractable issues.

Lack of resolution on appropriate monetary benefits

While responsible users of genetic resources understand that providers must benefit, the scale of those benefits remains unresolved in some cases. Non-monetary benefits are not generally a source of much controversy or confusion, although some provider countries appear to undervalue the importance of this type of benefit for their scientific and technological institutions and domestic industry. There remains much concern on the part of both providers and users, however, about appropriate monetary benefits, in particular up front payments and royalties. For the most part, companies are loathe to provide significant advance benefits unless they are attached to an agreed-upon workplan. Fees for samples and milestone payments, attached to progress in the research collaboration and a product's development, are familiar components of most industry R&D programs. Royalties are also standard practice, and the vast majority of companies agree that should a product be commercialized, provider countries should receive financial benefits, but the scale and nature of these benefits is often in dispute.

The greatest controversy remains the appropriate range for royalty rates. At the heart of this debate are different concepts of the value of genetic resources to commercial product discovery and development. A regular feature in current industry commentary on the CBD and ABS measures is the need to match expectations of value with commercial realities, and to appropriately value genetic resources in negotiations with companies. Lange (2004) refers to this as a 'mismatch of expectations' which she says grows from provider country inexperience with industry, and a lack of awareness on the part of national focal points and negotiators about the higher risks and costs involved in development, compared with discovery. In the absence of information on possible commercial values for genetic resources, providers make the assumption that genetic and biochemical resources have significant value for companies (See further discussion of this point in Sections 3.and 4.4).

Companies feel that the different research and development approaches and profit margins of industries, and existing practices in paying royalties for samples or leads, must inform the negotiation of royalties for genetic resources. The relative contribution of the partners to discovery and development, the information provided with samples, the degree of derivation of the final product from the original sample, and the novelty or rarity of samples all affect where in an established industry range a royalty rate will fall. [24]

[24] See ten Kate and Laird (1999) for a review of the factors influencing royalties for genetic resources.

In addition, provider countries should consider the time and cost it takes to develop a product; the volumes sold and average profit; and the likelihood that a product will be developed from a given collaboration. For example, industrial enzymes have a much lower profit margin than pharmaceuticals, and generally a lower royalty range (0.5 – 2% compared with 3-5%), but they cost between $2 – 20 million to develop compared with around $1 billion, and can yield commercial products in half or less the time (3-5 years compared with 10-15 years, with markets of $200 million compared with possibly $1 billion) (ten Kate, 1999; Laird and ten Kate, 1999; Ernst and Young, 2005).

A debate also exists about when royalty negotiations should take place. Cragg et al (in press) propose a two phase process of agreements between providers and users based on their experience with drug discovery and development at the US National Cancer Institute. The first stage is a research agreement that covers the discovery phase, and the second a commercial agreement that includes benefits related to drug development and royalties, triggered by a patent or selection of an agent for Phase II development. They feel that negotiation of these latter types of benefits are better left to the second stage, once a promising drug candidate has been identified and fully characterized, the breadth of any intellectual property determination is made, the disease category with known markets is clear, and resulting appropriate levels of benefit-sharing can more reasonably be discussed. It is not common practice within industry to lock down these terms in the earliest stages of a research collaboration, and they feel that requiring this serves to dampen demand for access. However, in industries where the likelihood of commercial product development is high, such as horticulture, it is common practice to merge discovery and commercial agreements, and in such cases royalties may be specified.[25]

The stakes for coming to agreement on the ways genetic resources are valued as part of commercial product discovery and development are quite high. A significant number of companies in the pharmaceutical, biotechnology, seed and other industries voiced the opinion that if provider countries set the bar too high, for example demanding royalties well outside of what is considered standard commercial practice, companies will withdraw from collection and research partnerships. Even if higher than normal royalties are agreed upon, some in industry feel that products with these conditions attached would fare poorly within the company and would not be developed. Products derived from genetic resources must compete with those originating from other research programs for development support, and they may look less financially promising if attached to large financial obligations.

The importance of partnerships

Many companies seek the benefits of better-developed and longer-term partnerships with source country institutions. Partnerships allow companies to access local expertise and resources in areas of interest, and in some cases companies build research capacity to undertake a greater share of discovery, more affordably, in provider countries. Partnerships also provide more insurance to companies that the resources they access are legally obtained. Because these more involved partnerships require a large investment of time and resources, however, companies tend to work in fewer countries than in earlier years, a trend further encouraged by developments associated with the CBD and ABS measures (see Section 3). The US biotechnology company Diversa has developed criteria by which it selects partners that include: the legal framework and political will within a country to support research and commercial activities; the scientific and institutional

[25] For example, see the Ball-NBI agreement in South Africa.

strength of potential partners; and the presence of unique and protected habitats (Mathur et al, 2004).

Partnerships also enhance the benefits accruing to provider countries and their institutions, particularly those that build the scientific and technological capacity of countries to undertake research on their own biological diversity[26]. Because provider country scientists play a larger role in discovery when part of partnerships, it also means that financial benefits derived from any commercial product will be more significant. Better-established partnerships also help provider countries monitor the ways samples are collected and used. This is of increasing importance as microorganisms come to dominate many natural products research programs, re-collection of samples becomes unnecessary with expression of DNA in the laboratory, and improvements in synthetic chemistry make it possible to create almost any compound in the laboratory (Koehn and Carter, 2005; Bull, 2004). As one US academic researcher that has brokered access and benefit sharing agreements in a number of countries put it: "This highlights again the value and importance of partnerships – for the benefit of everybody. People need to develop relationships so that they are comfortable working with each other. This kind of research is a difficult thing to regulate, and is becoming more so. Trust is a huge issue, and paramount to the process working. It is not enough to get a permit from a government agency that doesn't really know what the research is about - it is much better for all involved to also have full partnerships."

4. Industry and the CBD

Industry and researcher perceptions of the CBD, and ABS in particular, have become increasingly negative in the last decade. Some continue to cite the positive role the CBD can play in promoting equitable relationships, conservation and best practices in industry, but many more consider the negative impacts to far outweigh the positive. In 1999, ten Kate and Laird reported that over the course of the previous two years of their study many of the companies they interviewed had come to believe that implementation of the CBD had gone badly wrong. They cited lack of clarity in the regulatory framework; bureaucracy and delays in receiving permits; lack of understanding of business; confusion about national focal points; unrealistic expectations and transaction costs; restriction of scientific traditions of collaboration and exchange; and the pressures these new regulatory frameworks place on already taxed natural product research programs (ten Kate and Laird, 1999, p296). These concerns continue today, but are also increasingly accompanied by an underlying unease with what are characterized as "dangerous" and "political" minefields of fickle regulatory processes, and an absence of goodwill.

Increased mistrust and the absence of goodwill

From its inception, the CBD brought together a complex mix of scientific, conservation, trade, and legal elements that fit uneasily into a regulatory whole. ABS regulations exist at the juncture of many inter-lacing bodies of law, which "criss-cross" the same biological material, including international agreements on trade, environment, biological diversity, agriculture, IPR, and so on (Thornstrom, 2005). The ethical, legal and political implications of new biotechnologies, commercialization and ownership of life forms, patenting of gene sequences, the Human Genome Project, and broader concerns about globalization and corporate behavior, have found expression in the ABS policy process (Parry, 2004; Rosenthal and Katz, 2004; Dutfield, 2002; Laird, 2002).

[26] For example, Diversa's 18 partners have received more than $2 million in financial payments and $2 million in third-party grants to support research collaborations. Diversa has also supplied a range of non-monetary benefits, including training more than 100 scientists and students, and providing equipment and infrastructure improvements (Mathur et al, 2004).

These are critical issues to debate and resolve as part of international and national policy processes, but their effect on ABS policy has been divisive and has drained it of the goodwill necessary to come to agreement. Rather than coming together over the last 13 years to create simple, workable legal and regulatory frameworks for access and benefit-sharing, providers and users of genetic resources are increasingly estranged. [27]

The commercial activities upon which ABS is predicated are not sufficient in scope or scale to adequately support, or allow practical prescriptions, for a policy process that incorporates so many pressing but diverse ethical, political and legal issues[28]. The result is that ABS is all but stalled in practice, with only a small minority of governments enacting regulations that meet their obligations under the CBD, and companies being increasingly loathe to access genetic resources, or undertake research partnerships, in more than a handful of 'safe' countries that have strong institutions and relatively clear approaches to ABS. Industry involvement in the CBD has been erratic, in some cases becoming much stronger – as, for example, in the development of ABS guidelines by the biotechnology industry[29] - whilst in other sectors interest has waned. In general, however, involvement of industry and academic researchers in the ABS policy process has declined in recent years.

Charges of biopiracy and 'image problems'

As a result of an environment characterized by misunderstanding and mistrust, in recent years researchers and companies have become increasingly concerned about negative attacks and bad press associated with accessing genetic resources. In addition to the practical hurdles of gaining access, companies and researchers now consider the threat of 'biopiracy' charges a serious impediment to research (this concern did not feature prominently in the study undertaken by ten Kate and Laird (1999) in the late 1990s). One problem regularly cited is the broad definition of 'biopiracy'. Whereas its initial meaning focused on the patenting of genetic resources based on traditional knowledge without the consent of the knowledge holders, today it is popularly used to describe any commercial activity associated with genetic resources.

In a study of German companies using genetic resources, it was found that 'image' problems associated with accessing genetic resources were a major concern for companies from a range of sectors, and influenced their decision-making about whether and how to undertake collections (Holm-Muller et al, 2005). An academic researcher in the US said that both academic researchers and companies today are reluctant to access genetic resources overseas for fear of "…becoming part of a very dangerous socio-political environment in which anyone can claim they are biopirates at any time, and slander them without any legal recourse." An executive at a cosmetics and personal care company in the US similarly characterized research on 'new' ingredients or products as "very dangerous", and in the on-going absence of solid laws they currently avoid this research.

[27] As Rosenthal and Katz (2004) put it: "… suspicion, resentment, and misunderstanding, fueled by colonial history and the politics of trade and intellectual property rights, have frequently brought discussion of the issues to a stand-off in both multi-lateral and project-specific fora … In the policy vacuum that characterizes the current ABS situation in most countries, it is easy for anxiety and suspicion to proliferate."

[28] Finston (2005) describes a rush to "solutions" within the ABS policy process, without having adequately defined the "problem".

[29] In June 2005 BIO, the world's largest biotechnology industry association issued *Guidelines for Bioprospecting* for its members (www.bio.org/ip/international/200507guide.asp)

The rise in concerns about biopiracy is occurring at the same time most in industry have come to accept the need to negotiate access and benefit-sharing agreements. As one biotechnology company executive put it: " The agreements are not onerous; they [companies] can afford royalties. Furthermore, the parties to the CBD can seek some form of reprisal with any firm they feel has gathered samples without permission… I can't imagine any reasonably sized company trying to build a business on hidden material."

Leif Christofferson of Diversa notes that attacks on companies for 'biopiracy' almost always focus on the companies that are most transparent, which has the effect of encouraging greater secrecy on the part of industry. He cites the case of Diversa in Yellowstone National Park in the US, because in this case both the Park and the company felt that their agreement was a 'win-win' and presented it to the public with the expectation that others would share their views. The firestorm that erupted and put their collaboration on hold for many years has served as a warning to other companies, he says.

Rosenthal and Katz (2004), reporting on the work of the ICBGs, note: "Sometimes, regardless of how thoughtfully, transparently, or collaboratively a collection-based project and its approach to ABS are formulated, the political context in which it operates may ultimately make certain partnerships controversial. This is particularly the case when working with indigenous peoples."

Sometimes, however, charges of biopiracy have been necessary stimulants towards attaining equitable agreements and persuading reluctant parties to negotiate. For example, public outrage was expressed about the filing by the South African-based Council for Scientific and Industrial Research of a patent for active constituents of *Hoodia* spp. responsible for suppressing appetite. The indigenous San had long used the plant for these purposes yet did not give consent to the use of their knowledge and were not acknowledged by the inventors. International media coverage forced a turn-about of the situation, and the development of an agreement and partnership of mutual benefit to the CSIR and the San (South African San Council and CSIR, 2003; Wynberg, 2004).

In some cases, claims of biopiracy also have positive commercial spin-offs. For example, an agreement between Chicago-based Ball Horticulture and the South Africa-based National Botanical Institute was the subject of much publicity and controversy (Wynberg, 2003). However, greater profile for the agreement is believed to have led to an improved image for Ball and increased interest from other provider countries in partnerships (Brian Corr, Ball Horticulture, pers. comm., 2005).

Lack of awareness of the CBD and new ethical and legal obligations

Other companies, however, appear to be unaware of the complexities of their obligations under the CBD, and attract attention because of deficiencies in their agreements, or the information made available to the public, rather than as a result of efforts at transparency. For example, the Netherlands and US biotechnology company, Genencor International, have been in discussions with the Kenyan government about claims that it developed enzymes from samples collected in the 1990s from alkaline lakes, which were subsequently licensed to Proctor and Gamble and used in Tide laundry detergent (Mbaria, 2004). This case was brought to public attention after a feature in Genencor's 2000 annual report suggested that the lakes served as a source of a useful enzyme – a powerful image in an annual report, perhaps, but bound to raise concerns on the part of provider countries.

Although many in industry are well-versed in the CBD and resulting obligations, other companies, and indeed entire sectors, remain largely ignorant of these issues. Ten Kate and Laird

(1999) found awareness significantly lower in companies in botanical medicine, personal care and cosmetic, and horticulture than in pharmaceuticals, biotechnology, the seed industry and crop protection, and this continues today[30]. Holm-Muller et al (2005) found that only a small minority of the German companies they interviewed, including only 14% of those that access genetic resources, are aware of the CBD and its legal obligations, and fewer still are familiar with terms such as "access and benefit-sharing".

Ignorance of the CBD is not confined to industry, however. Many academic researchers continue to see the CBD as having no bearing on their work. For example, the Scientific Council for Biological Diversity of the Swedish Environment Protection Agency sent an enquiry to 39 universities about ABS provisions of the CBD. Of the 17 that responded, 50% said that ABS issues did not impact or relate to their work (Thornstrom, 2005). Some academic researchers express concern about colleagues that do not take the CBD seriously, and while paying lip service prefer in practice to "ask forgiveness rather than ask permission". Some see the new obligations as too burdensome and expensive in time and funds, and others say that whatever they do, they will be tarred 'biopirates'.

Lack of understanding of commercial practices and risks

Numerous researchers and companies expressed concern that few in government responsible for ABS are familiar with the rapid scientific and technological developments in industries that use genetic resources, or with the market, legal and other factors that influence corporate behavior. They see this as a serious impediment to the development of effective ABS frameworks.

Many thought government ministries dealing with trade and industry, or scientific research, should be the home for national focal points, rather than ministries of environment and natural resources. Some feel that the role of those with relevant scientific expertise in provider countries has diminished over the last ten years, and that the ABS policy process is now dominated by groups with little scientific or commercial experience.

For example, there are common misunderstandings about the value of genetic resources for R&D and commercialization, including the lower expenditure and risk associated with discovery compared with development, and the low odds of commercial product development from any one sample (although this varies by sector)[31]. Companies have also remarked that the internal competition genetic resources research programs (eg natural products in the pharmaceutical and cosmetics industries, and wild germplasm in seed) face from other research programs within companies is often poorly appreciated[32]. Overall there is a perception that the actual activities

[30] Nutraceuticals and botanicals companies, which tend to be small, are often completely unaware of the CBD, and yet as a researcher at a French personal care and cosmetics company put it: "they prospect for leads and use traditional knowledge more directly in new product development". Ingredient suppliers in these sectors undertake a significant portion of the prospecting and new product development, but rarely see the CBD as relevant to their business model (Kodzo Gbewonyo, Bioresources International, pers. comm., 2005).

[31] It is estimated that one in 10,000 samples makes it into a commercial pharmaceutical product, and Cragg et al (in press) estimate that less than 4% of patented pharmaceutical drug candidates become commercial drugs.

[32] As one researcher said of bioprospecting for fragrances: "…if it becomes too difficult to do this research from a legislative perspective then it will stop, which would be a terrible shame." (Roman Kaiser, Givaudan, pers.comm., 2005).

governments seek to regulate are unclear[33], and that standard, and largely non-negotiable, commercial practices like the premium placed on confidentiality associated with R&D and agreements[34], and the role of intellectual property is not well understood. One company representative said that when they work in countries with low levels of ABS capacity, the company "must sit on both sides of the negotiating table, explaining what a contract is, a patent, and so on," and that this process is "wearing" and "unsustainable".

Increasingly contested intellectual property rights

There are sharp differences in perspective between groups about the positive and negative impacts of intellectual property rights (IPRs), and as a result this issue has been found at the center of much of the ABS dialogue. In particular, there are divergent perceptions about the role of intellectual property protection in stimulating innovation and revenue; the ethics of patenting life; and the effects of intellectual property protection on food security, and health service provision (CIPR, 2002; Oldham, 2004; GRAIN, 2005). Ongoing efforts to introduce 'disclosure of origin' requirements for IPR applications, the lodging of multi-genome patent claims, and differences of opinion as to the placement of genetic information in public databases have been three recent debates that illustrate these divergences.

The possibility of requiring applicants for patents or other IPRs to declare if any genetic resources or traditional knowledge have been utilized in their applications has been brought into focus in recent years. Although a number of countries have adopted these disclosures of origin measures, there are conflicting opinions about their introduction at the international level, with some making a strong calls for patents to be granted only on evidence of PIC and benefit-sharing, and others arguing that a contract-based system suffices for securing the ABS objectives of the CBD. An industry-wide survey in Germany revealed wide support for disclosure requirements amongst users, predominantly Holm-Muller et al (2005) remark because the requirement is without prejudice to the processing of patent applications or the validity of rights arising from granted patents. Although the debate has predominantly focused on moral and ethical issues, Tobin (2005) notes an important shift in focus towards the use of disclosure as an economic tool to promote facilitated access, reduced transaction costs for ABS and legal certainty. This could go a long way to resolving the 'biopiracy' claims described earlier.

Industry and researchers view IPRs as important elements of the research and commercialization process, but there are also differences in approaches to intellectual property protection and the publication of research findings. For example, Diversa has patented results of their research on microbial diversity, while the Venter Institute is working in similar areas and publishing a freely-shared genomics database even though this may "decrease a nation's benefits arising from potential commercial utilization" (Biological Resources Access Agreement, 2004). In Bermuda's Sargasso Sea, a six-year process by Diversa to develop a biodiversity research partnership with a local biological station is in contrast to the Venter Institute's open publication of 1.2 million gene fragments from the same area. This might mean that Diversa and other companies like it may now find it harder to justify to their shareholders that they should continue to pay for something that they can now initiate for free from a public database (Diversa, 2005).

[33] For example, in many instances policy makers confuse collection of samples for discovery (bioprospecting) with sourcing and export of bulk botanical raw materials – two very distinct activities raising very different legal and ethical issues regarding ABS (Kodzo Gbewonyo, BRI, pers.comm., 2005).

[34] For example, a biotechnology company representative said: "…Some interest groups, such as journalists searching for a story, or environmental groups in need of controversy to help boost fundraising efforts, may find the mere fact that these benefit-sharing terms are confidential is unethical".

Increasingly, genome mapping with its identification of key genetic material across varieties, species, and genera, and the increasing realization of relatedness between organisms, is resulting in a surge of very broad intellectual property claims (Oldham, 2004). With continued scientific and technological changes, an increased ability to turn genetic resources into new informational products, and reduced dependency on wild genetic resources in certain sectors, the ground for continued contestations of IPRs is fertile.

Competent National Authorities

The Bonn Guidelines recommend each country designate competent national authorities (CNAs) or focal points for ABS. Most countries have yet to designate or clearly define the tasks of CNAs, and companies and researchers regularly experience difficulties locating groups within government that can clearly explain and execute permitting for collections and research. German companies cited difficulties identifying an appropriate focal point with whom to negotiate and receive permits or prior informed consent as one of the most common problems associated with accessing genetic resources (Holm-Muller et al, 2005). As a researcher at a French personal care and cosmetics company said: " Companies need security and for things to be clear. We want to know what we can do, where we go to ask for authorization, what partners are allowed to work with us, who can collect and send plants to the company. We are happy to apply for authorization and share benefits, but it can be very difficult to know how to do this."

A biotechnology industry representative in Europe made the additional point that because many countries have not established effective PIC procedures or authorities, "… industries will have to choose their countries of CBD collaboration not only based on where the interesting biodiversity is, but also where PIC procedures and the CBD legislation are in place" (Lange, 2004).

Acquiring prior informed consent poses particular difficulties for companies. The CBD gives legal authority to national governments, however in practice there are a range of stakeholders in provider countries whose consent is required. Most companies consider it beyond their expertise to navigate the complex political and social issues that underlie seeking prior informed consent from many parties within a country[35]. Almost all companies prefer to negotiate with scientific research institutions that share their experiences and worldview[36], and many would prefer to work entirely through these groups for all permitting as well as PIC requirements, rather than having to work through complex government bureaucracies. Indeed, in most cases partnerships between companies and research institutes (both domestic and provider country) are still the most common model through which companies gain access to genetic resources.

While many governments remain ill-informed about the scientific and commercial realities of bioprospecting, some of the problems that have arisen in this regard are magnified by striking differences in experience and perspective in a new and evolving regulatory field. The ICBG

[35] In the ICBG program, academic researchers tend to broker relationships between parties, but even they have run into problems obtaining prior informed consent in cases where the 'community' that can legitimately make decisions regarding the sharing of knowledge or resources is unclear, and where an "established, credible and politically representative governance system" does not exist for the indigenous communities involved (Rosenthal and Katz, 2004; Rosenthal, in press).

[36] The US National Cancer Institute (NCI), for example, found that companies are reluctant to negotiate directly for PIC with local communities and indigenous peoples, and prefer to leave these to local partner institutions with the necessary experience in the country. NCI has found that it is most effective for local partners to obtain all necessary permits and PIC from relevant government authorities as well as local communities (Cragg et al, in press).

program, for example, has found numerous challenges in bridging the expectations and practices of users and providers. Companies are typically concerned about losing their competitive edge if proprietary bioassays and related methodology, as well as the nature of any specific leads or the financial terms of an agreement, are shared with parties peripheral to the work. The unfamiliar concerns of indigenous peoples, conservationists and others raise concern among industrial partners that their needs for secrecy will not be respected, and vice versa (Rosenthal and Katz, 2004). However, the ICBG program has produced approximately 125 contracts, including research and benefit sharing, material transfer, confidentialty, know-how licenses, license option agreements, and trust funds, and has managed to build partnerships that address both provider and user expectations and priorities. While this has 'been a significant rate-limiting factor in some projects", the development of models for collaboration is considered perhaps the single most significant contribution of the program to date (Rosenthal and Katz, 2004).

Regulatory confusion, complexity and shifting goalposts

Although more than 75 Contracting Parties have been involved in ABS law and policy development, only 26 of the 188 Contracting Parties to the CBD have adopted ABS laws and procedures. Development of national ABS measures has proven difficult for many countries due to a number of factors, including lack of technical expertise, budgetary constraints, weak government structures and political support, local social conflicts, and conflicts over ownership of genetic resources (UNEP/CBD/WG-ABS/3/2, 2004; Carrizosa et al 2004; Nnadozie et al, 2003). It is also the case that many governments are juggling competing priorities, and do not see bioprospecting as an area active enough to warrant allocating the resources necessary to develop ABS laws and institutions. At the same time, many countries have yet to identify the objectives ABS measures are intended to serve, and a strategy for achieving them[37]. The result is that even existing ABS measures are often sectoral and patchy.

But even in countries with well-developed ABS measures, and national focal points, there remains confusion associated with implementation. For example, in the Galapagos Islands, Thorstrom (2005) found that – despite Ecuador's membership in the Andean Pact and active participation in ABS policy dialogue over the last 15 years - negotiation of an agreement in line with current ABS norms was haphazard and imperfect, and "…the CBD's guidelines on ABS, coupled with the 391/96 provisions did not work very well in practice". (p3) This was due to a lack of awareness of new regulatory frameworks on the part of the local research institution and the company involved.

In other cases, countries with well-developed measures can fine-tune measures, in ways that shift goalposts and create uncertainty for users. For example, in the 1990s the University of Utah was the first group to enter into a commercial research agreement with the Philippine government under Executive Order 247. A process underway today to refine ABS laws has produced a framework that is at odds with the earlier agreement. New rules include, for example, royalties of 3% on gross sales to shareholders in the Philippines. At present, the University of Utah will split any royalties from their marine bioprospecting with the University of the Philippines, as an agent of the national government, and considers royalties of 3-5% of net sales the most likely range possible. Under this scenario, 2.5% of net sales possible for the University of the Philippines falls well below the 3% of gross sales anticipated in the new rules. It is extremely unlikely any company will agree to royalties based on gross, rather than net, sales, and it is unclear where this

[37] See ten Kate and Wells, 2000. Finston (2004) described it this way: "To paraphrase Lewis Carroll, if you do not know where you are going any road will get you there. Now more than ever, it is important for the developing country Members of the CBD to identify their destination in terms of their strategic commercial interests, and to map out a strategy for reaching their goals".

leaves the research programs. The Bureau of Fisheries and Aquatic Resources, in the Department of Agriculture (DA-BFAR) is willing to consider compromise language, however, and discussions for renewal are currently underway (Chris Ireland, University of Utah, pers.comm., 2005).

Another major problem with coherent implementation of ABS regulations appears to be what some in industry refer to as a lack of "political will" within governments (Mathur et al, 2004). Researchers and industry now widely believe that in many countries government officials are reluctant to grant access, even if regulatory procedures are in place. One US researcher described his unsuccessful efforts to gain access in one country over many years as follows: "People in government see this as a political hot potato, and are afraid to stick their neck out and even prepare an agreement for fear of the criticism that will result, and they will be fired… We finally came to realize that this is a political issue, and concerns had nothing to do with coming up with a fair and satisfactory agreement, or not. "

The cost and time required to develop partnerships within complex and evolving regulatory frameworks are significant, and many companies report a retraction of collections into fewer countries with more straightforward procedures. Countries like Brazil and India, for example, are regularly avoided; it takes 1-3 years to get a permit, and researchers fear both the hostility they find to any research on genetic resources, and what one observer called the "national regulatory labyrinths" (Thorstrom, 2005). In The Philippines, the University of Utah undertook negotiations for 3 years for their first commercial research agreement, and a year and a half for the first renewal (Chris Ireland, pers comm., 2005). The US National Cancer Institute has found that it can take many years to reach agreements, and that delays have resulted in promising compounds or their derivatives being synthesized and partnerships stalling (Cragg and Newman, pers. comm., 2005). Syngenta, noting their frustration at finding a government body to give PIC, and a partner with whom to develop agreements, have remarked that "…if you don't move for two years, you lose interest and move on" (Alwin Kopse, Syngenta International, pers. comm., 2005).

Legal certainty concerns

All of these factors combine to create concerns about 'legal certainty' for users of genetic resources, something a party would have regarding an instrument if "he was fully aware of all relevant laws, and certain that they were consistently and predictably in force and enforceable" (IUCN-Canada, 2005)[38]. Legal certainty grows from a broader body of law than ABS or biodiversity law, but confusion in the ABS regulatory process makes many companies very nervous. As one researcher put it, "…even if one comes to an agreement that is satisfactory to both researchers and governments, in a few years another individual with more political influence will come along and say the agreement is invalid." Companies want to know that during the course of the 10-15 years it takes to develop a pharmaceutical, for example, and following

[38] In its analysis of legal certainty in ABS measures, IUCN-Canada (2005) focused on three elements: (1) process certainty (establishment and empowerment of competent national authorities, specifying the rights and duties of others (eg landowners and communities) who may be involved; clarity in procedures for applying for ABS rights, various deadlines, and appeal); (2) scope and nature of the grant (clearly defining the right granted, and enunciating mandatory provisions and conditions that must be included within 'mutually agreed terms'); and (3) legitimate expectations and vested rights (eg clear and specific statutory requirements and limitations regarding subsequent challenges to the user's activities after receiving ABS rights, and a clear delimitation of the nature of government's power to alter, cancel, repudiate, amend or suspend an ABS right, once it has been received).

expenditures in the hundreds of millions of dollars, questions will not be raised about the company's rights to the original material.

Some companies find that through more involved partnerships with provider country research institutions they gain greater confidence in their legal title to resources. Others work only in countries with which they feel comfortable, whether through historical ties (eg French companies working in French territories under French law), or as a result of the legal framework meeting their needs for legal certainty (eg Costa Rica).

Impacts on science and development

Researchers in both academia and industry express significant concern about the negative impact ABS is having upon basic science and upon traditions of trust and collaboration among scientists. Just as scientific and technological developments have dramatically improved our ability to study and use genetic and biochemical resources, the availability of organisms to research has diminished, including in countries with extremely threatened ecosystems where the future of these organisms is uncertain. Many felt that countries were shutting themselves behind an 'iron curtain' and setting back their own capacity and development. Craig Venter, Director of the Venter Institute, remarked at a recent public lecture, "If Darwin were alive today, he would not have been able to have done his research."

A marine researcher in the US feels that "… closing off collaboration and collegiality has very serious consequences for science worldwide. People don't seem to appreciate that it isn't just pharmaceutical companies that have an interest in natural products, it is also academic researchers. We used to work in many parts of the world from which we are now excluded, and train students from countries with which we no longer have working relationships. How is this a positive development?" (William Fenical, SCRIPPS, pers. comm.., 2005). Rosenthal and Katz (2004) consider the need to develop effective models for collaboration an urgent one. They argue that the research community must "demonstrate that this work can be done in a flexible and accommodating manner that recognizes the environmental and socioeconomic context in which these organisms exist, or we will lose access to them in the near term through politics, and eventually through extinction…".

A representative from the seed industry believes that the CBD and FAO agreements have led to a narrow band of collaboration between companies in the North who know and trust each other, and that new collaborations with new institutions are considered with increasing reluctance. The net effect is a stifling of research and innovation (Alwin Kopse, Syngenta International, pers. comm., 2005). Others have expressed concern about the effect of the CBD on collection of genetic material for agricultural genebanks, and the reduced *ex situ* conservation of agricultural diversity, as a result.

Another researcher is working on a project called "The Scent of the Vanishing Flora" as a way of educating people about the many reasons why nature conservation is important (Kaiser, 2004). A number of countries would not let him undertake research on the scents of extremely endangered species, although they were found in botanic gardens. "As soon as they know you are from industry, they become very suspicious… There are amazing things in nature, and this research should continue" (Roman Kaiser, Givaudan, pers.comm., 2005).

But it is not only negative impacts on science that has researchers and other worried about trends in ABS. Many groups also feel that local communities and rural producers suffer when opportunities for commercialization of local products are cut off. PhytoTrade Africa, for example, has established partnerships with companies in the cosmetic and personal care sector like Aldivia

(France) around the commercialization of products from Southern Africa (Aldivia and PhytoTrade, 2005). In order to develop products, producers need to do research and development, and this requires funds. One option is through charitable donations and public support, and the other is through commercial partnerships. The former is limited, and the latter depends on companies benefiting from the arrangement. They have found that their association can best bring benefits to local producers through industry partnerships, including shared intellectual property and benefit-sharing agreements. Although royalties are built into negotiations, the primary benefits they see are partnerships with reliable buyers, who sign long term supply contracts, paying a fair price. At the same time, PhytoTrade is working on innovative models for capturing benefits from intellectual property, including through a trust. But they see the most important goal as developing "long term supplementary income sources for poor rural people in the region from the sustainable exploitation of indigenous NTFP [non-timber forest products]" (Lombard, 2004; Lombard, PhytoTrade Africa, pers.comm., 2005).

4. Recommendations

During the course of this project, researchers and representatives from industry and academia were asked for their recommendations on ways to improve the ABS policy process. A range of invaluable recommendations relating to ABS in general, and ABS and industry in particular, have also emerged in the literature, but these will not be repeated here[39].

Industry and researcher recommendations for providers:

1. Undertake national consultations that comprehensively and overtly address the range of issues that touch upon or underlie ABS – eg patenting of life forms, relationships with external companies, implications of new biotechnology – and tease out the distinct concerns associated with each, and their relationship to ABS frameworks.

2. Define biopiracy and what would constitute acceptable bioprospecting activites.

3. Clarify the types of activities ABS measures regulate.

4. Identify the objectives ABS measures are intended to serve – eg biodiversity conservation, scientific and technological development - and develop a strategy for achieving them

5. Improve capacity within government to address these issues, including understanding of the scientific and technological, market, and legal aspects of bioprospecting and the industries of which it is a part.

6. Improve the capacity of national focal points, clarifying their roles and responsibilities, and ensure that individuals with relevant scientific, commercial and other expertise are part of the staff, and part of national ABS policy dialogues.

[39] See, for example, IUCN-Canada, 2005; UNEP/CBD/WG-ABS/3/2, 2004; Carrizosa et al, 2004; Nnadozie et al, 2003; Rosenthal and Katz, 2004; Cragg et al, in press; Parry, 2004; Laird, 2002; ten Kate and Laird, 1999.

7. Clarify expectations for permitting (time to process, content of application, requests for additional information, criteria by which applications will be judged, etc.) and identify the ways PIC is to be sought from groups outside of government.

8. Promote the role of research institutions as intermediaries between companies and providers, and brokers of permitting and PIC procedures.

9. Build domestic capacity and infrastructure to support higher levels of scientific collaboration, and to maximize the gains from bioprospecting partnerships.

10. Create a legal and scientific environment receptive to research and commercial partnerships, including providing legal certainty to users adhering to national laws.

11. Avoid a 'one-size fits all' approach to ABS measures, taking into account the diversity in user industries, including differences in research and development, the value of genetic resources to industry R&D, the types of commercial products that result, and the profitability of products.

12. Retain flexibility to allow laws to adapt to the rapid scientific and technological change that characterize industries using genetic resources. Use a 'stepwise' approach to ABS law and development and keep the permitting and regulatory process simple and predictable.

13. Don't lock companies into a commercial agreement and a predetermined set of benefits at the earliest stages of discovery, but rather provide indicative benefits, or a package of benefits triggered by different stages in the R&D and commercialization process. A research agreement might cover the discovery phase, for example, followed by a commercial agreement triggered by patents or selection of an agent for development.

14. Distinguish between academic and commercial research in regulations, with different levels of complexity in agreements, and different expectations associated with benefit-sharing.

15. Do not sacrifice the invaluable benefits of scientific collaboration, or academic research on biodiversity, out of fear that commercial research cannot be adequately regulated or monitored.

16. Promote transparency and partnerships, rather than illegal collecting. Byzantine regulatory frameworks and mistrust do not appear to deter the more unscrupulous collectors and only serve to put off more responsible companies.

17. Promote more involved partnerships between domestic research institutions and companies, as a way of ensuring more significant benefits and – particularly in light of advances in synthetic chemistry and the increasing focus on microorganisms – more effectively monitoring commercial activities.

18. Bring more individuals from trade and industry, and academic scientists with experience in these fields, onto delegations to the CBD.

Recommendations for user country governments:

1. Build the capacity of national focal points to provide information (eg corporate policies, standardized contracts, information on ABS measures) and technical assistance to researchers and companies. National focal points might also collaborate across regions to ensure more effective use of limited resources.

2. Promote the involvement of companies and industry associations[40], and academic researchers working in these fields, in the CBD policy process. This might include actively soliciting their feedback and input on ABS issues prior to key meetings.

Recommendation for Parties to the CBD:

1. Develop a regional or international clearing house for information on the commercial use of biodiversity. This would include information on the range of sectors undertaking research on genetic resources, including scientific and technological developments, demand for access, trends in benefit sharing, and new ABS agreements. The information would be regularly updated, and summaries of recent developments and emerging issues submitted to each meeting of the ABS Working Group, the COP, etc. In this way, Parties might be better able to stay abreast of the commercial activities they seek to regulate.

[40] For example, a new industry association, the American BioIndustry Alliance, has been formed to represent a range of sectors involved in bioprospecting at the CBD, WIPO and other international policy processes (www.abialliance.com).

ANNEX

PHARMACEUTICAL INDUSTRY: TABLES AND CHARTS

Table 1. Top 10 Pharmaceutical Markets

	June 2003- June 2004 ($ billions)	**Share of global sales**	**Annual change**
US	$228.7	46.0%	10%
Japan	55.4	11.1	3
Germany	27.8	5.6	6
France	26.4	5.3	7
UK	18.4	3.7	11
Italy	17.9	3.6	6
Spain	12.8	2.6	11
Canada	10.5	2.1	1
China	6.6	1.3	19
Mexico	6.3	1.3	11
Total	410.8	82.6%	9%

Source: IMS Health, Moving Annual Total (MAT) to September 2004

Table 2. Five year merger history of the top 10 pharmaceutical companies

	Market share, based on 2003 sales	**Market share, based on 1998 sales (pro forma)**	**Major component companies**
Pfizer	10.1%	9.0%	Pfizer, Pharmacia, Upjohn, Warner-Lambert, Searle
GlaxoSMithKline	6.6	7.2	Glaxo, Wellcome, SmithKline French, Beecham
Sanofi-Aventisa	5.4	5.8	Sanofi, Synthelabo, Hoechst, Rhone-Poulenc, Fisons
Merck & Co	4.8	4.2	
Johnson & Johnson	4.8	3.6	
Novartis	4.3	4.2	Ciba-Geigy, Sandoz
AstraZeneca	4.1	4.3	Astra, Zeneca
Bristol-Myers Squibb	3.4	4.2	Bristol-Myers Squibb, DuPont Pharma
Roche	3.3	3.1	
Abbott	2.8	3.3	Abbott, BASF Pharma (Knoll)
Top 10 companies	49.6%	48.9%	

Source: IMS Health, 2004

Table 3. Top 15 pharmaceutical companies 2004

Company	Location	Healthcare revenues ($bn)	% change from 2003
Pfizer Inc	US	$52.5	17.4%
Johnson & Johnson	US	47.3	13.1
GlaxoSmithKline Plc	UK	37.3	(5.1)
Sanofi-Aventis Group	France	31.6	9.0

Novartis	Switzerland	28.2	13.6
Roche	Switzerland	25.2	0.2
Merck & Co.	US	22.9	2.0
AstraZeneca Plc	UK	21.4	13.7
Abbott Laboratories	US	19.7	13.9
Bristol-Myers Squibb	US	19.4	3.9
Wyeth	US	17.4	9.5
Eli Lilly and Co.	US	13.9	10.1
Bayer	Germany	10.6	(4.4)
Amgen Inc.	US	10.6	26.3
Boehringer Ingelheim GmbH	Germany	10.1	10.5

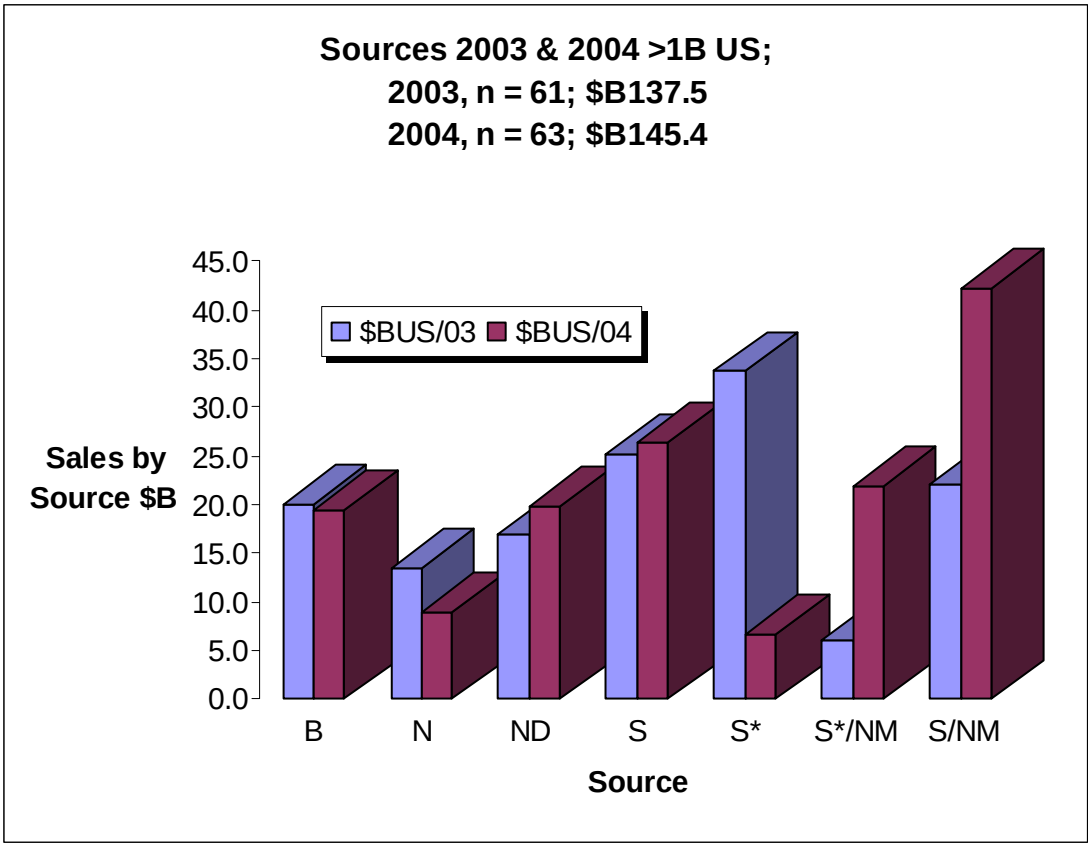
Source: MedAd News, 2005.

Table 4. Drug Discovery and Development

	Average time (years)	**Average # compounds**	**PhrMA member company investments ($bn)**
Drug discovery	5 years	10,000	$11.0 billion
Pre-clinical	1.5	250	
IND Submitted			
Clinical Trials Phase I, II, III	6	5	14.1
NDA submitted			
FDA Review	2	1	4.1
Large scale manufacturing/Phase IV	2	1	3.7

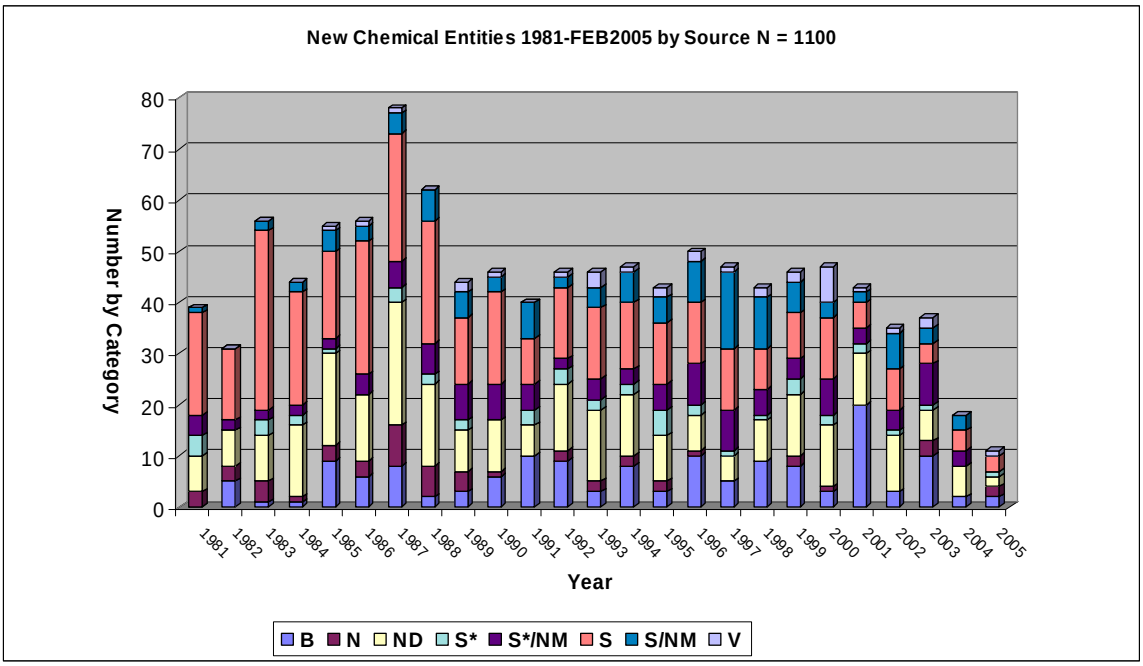
Source: PhRMA, 2005

Chart 1. Sales by all categories, drugs >$1 billion, 2003 and 2004



Source: Newman, 2005
B=biologicals; N = natural products without modification; ND = modified natural products; S= synthetic; S/NM= synthetic by natural product mimic; S*=natural product pharmacophore; S*/NM=natural product pharmacophore or mimic

Chart 2. New Chemical Entities 1981-2005



Source: Newman, 2005

BIOTECHNOLOGY INDUSTRY TABLES

Table 5.

Global biotechnology at a glance in 2004					
	Global	**US**	**Europe**	**Canada**	**Asia-Pacific**
Public company data					
Revenues ($m)	54.613	42.740	7.729	2.091	2.052
R&D expense ($m)	20.888	15.701	4.151	782	253
Net loss ($m)	5.304	4.317	484	408	94
Number of employees	183.820	137.400	25.640	7.370	13.410
Number of companies					
Public companies	641	330	98	82	131
Private companies	3.775	1.114	1.717	390	554
Public and private companies	4.416	1.444	1.815	472	685

Source: Ernst and Young, 2005

Table 6. World's Top 10 Biotechnology Companies

Company	**2002 sales (US $millions)**
Amgen	5.523
Genentech	2.212
Amersham	2.305
Serono	1.546
Genzyme	1.329
Chiron	1.276
Biogen	1.148
MedImmune	848
Invitrogen	649
Cephalon	507

Source: ETC Group, 2003

SEED, CROP PROTECTION, AND PLANT BIOTECHNOLOGY TABLES

Table 7. Top Seed Companies and their Business Areas (2004)

Company	2004 sales (US$ millions)	Nature of business
Monsanto (US)	**2.800**	**Corn, soybean, cotton. Traits, Vegetables through acquisition of Seminis**
Dupont / Pioneer (US)	**2.600**	**Corn, soybean, traits**
Syngenta (Switzerland)	**1.200**	**Corn, soybean, sugarbeet, vegetables, flowers, traits**
Groupe Limagrain (France)	**1.044**	**Corn, cereal, vegetables**
KWS AG (Germany)	**622**	**Corn, sugarbeet, cereals, oilseeds**
Land O'Lakes (US)	**538**	**Alfalfa, maize, soybean, forage and turf grasses**
Sakata (Japan)	**416**	**Vegetables, flowers**
Bayer Crop Science (Germany)	**387**	**Vegetables, traits**
Taikii (Japan)	**366**	**Vegetables, flowers**
DLF-Trifolium (Denmark)	**320**	**Cool season clover and grass; grains and flax**
Delta & Pine Land (US)	**315**	**Cotton, soybean**

Source: ETC Group (2005); International Seed Federation (2005a); Smolders (2005)

Table 8. Top Agrichemical Companies, 2002.

Company	US$Billions
Syngenta (**Switzerland)**	5.260
Bayer **(Germany)**	3.775
Monsanto **(US)**	3.088
BASF **(Germany)**	2.787
Dow **(US)**	2.717
DuPont **(US)**	1.793
Sumitomo Chemical **(Japan)**	802
Makhteshim-Agan **(Israel)**	776
Arysta LifeScience **(Japan)**	662
FMC **(US)**	615

Source: Agrow (2003)

Table 9. Value of exported seed of major crops (in US$ millions) (1998)

Crops	Seed export
Maize	**530**
Herbage crops	**427**
Potato	**400**
Beet	**308**
Wheat	**75**
Other agricultural crops	**750**
Horticultural crops	**1.150**
Total	**3.640**

Source: International Seed Federation (2005a)

Table 10. Areas planted to GM crops in adopting countries

Country	Area planted to GM crops (million ha)
United States	47.6
Argentina	16.2
Canada	5.4
Brazil	5
China	3.7
Paraguay	1.2
India	0.5
South Africa	0.5
Uruguay	0.3
Australia	0.2
Romania	0.1
Mexico	0.1
Spain	0.1
Philippines	0.1

Source: James (2004)

HORTICULTURE INDUSTRY TABLES

Table 11. Top importers of live plants 2001-2004

Importing country	Trade Value 2001-2004 (US$1,000)
Germany	$3.400
France	$1.877
United Kingdom	$1.493
USA	$1.451
Netherlands	$1.099
Others	$7.670

Source: UN Comtrade, October 2005

Table 12. Top exporters of live plants 2001-2004

Exporting country	Trade Value 2001-2004 (US$1,000)
Netherlands	$7.441
Denmark	$1.639
Belgium	$1.561
Italy	$1.434
Germany	$1.002
Others	$4.718

Source: UN Comtrade, October 2005.

Table 13. Top 10 cut flowers at Dutch auctions, 2004

Product	Auction turnover 2004 (Euro 1,000,000)
1. Rosa	705.9
2. Chrysanthemum (raceme)	285.3
3. Tulipa	185.0
4. Lilium	158.3
5. Gerbera	115.9
6. Cymbidium	65.2
7. Freesia	59.6
8. Anthurium	39.7
9. Chrysanthemum	38.9
10. Alstroemaria	38.4

Source: Dutch Flower Council, October 2005

Table 14. Top 10 pot plants at Dutch auctions

Product	Auction turnover 2004 (Euro 1,000,000)
1. Phalaenopsis	109.7
2. Dracaena	42.2
3. Kalanchoë	40.2
4. Anthurium	36.0
5. Ficus	32.5
6. Chrysanthemum	25.7
7. Rosa	25.0
8. Hydrangea	24.4
9. Spathiphyllum	22.8
10, Hedera	20.0

Source: Dutch Flower Council, October 2005

Bibliography

Agrow (2003), *Agrow: World Crop Protection News*, February 26, 2003. www.agrow.co.uk

Aldivia and PhytoTrade Africa (2005), *Maruline, the first African active botanical ingredient from fair trade and sustainable sources*, Press release. www.phytotradeafrica.com.

Arico, S and C Salpin (2005), *Bioprospecting of Genetic Resources in the Deep Seabed: Scientific, Legal and Policy Aspects*, United Nations University Institute of Advanced Studies, Yokohama, Japan.

Beverage Daily (2004), *EU to promote plant sustainability*. 12 January, 2004, www.beveragedaily.com

Bijman, J (2001), Restructuring the life science companies. *Biotechnology and Development Monitor*, 44/45:26-31.

Biological Resources Access Agreement (2005), Biological Resources Access Agreement between Commonwealth of Australia and J. Craig Venter Institute, www.venterinstitute.com

Bioresources International (2003), *Unigen partners with BioResources International; Botanical Liaisons*. Functional Food Wire, Press Release. BioResources International, www.miraculin.com/functional_foodwire.htm.

Biotechnology Industry Association (Bio), (2005), *Guide to Biotechnology*, www.bio.org.

Bull, AT (ed) (2004), *Microbial Diversity and Bioprospecting*. ASM Press, Washington DC.

Carrizosa, S, SB Brush, BD Wright, and PE McGuire (eds) (2004), *Accessing Biodiversity and Sharing the Benefits: Lessons from Implementing the Convention on Biological Diversity*. IUCN, Gland Switzerland and Cambridge UK.

Commission on Intellectual Property Rights (2002), *Integrating Intellectual Property Rights and Development Policy*. Report of the Commission on Intellectual Property Rights.

Class, S (2004), Healthcare in Focus, *Chemical and Engineering News*, December 6, 2004, pp 18-29. www.cen-online.org.

Coetzee, JH (2002), Benefit sharing from flowering bulbs – is it still possible? Proceedings of the 8th International Symposium on Flowerbulbs, *Acta Hort* 570: 21-27.

Cosmetics design (2005), Natural products breath life into stagnant sector, *Cosmetics design.com*, September 30, 2005.

Cragg, GM, DJ Newman, and BJ Gabrielsen (in press), *Access Issues Related to the US National Cancer Institute's (NCI) Natural Products Drug Discovery and Development Program.*

Cragg, GM, DGI Kingston, DJ Newman (eds) (2005), *Anticancer Agents from Natural Products*, Taylor and Francis Group, CRC Press, Boca Raton FL.

CropLife International (2002), *Facts and Figures 2002*, www.croplife.org/website/pages/facts_and_figures_2002.aspx

Diversa (2005) (2005). *Diversa Inc.: Ethical issues in bioprospecting partnerships.* Unpublished and confidential draft (Bensimon, C and D Finegold).

Diversa (2005), *Products*, www.diversa.com.

Dutch Flower Council (2005), www.flowercouncil.org.int

Dutfield, G (2002), Sharing the benefits of biodiversity: is there a role for the patent system? *Journal of World Intellectual Property*, November 2002.

Ernst & Young (2005), *Beyond Borders: A Global Perspective*.

ETC Group (2005), Global Seed Industry Concentration – 2005. *Communiqué*, Issue no. 90, September/October 2005.

EuropaBio (The European Association for Bioindustries) (2005), *Biotechnology in Europe: 2005 Comparative Study*, BioVision, Lyon, 12 April 2005.

EuropaBio (2005), *White biotech, Green biotech, healthcare biotech*, www.europabio.org.

European Commission (2003), The horticulture sector in the European Union, European Commission Directorate-General for Agriculture. http://www.europa.eu.int/comm/agriculture/index.enhtm

Fernandez,-Cornejo, J. and D Schimmelpfennig (2004), Have seed industry changes affected research effort? *Amber Waves* 2 (1): 14-19. Economic Research Service, USDA, http://www.ers.usda.gov

Finston, SK (2004), *The Relevance of Genetic Resources to the Pharmaceutical Industry: The Industry Viewpoint.* Paper presented at the International Society of Environmental Biotechnology Seventh Biennial Symposium, 21 June 2004, Chicago, Illinois.

Finston, SK (2005), *Access and Benefit-Sharing (ABS) in the CBD; Perspectives of the Research-based Bio-pharmaceutical Industry*.

Florigene (2005), http://www.florigene.com

Fowler, C and P Mooney (1990), *The Threatened Gene. Food, politics and the loss of genetic diversity*, Lutterworth Press, Cambridge.

Gbewonyo, K (2003), Botanicals move out of Africa, *Functional Foods and Nutraceuticals*, November 2003, www.ffnmag.com.

GRAIN (2005), various at www.grain.org /rights

Hall, CR (2004), Impacts of technology on the development, production and marketing of nursery crops. *Acta Hort* 630: 103-111.

Handelsman, J (2005), How to Find New Antibiotics, *The Scientist*, vol 19, issue 19, page 20, October 10, 2005.

Heywood, V (2003), Conservation and sustainable use of wild species as sources of new ornamentals. *Acta Hort* 598: 43-52.

Holm-Muller, K, C Richerzhagen and S Tauber (2005), *Users of Genetic Resources in Germany: Awareness, Participation, and Positions regarding the Convention on Biological Diversity*, Federal Agency for Nature Conservation (BfN) – Skripten 126, Bonn, Germany.

International Food Policy Research Institute (IFPRI) (2005), Can public and private sectors work together for the poor? *IFPRI Forum*, June 2005.

IMS Health (2005), www.imshealth.com.

International Seed Federation (2005a), *Seed statistics*, www.worldseed.org

International Seed Federation (2005b), *What is benefit sharing?*, www.worldseed.org/FAQ/FAQbs.htm

IUCN-Canada (2005), *Summary Analysis: Legal Certainty for Users of Genetic Resources under Existing Access and Benefit-Sharing (ABS) Legislation and Policy*, UNEP/CBD/WG-ABS/3/INF/10, 2 February 2005.

James, C (2004), *Global status of commercialised biotechnology/GM crops*. No 32 – 2004, International Service for the Acquisition of Agri-Biotechnology Applications,

Jørgensen, B (2004), Sustainable trade in ornamental horticulture. *Acta Hort* 630: 119-123.

Kaiser, R (2004), Vanishing Flora – Lost Chemistry: The Scents of Endangered Plants around the World. *Chemistry and Biodiversity*, vol 1, pp 13 – 27.

ten Kate, K and A Wells (2000), *Preparing a national strategy on access to genetic resources and benefit sharing: a pilot study*. Royal Botanic Gardens, Kew, UK.

ten Kate, K. and SA Laird (1999), *The Commercial Use of Biodiversity: Access to genetic resources and benefit-sharing*. Earthscan, London.

ten Kate, K (1999), 'Biotechnology in Fields other than Healthcare and Agriculture', in K. ten Kate and SA Laird, *The Commercial Use of Biodiversity: Access to genetic resources and benefit-sharing*. Earthscan, London.

ten Kate, K. (1999), 'Horticulture', In: *The Commercial Use of Biodiversity*, edited by K. ten Kate and S.A. Laird, Earthscan, UK.

Koehn, FE and GT Carter (2005), The Evolving Role of Natural Products in Drug Discovery, Nature Reviews, *Drug Discovery*, vol 4, March 2005. www.nature.com/reviews/drugdiscovery.

Laird, SA (2002), *Biodiversity and Traditional Knowledge: Equitable Partnerships in Practice*, Earthscan, London.

Laird, SA and K ten Kate (1999), 'Natural Products and the Pharmaceutical Industry', In K. ten Kate and SA Laird, *The Commercial Use of Biodiversity: Access to genetic resources and benefit-sharing*. Earthscan, London.

Lange, L (2004), 'Tropical biodiversity, an industrial perspective', *Luna*: 2004-30488-01.

Lawrence, F (2005), *Why I won't be giving my mother Fairtrade flowers*. www.guardian.co.uk

Lewis, G, S Class, and E Edery (2005), Growth, in moderation, *Scrip Magazine*, pp 2-4, February 2005. www.scripmag.com.

Lombard, C (2004), PhytoTrade Africa and Fair Trade: Constraints to conventional agricultural production. *Tropical Agriculture Association Newsletter*, vol 24, no 1, March 2004.

Mathur, E, C Constanza, L Christoffersen, C Erickson, M Sullivan, M Bene, and JM Short (2004), 'An Overview of Bioprospecting and the Diversa Model', *IP Strategy Today*. No 11 – 2004, 1 –21.

Mbaria, J (2004), 'KWS Wants Millions for 'Extreme Bugs': Proctor and Gamble Used in Organisms in Its Detergent', *The East African*, August 23-29,2004, Nairobi.

McAlpine, JB, BO Bachmann, M Piraee, S Tremblay, AM Alarco, E Zazopoulos, and CM Farnet (2005), Microbial Genomics as a Guide to Drug Discovery and Structural Elucidation: ECO-02301, a Novel Antifungal Agent, as an Example. *Journal of Natural Products*, 68, pp 493-496.

MedAd News (2005), Annual Report, Top 50 Pharma, *Med Ad News*, vol 24, no 9, September 2005.

Newman, D (2005), *Mother Nature's Pharmacopoeia: Antitumor Agents from Nature.* Unpublished manuscript.

Newman, DJ, GM Cragg, and KM Snader (2003), Natural Products as Sources of New Drugs over the Period 1981-2002, *Journal of Natural Products*, 66, pp 1022-1037.

Nnadozie, K, R Lettington, C Bruch, S Bass, and S King (eds) (2003), *African Perspectives on Genetic Resources – A Handbook on Laws, Policies, and Institutions*, Environmental Law Institute.

Novozymes (2005), *Fast facts*, www.novozymes.com.

Oldham, P (2004), Global status and trends in intellectual property claims: genomics, proteomics and biotechnology. *Global Status and Trends in Intellectual Property Claims*, issue no 1, October 2004. http://cesagen.lancs.ac.uk/resources/docs/genomics-final.doc. Also available as UNEP/CBD/WG-ABS/3/Inf/4.

Organisation for Economic Co-operation and Development (OECD) (2005), *Statistical Definition of Biotechnology*, www.oecd.org.

Parry, B (2004), *Trading the Genome: Investigating the Commodification of Bio-information.* Columbia University Press, New York.

Pharmaceutical Research and Manufacturers of America (PhRMA) (2005), *Pharmaceutical Industry Profile 2005*, Washington, DC, PhRMA, March 2005.

Phillips McDougall (2005), *Agrochemical industry research and development expenditure, A Consultancy Study for CropLife International*, September 2005.

Rangnekar, D (2005), *The impact of patents and plant breeders rights on agricultural research*, unpublished policy brief.

Rosenthal, JP (in press), Politics, Culture and Governance in the Development of Prior Informed Consent in Indigenous Communities, *Current Anthropology*, vol 47, no1.

Rosenthal, JP and FN Katz (2004), Natural products research partnerships with multiple objectives in global biodiversity hot spots: nine years of the International Cooperative Biodiversity Groups Programs. In Bull, AT (ed) (2004), *Microbial Diversity and Bioprospecting*. ASM Press, Washington DC, pp 458-466.

Rubenstein, KD, P Heisey, R Shoemaker,J Sullivan, and G Frisvold. (2005), *Crop genetic resources: an economic appraisal*. A report from the Economic Research Service, United States Department of Agriculture, Economic Information Bulletin Number 2, May 2005. www.ers.usda.gov

Short, PL, (2005), Growing AgChem R&D. *Chemical & Engineering News*, 19 September 2005, 83(38): 19-22.

Smolders, W (2005), *Commercial practice in the use of plant genetic resources for food and agriculture*. Background study paper no. 27, prepared for the Commission on Genetic Resources for Food and Agriculture, Food and Agriculture Organisation of the United Nations.

South African San Council and CSIR (2003), Benefit-Sharing Agreement, March 2003.

Syngenta (2005), Syngenta enters into research collaboration on natural products in China. Basel, Switzerland, May 17, 2005. http://www.syngenta.com/en/media/article.aspx?pr=051705&Lang=en)

Thornstrom, CG (2005), *The green blindness: microbial sampling in the Galapagos – the case of Craig Venter vs the Darwin Institute and the lessons for the trip to China by S/V 'Gotheberg'*. Unpublished manuscript.

Tobin, B (2005), *Disclosure of origin: A tool for legal certainty and equity or another empty gesture?* Unpublished manuscript.

UN Comtrade (2005), http://unstats.un.org/unsd/comtrade

UNEP/CBD/WG-ABS/3/2 (2004), *Analysis of existing national, regional and international legal instruments relating to access and benefit-sharing and experience gained in their implementation,*

including identification of gaps. Ad Hoc Open-Ended Working Group on Access and Benefit-Sharing, Bangkok, 14-18 February 2005.

US Department of Commerce (2003), *A Survey of the Use of Biotechnology in US Industry*, US Department of Commerce, Technology Administration, Bureau of Industry and Security, October 2003.

Venter, CJ (2005), "*A history of genomics: from human to the environment*", Vice-Chancellor's Open Lecture, University of Cape Town, November, 2005. www.venterinstitute.com

Wynberg, R (2004), Rhetoric, Realism and Benefit-Sharing—Use of Traditional Knowledge of *Hoodia* Species in the Development of an Appetite Suppressant, *World Journal of Intellectual Property* 6(7): 851-876.

Wynberg, R (2003), A review of benefit-sharing arrangements for biodiversity prospecting in South Africa. In: *Developing Access and Benefit-Sharing Legislation in South Africa. A review of international and national experiences.* IUCN, Pretoria. pp. 56-80

Yu, Tin-Wein and HG Floss (2005), Ansamitocins (Maytansinoids), In Cragg, GM, DGI Kingston, DJ Newman (eds) (2005), *Anticancer Agents from Natural Products*, Taylor and Francis Group, CRC Press, Boca Raton FL.

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