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Microbial Genetic Resources

ISSUE: The lack of interest in microbial genetic resources is disproportionate to the role they play in nature, in supporting human society, and the extent to which they have been and will continue to be commercially exploited. The vast majority of microbial culture collections are located in the North, and there is a strong and growing trend towards privatization and patenting of microorganisms.

IMPACT: All countries that are signatories to the World Trade Agreement, including some 70 developing countries, are now obligated to adopt and implement patent laws for microorganisms and for biotech processes applied to living organisms. The Convention on Biological Diversity does not cover genetic materials held in *ex situ* collections gathered before the Convention entered into force at the end of 1993.

ECONOMIC STAKES: A systematic analysis of the value of microbial genetic resources to the North has never been calculated, but microbial materials originating in the South are being patented by industry in the North, or placed in private industry collections that are not accessible to the public.

What is a Microbe?

"Microbes" or microorganisms are tiny living things which are not visible except with the powers of a microscope. These include algae, bacteria, fungi (including yeasts), certain protists (one celled animals that are not bacteria) and viruses. For the purposes of patent protection, the term microorganism often applies to other types of biological material including cell lines of plant or animals--and *not* excluding human genetic material. As discussed below, there is considerable confusion and uncertainty regarding the scope of the term "microorganism."

Given the fact that you can't see microorganisms with the naked eye, it's not surprising that microbial genetic resources receive scant attention in the overall panorama of biological diversity. Microbials lack the aesthetic and emotional appeal of panda bears or rainforests, and are rarely perceived as vital or as useful as a food crop. It's hard to be passionate about something you can't see. So it's not surprising that popular campaigns for equitable conservation and use of biodiversity rarely champion the cause of bacteria or fungi. But the general lack of interest in microbial genetic resources is disproportionate to the key role they play in nature, in supporting human society, and the extent to which they have been and will continue to be commercially exploited.

Politically speaking, microbial genetic resources can no longer be disregarded as ubiquitous life forms outside of the mainstream of biodiversity debates. The genetic resources of microorganisms are very much an issue in the international policy arena:

"The role of the infinitely small is infinitely large." **-- Louis Pasteur**

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- The Convention on Biological Diversity excludes from its scope all *ex situ* germplasm collected prior to the Convention coming into force. This means that all microbial culture collections, the vast majority of which are located in the industrialized world, are the legal property of the depositor and not of the donor country, regardless of where the germplasm was collected. RAFI's research reveals that many microorganisms originating in the South are being patented by pharmaceutical and biotechnology companies in the North.

- There is a strong and growing trend towards privatization and patenting of microorganisms. The GATT/Trade-Related Aspects of Intellectual Property Rights (GATT/TRIPs) agreement specifies that microorganisms may not be excluded from patent protection (Section 5, Article 27.2). All countries that are signatories to the World Trade Agreement, including some 70 developing countries, are now obligated to adopt and implement patent laws for microorganisms and for biotech processes applied to living organisms.[1]

- As a rule, far greater concentrations of plant and animal genetic diversity are found in the tropics and subtropics. Some microbial ecologists are reluctant to state unequivocally that microbial diversity is greatest in the South, simply because so little is known about microbes. Most agree, however, that it is a reasonable hypothesis, especially because of the symbiotic relationship between plants and microbes. While microbial diversity is greatest in the South, the overwhelming majority of culture collections are located in the North.

Ex Situ Collections

The number of microorganisms contained in culture collections worldwide represents only a small percentage of the total number of estimated species available. [2] A handful of dirt from anywhere in the world may yield thousands of new species of microbes, but the microbial diversity currently maintained in culture collections is "scarcely representative" of the global genetic resource. The economic potential of only a small percentage of those microorganisms already present in culture collections has been investigated. For example, less than 4% of an estimated 1.5 million species of fungi have been examined for any reason.[3] The U.S. National Research Council's 1993 report, *Managing Global Genetic Resources*, concludes that "a much greater proportion of the microbial gene pool must be captured in world collections."[4]

The role of *ex situ* collections of microbial genetic resources assumes utmost importance because of the limitations in conserving already isolated and characterized microbials in their natural habitats. The National Research Council finds that, "...in general, *in situ* conservation is not a viable option for the supply of already isolated and characterized microbial genetic material to researchers."[5] This is because the isolation and identification of microorganisms is both a time-consuming and uncertain task. Interesting and novel strains are often found at low frequencies, many species are seasonal in occurrence (some may not be visible in every year, or have fruiting bodies that mature and disappear within a few hours). In its review of conservation of microbial genetic resources, the National Research Council concludes: "Once isolated in culture and found to be new or to have new properties, the only realistic option available to ensure that it continues to be available is in most cases *ex situ* conservation in a culture collection."[6]

The following table, based on data from the U.S. National Research Council, conservatively estimates the number of microorganism species worldwide. With respect to culture collections, only 2 percent of the species expected to be found are currently preserved. Species numbers alone do not provide an adequate representation of the gene pool because of the immense genetic diversity within a single species.

Estimated Numbers of Species of Microorganisms Maintained in Culture Collections Compared with the Probable World Species Totals ‡

Group	Species in Culture Collections	Estimate of Total World Species	Proportion of Species Maintained as % of World Estimate
Algae	1,900	60,000	3%
Bacteria	2,200	30,000	7%
Fungi	30,000	1,500,000	2%
Viruses	2,900	130,000	2%
Protoctists	300	100,000	0.3%
TOTAL	37,300	1,820,000	2%

‡This table is adapted from a table appearing in the National Research Council's "Managing Global Genetic Resources," National Academy Press, Washington, D.C., 1993, p. 243. Estimates on total species in culture collections and total world species have been updated based on new estimates cited in literature, and on the basis of conversations with scientists who are working with collections of fungi and microalgae.

Patent Depositories for Biological Materials

Patent applications in biotechnology usually involve the deposit of biological material in "culture collections"–institutions designed to preserve living biological materials (microorganisms, cell lines and special gene and cellular products) "in perpetuity." The patent laws of the US and most countries require an inventor to give a full disclosure of their invention to the Patent Office. In cases where novel microorganisms are involved, patent law usually requires the deposit of a sample with a recognized patent culture depository. Patent culture depositories are regulated internationally by the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure administered by the World Intellectual Property Organization (WIPO) in Geneva. Since 1981, 26 institutions in 15 states have been officially recognized as "International Depository Authorities" (IDAs) for the purpose of patent procedure. These institutions contain the living materials (microorganisms, genes, seeds, animal embryos, human and animal cell lines, etc.) that are the basis for virtually all biopatents.

Countries that have signed the Budapest Treaty must recognize deposits made in any International Depository Authority (IDA). In other words, a single deposit made in any IDA is acceptable by each country party to the Treaty as meeting the deposit requirements of its own national laws. A single culture deposit in an approved collection will satisfy all countries selected in multi-country patent filings. Currently, 32 countries are signatories to the Budapest Treaty: Australia, Austria, Belgium, Bulgaria, Cuba, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Hungary, Japan, Latvia, Liechtenstein, Netherlands, Norway, Philippines, Poland, Rep. of Korea, Rep. of Moldova, Russian Federation, Singapore, Slovakia, Spain, Sweden, Switzerland, Tajikistan, Trinidad and Tobago, UK, USA, Yugoslavia.[7]

Samples of genetic materials deposited in culture collections (for which patents are pending), are not always made freely available to individuals and/or institutions that request them. At the American Type Culture Collection in Rockville, Maryland, the world's largest microbial culture depository, written authorization must first be obtained from the depositor, or the European Patent Office. Once a patent is issued, the restrictions are lifted because the patent holder assumes the right to restrict unauthorized use of the patented material. The biotechnology industry is pushing for global adoption of stronger restrictions governing access to biomaterials in patent depositories.[8]

Not surprisingly, the overwhelming majority of the institutions that preserve microbial genetic resources are located in industrialized countries of the North. (See table below.)

International Depositories for Patented Microbiological Materials Under the Budapest Treaty

STATE	Facilities
NORTH	
United Kingdom	7
Russian Federation	3
United States	2
Japan	1
Germany	1
France	1
Netherlands	1
Belgium	1
Spain	1
Bulgaria	1
Czech Republic	1
Slovakia	1
Hungary	1
Australia	1
SOUTH	
Korea (Republic of)	3
TOTAL	26

Patentability of Microorganisms

When is a microorganism patentable? What is the definition of a microorganism? There is considerable uncertainty regarding the answer to these questions. Some patent experts observe that, "the word is intentionally not defined in the Budapest Treaty so as to avoid undue constraints being imposed upon the application of the Treaty. "[9] It is important to note that the word "microorganism" is not scientifically defined, nor does it correspond to any standard usage in scientific circles.

In many countries, the term microorganism extends to cell lines and plasmids–including human genetic material.[10] There is nothing in the Budapest Treaty that prohibits the patenting of human genetic material, although individual depositories may elect to accept only certain types of microorganisms.

Traditionally, industrial patent law makes a distinction between "discovery" and "invention." A previously unknown naturally-occurring microorganism (in its natural state) is universally regarded as a discovery and is not patentable. However, the degree of human intervention that is required to turn a discovery into a patentable invention varies between countries. In the United Kingdom and the European Patent Office, only previously undiscovered microorganisms can be patented. In Germany, isolating a strain of a microorganism allows for patentability, since these organisms are no longer "in nature". In the United States, a "biologically pure culture" may be patentable (assuming it meets the standard criteria for patentability). Products of living things such as enzymes and antibiotics, are also patentable and can fall under the category of microorganisms. Processes, end-products and commercial uses of microorganisms are patentable, so that while a microorganism may not be patented as such, the use of a microorganism, the biochemical reactions a microorganism may produce, or the genetic sequence of a microorganism is patentable.[11] In the United States, the 1980 Supreme Court ruling Diamond v. Chakrabarty allowed for the patenting of a genetically modified microbe. This precedent has made it relatively easy to obtain patents on genetically engineered microorganisms in the United States.

The world's largest patent culture depository is the American Type Culture Collection (ATCC) based in Rockville, Maryland (USA).The ATCC became the first approved international patent depository in 1981. Patrick Burke, Director of Marketing and Public Relations for the ATCC estimates that the ATCC now accounts for 50% of all microorganisms on deposit worldwide for purposes of patent procedure..[12] In 1993, the ATCC distributed approximately 150,000 cultures worldwide. But only 20% of those cultures were distributed outside of the United States. And only 2% of the cultures distributed to foreign countries went to countries other than Canada, Europe and Japan.[13]

Microbial BioPiracy: A Sample of Industrial Patents on Microbials from the South

Patent depositories contain microbes collected worldwide, yet there is no requirement that patent applications and/or deposited bio-materials list the source country. As a result, the number of microbes originating from the South that are currently held in microbial collections (patented or not) is impossible to estimate. RAFI's search of the ATCC database reveals that considerable numbers of microbes from the South are now subject to exclusive monopoly under industrial patent claims.

To illustrate, RAFI compiled data on microbial patents for three biotechnology/pharmaceutical companies: Bristol-Myers; Merck, and Eli Lilly. It should be noted that patent holders are not required to divulge the original source of either a naturally occurring organism or one that has been altered after it was isolated from nature. Therefore, it is unlikely that companies have listed the source for all foreign strains. The tables below were compiled from ATCC databases as of January 1995. [Note: The total number refers to the total number of deposits made by a certain company, regardless of whether it had been patented or not.]

Bacterial Cultures deposited by Bristol-Myers, or Bristol Labs in the ATCC

Original Source Country of Bacterial Culture	Number of patents owned by Bristol
India	28
El Salvador	1
Fiji Islands	2
Philippines	3
Argentina	2
Peru	3
Mexico	1
Guatemala	2
Colombia	1
Brazil	2
S. America--unspecified	1
subtotal	43
total of Bristol deposits	110*
% from developing countries	38%*

*While Bristol had 110 deposits in the ATCC, not all of them were patented, so the actual percentage of patents from the developing world is higher than the figure given. Furthermore, depositors are not required to label the source of each strain, so it is possible that other strains were also derived from developing countries.

Eli Lilly's Bacterial Deposits in the ATCC

Original Source Country	Deposits by Eli Lilly	Patents by Eli Lilly
Mexico	1	0
Venezuela	3	1
East Indies	2	1 or 2
Costa Rica	1	0
Marshall Islands	1	1
Philippines	1	1
S. America	1	1
subtotal	10	6-7
total Eli Lilly deposits	45	
% from developing countries	22%	13-16%

Note: Eli Lilly has many deposits that are not patented.

Pfizer bacterial deposits in the ATCC

Original Source Country	Patents by Pfizer, Inc. or Chas. Pfizer Inc.
Turkey	1
Nigeria	2
India	3
Egypt	4
China	1
Jamaica	1
Venezuela	1
Malaysia	4*
Ghana	2
Philippines	1
Guatemala	1
subtotal	17-22
total Pfizer deposits	210
% from developing countries	8-11%

*The deposits listed for Malaysia were identified based on the species name, but are not specifically listed as originating from Malaysia. As a result, it cannot be confirmed whether or not all such samples originated in Malaysia

Microbial biopiracy is not new. In 1949, Filipino scientist Abelardo Aguilar sent his employer, Eli Lilly Co., samples of an antibiotic isolated from a soil sample that he collected in his home province of Iloilo. Three years later, Eli Lilly sent a congratulatory letter to Aguilar, promising to name the new antibiotic, "Ilosone", after the Filipino province where the soil sample was found. The drug, erythromycin, sold under the brand name "Ilosone" has since earned Eli Lilly billions of dollars, but neither Aguilar nor the Philippines received any royalties, despite Aguilar's 40-year battle to be recognized and rewarded. Aguilar died last year; the Philippine government is now attempting to assist Aguilar's family in negotiations with Eli Lilly.[14]

MIRCEN's: Microbial Resource Centres for the Developing World

MIRCENs (Microbial Resource Centres) were conceptualized in the 1970s by United Nations Environment Programme (UNEP) and UNESCO as a network of microbial centres directed to the needs of developing countries. MIRCENs are active in the collection, preservation, identification and distribution of microbial germplasm. The first 6 resource centres designated as MIRCEN's were established in Brazil, Egypt, Guatemala, Kenya, Senegal and Thailand. By 1991 there were 23 centers located in developing and developed countries. While MIRCEN's were established to extend microbial biotechnology to developing countries, there are now more facilities designated as MIRCENs in developed countries than in developing countries.[15] The goals of MIRCENs are[16]:

- to provide a global infrastructure for the management, distribution of the utilization of microbial gene pool for international cooperation;
- to help conserve microbial diversity, with emphasis on *Rhizobium* in developing countries;

of microbial gene pool for international cooperation;
- to help conserve microbial diversity, with emphasis on *Rhizobium* in developing countries;
- to promote economic applications of microbial technologies;
- to foster development of new, inexpensive technologies native to specific regions;
- to serve as foci for training of human resources and diffusion of knowledge.

Most MIRCEN's in the developing world specialize primarily on Rhizobium bacteria, for the development of "biofertilizers" that can improve yields for agriculture and lessen dependency on the purchase of costly, chemical-derived fertilizers. The MIRCENs holding the largest Rhizobium culture collections are in the United States (Hawaii with 2000 strains and Beltsville, Maryland with 938 strains) accounting for approximately 76% of all collected Rhizobia strains held by MIRCENs.[17]

As a collective group, MIRCENs do not have a defined policy on intellectual property rights. Policy on intellectual property may be guided by the research institutes that host the MIRCEN. Normally, MIRCENs have a policy of free exchange of microbial materials within the network, but each MIRCEN may decide on a case by case basis.[18] Although the ATCC is designated as a MIRCEN, for example, microbials under pending patent claim would not necessarily be available to developing country MIRCENs, even if the country of origin requested the culture. Because the legal status of many microbial collections in the developing world is ill-defined, these microbials could be subject to claims of exclusive monopoly control in the industrialized world.

Value of Microbial Markets

Worldwide, the economic value of microorganisms is estimated to be "at least many tens of billions of U.S. dollars."[19] It is the invisible world of microbes that has given us more than 3,222 antibiotics, for example. Today, five of the pharmaceutical industry's top-selling pharmaceuticals are derived from microbes.[20] These blockbuster drugs alone account for more than $4.5 billion in annual sales:

- Mevacor (1991 sales of $1.1 billion for this lipid-lowering agent) -- Merck
- Ceclor (an antibiotic generating $950 million) -- Eli Lilly
- Augmentin (a $900 million antibiotic) -- SmithKline Beecham
- Rocephin (a $875 million antibiotic) -- Hoffman-LaRoche
- Sandimmune (a $700 million immunosuppressive drug) -- Sandoz

The beta lactam antibiotics produced by penicillin fungi had worldwide revenues of $2.25 billion in 1992. Cephalosporins, another group of fungi, produced antibiotics generating $8.5 billion in sales. Mevinolin fungi produce cardiovascular drugs with worldwide sales of an estimated $1.6 billion. Cyclosporin fungi produce immunosuppressive drugs with worldwide sales of approximately $820 million.[21]

There is growing demand for new anti-fungal therapies because of the growing numbers of immunocompromised people, the alarming spread of drug resistance and shortcomings of current therapies. Companies like Myco Pharmaceuticals and Xenova Ltd. are pursuing novel pharmaceuticals from genetically engineered fungi collected around the world. The potential markets are staggering: The anti-fungal market was estimated at $2.1 billion in 1993 and is expected to rise to about $3.5 billion by 1995. Industry analysts put the annual growth rate of the anti-fungal market at 19%, with the world market projected to reach $4.9 billion in 1997.[22]

The value of microbials extends beyond pharmaceuticals. The total world market for industrial enzymes, all produced by microorganisms, is (US) $1.3 billion. Enzymes are natural catalysts that can speed up a chemical reaction. Because the process is biological, they are biodegradable and can be used instead of synthetic chemicals. Industrial enzymes are used to enhance detergents, as biopesticides, to clean up toxic wastes, replace chemicals in paper and pulp processing, oil extraction, etc.

With the use of modern biotechnology, the potential applications of microorganisms is vast. Scientists are able to take a gene coding for a valuable enzyme and transfer it to a more suitable host that thrives and produces large quantities in an industrial setting. Today, microbe hunters are especially interested in both exotic and hostile environments as the source of new microbial diversity. Bioprospecting for microbes goes, quite literally, to

the ends of the earth. The following are just a few examples:

- According to a recent article in *Business Week*, when employees of Novo Nordisk go on holiday, they take along soil-collection kits to gather exotic, enzyme-producing microbes. The father of one Novo scientist collected a soil sample from Indonesia which yielded an enzyme that is now widely used by soft-drink suppliers to change starch into sugar.[23]

- Sponges growing on a coral reef near South Lion Island off the coast of Papua New Guinea are the source of a powerful antifungal agent "Papuamine." Because the sponges yield only minute quantities of the antifungal agent, Myco Pharmaceuticals is now attempting to synthesize papuamine in the laboratory.[24]
- Bacteria found in the whale gut from the last legal Eskimo whale hunt are capable of breaking down toxic petrochemicals.[25] Scientist A. Morrie Craig of Oregon State University has applied for patents on some of the whale gut bacteria, and Pioneer Hi-Bred has already secured rights over commercial products that may someday result from the bacteria.

- Researchers from the Spanish biotech company, PharmaMar, travel aboard the ships of Pescanova--one of the largest fishing fleets in the world-- in search of elusive microorganisms. PhamaMar is "fishing" for pharmaceuticals. The company isolates bioactive materials from the marine environment in hopes of discovering new treatments for cancer and AIDS.[26] According to published sources, PharmaMar already has 250 active ingredients, 30 patents and 13 compounds in preclinical and clinical development. The company sells marine organisms for use in research to Glaxo, Sandoz and Pfizer, among others.[27]

Multinational Microbe Hunters:
A Few Examples of Proprietary Culture Collections

Xenova, Ltd., United Kingdom -- Maintains a library of 23,000 fungi and bacteria, coupled with a sophisticated assay technology that uses disease-specific targets to identify promising compounds for drug development.

Myco Pharmaceuticals, Boston, USA -- Maintains a fungal library of 30,000-40,000 accessions, collecting at the rate of 10,000 per year. Myco is a new biopharmaceutical company with the focus of discovering drugs through fungal genetic engineering.

Mycogen Inc., Maryland, USA -- Specializes in collection of naturally occurring soil microbe, *Bacillus Thuringiensis* from all over the world for insecticidal proteins. Mycogen has more than 3,000 strains of *B.t.* in-house, with 60 *B.t.*-related patents.[28]

Martek Inc., Maryland, USA -- Specializes in microalgae in biotechnology, and is developing proprietary nutritional, pharmaceutical and diagnostic products from microalgal compounds. Martek's library holds over 1900 microalgal strains collected from all over the world. It is the second largest commercial collection of microalgae in the world.[29]

Novo Nordisk, Denmark -- Industrial enzyme giant, controls 50% of the world enzyme market with approximately $575 million in annual sales. In 1993, Novo created a new, research and development effort based in California that is charged with finding new microbes in extreme environments such as boiling springs of Yellowstone National Park, the deep ocean or frozen tundra of Antarctica.[30]

Conclusion

Microbial genetic diversity has been under-valued and under-recognized in the scope of biodiversity debates despite its economic importance and potential. Microorganisms are routinely taken from the South, and used for commercial purposes by corporations and researchers in the North.

The vast majority of microbial culture collections are located in the North, and there is a growing trend toward privatization and patenting of this material. *Ex situ* microbial collections, gathered prior to the Convention on Biological Diversity entering into force, are not covered by the terms of the Convention. The issue of *ex situ* germplasm will

be addressed at upcoming meetings of the Conference of Parties to the CBD.

For patent purposes, the term "microorganism" is not based on a scientific definition, and this vagueness accommodates the biotechnology industry in its desire to patent all life forms. Developing countries that are obligated to implement patent laws for microorganisms should be aware of the fact that they may unknowingly accept/endorse patent protection for human genetic material unless specific restrictions are adopted. Transparency and debate on these and related concerns are necessary in a number of international fora:

Microbial culture collections housed in the developing world, particularly in the MIRCEN network, account for a shockingly small percentage of the world's total microbial genetic resources. There is no policy in place to insure that these microbial resources are not subject to claims of exclusive monopoly under industrial patent laws. UNESCO or another UN body should work with member states to develop policies to protect microbial genetic resources from privatization and to insure equitable exchange of microbial genetic resources in culture collections worldwide. A possible model for UNESCO to consider is the historic agreement made in October, 1994 to place *ex situ* plant germplasm held by the Consultative Group on International Agricultural Research (CGIAR) gene banks under the legal, inter-governmental control of the United Nations Food and Agriculture Organization (FAO).

Signatories to the World Trade Agreement must determine whether or not human genetic materials are included in its definition of microbial materials.

Similarly, contracting parties to the Biodiversity Convention must come to a clear decision on the role of intellectual property with respect to biological materials and especially whether or not human genetic materials are part of the Convention.

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[26]Bio/Technology, Vol. 12, August, 1994.
[27]Market Letter, June 8, 1992.
[28]Personal conversation with Guy A. Cardineau, Director of Molecular Biology, Mycogen, February 17, 1995.
[29]Personal conversation with Dr. Paul Behrens, Head of Physiology, Martek, Inc., February, 1995. The largest collection of microalgae is housed at University of Texas, Austin, USA.
[30]"Novo Nordisk's Mean Green Machine", in Business Week, November 14, 1994, pp. 72-75.

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A Case Study of a Celebrated Microbe: The Privatization of *Thermus Aquaticus*

When bacteriologist Thomas D. Brock discovered a bacterium, *Thermus aquaticus*, that thrived in the boiling hot springs of Yellowstone National Park in 1966, he had no idea that he had stumbled across a microbe that would become the source of one of the most important tools of modern molecular biology--the polymerase chain reaction (PCR). Nor did he know that patent claims on his discovery would later bring royalties valued at hundreds of millions of dollars annually to Swiss pharmaceutical corporation Hoffman-LaRoche.

An enzyme isolated from *Thermus aquaticus* is the catalyst for the polymerase chain reaction, or PCR, a technique that is routinely used for producing millions of copies of any DNA sequence. Using PCR a scientist can start with a few molecules of DNA and scale-up to a workable sample. The PCR technique enables forensic scientists to identify people from tiny samples of hair, skin or blood, for example.

Thomas Brock put his heat-loving microbe into the public domain by depositing it in the American Type Culture Collection--the world's largest repository for microorganisms in Rockville, Maryland (USA). More than a decade later, scientists at Cetus, a California-based biotech company, requested samples of *Thermus aquaticus*, isolated and purified the Taq enzyme from the bacterium, and received patents on both the enzyme and the PCR process using the enzyme. In 1991, Cetus sold worldwide rights to PCR to the Swiss pharmaceutical giant, Hoffman-LaRoche, for (US) $300 million. The patent allows Roche to claim a royalty on every use of the enzyme to perform a PCR--even in research laboratories with no commercial applications.

Thomas Brock was shocked to learn that the organism he donated to the scientific world became subject to exclusive monopoly. "I am not concerned about the money involved," wrote Brock in a letter to *Science* magazine, "but with how such practices (legitimate or not), stifle the development of scientific research."[1] Other researchers share Brock's concern. Molecular biologist Ronald Sederoff of North Carolina State University (North Carolina, USA) protested publicly when Hoffmann-LaRoche refused to grant his laboratory permission or a license to produce its own enzyme for PCR experiments which have no direct commercial application. Purchase of the enzyme from Roche would cost several times the laboratory's annual budget, yet the company refused to negotiate. In a letter to *Science*, Sederoff observed:

> "The position taken by the holders of the rights to PCR has created a major impediment to our progress. This position is contrary to the spirit of the traditional relationship between industrial and university research and inimical to the philosophy of the patent process, which is intended to encourage innovation."

Ultimately, Sederoff's laboratory was forced to pay Roche's price and scale-back their research accordingly. In an interview with RAFI, Sederoff observed that public research programmes are at a distinct disadvantage under the industrial patent system, "We are required to play by the same rules, but we don't have the resources to compete with them."[2]

The celebrated case of *Thermus aquaticus* illustrates the potential value of elusive microbes. Bioprospectors from at least 39 different companies, research and educational institutes are now prospecting for valuable microbes in Yellowstone's thermal waters. All of the microbe hunters have permits to do their work, but none of them pay for the privilege, nor are they obligated to return a share of their profits if the microbes they find someday result in commercial products. While this scenario is all-too-familiar in diversity rich countries of the South, the corresponding inequities are less often seen within the United States context.

In 1994, the Director of the U.S. National Park Service, Roger Kennedy, ignited the wrath of the biotechnology industry when he suggested that commercial bioprospectors should pay royalties to the National Park Service as a way to contribute to long-term conservation of the natural areas. In an interview with the *Los Angeles Times*, Kennedy asked: "Doesn't the public, which pays for the upkeep of these places, have a right to expect some sort of contribution from those who are enriching themselves?"[3]

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[1]Brock, Thomas D., Letter to the Editor in Science, Vol. 259, 22 January 1992, p. 441.
[2]Personal communication with Ronald R. Sederoff, 21 February 1995.
[3]Clifford, Frank. "Simpson Case Boosts Microbe Conservation," Los Angeles Times, August 31, 1994.

Source:

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