Global Status and Trends in Intellectual Property Claims:

Microorganisms

Submission to the Executive Secretary of the Convention on Biological Diversity by
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Global Status and Trends in Intellectual Property Claims. Issue No. 2.
ISSN: 1745-3941 (Print)
ISSN: 1745-395X (Online)
Available from: <http://www.cesagen.lancs.ac.uk>

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The ESRC Centre for Economic and Social Aspects of Genomics (CESAGen) is a Research Centre of the Economic and Social Research Council, United Kingdom and is a collaboration between Lancaster and Cardiff Universities (http://www.cesagen.lancs.ac.uk). CESAGen forms part of the national ESRC Genomics Network. CESAGen's work is directed towards analysis of the social, economic, ethical and environmental implications of genomics across the spectrum of red and green genomics issues.

About this Series:

This series has been established as a contribution to the development of evidence based approaches to analysis of the potential role of intellectual property instruments within the development of an international regime on access to genetic resources and benefit-sharing under the Convention on Biological Diversity. The series aims to provide independent information and analysis on intellectual property issues to assist policy-makers and other participants within debates surrounding the development of the international regime.

Acknowledgements:

The support of the Economic and Social Research Council (ESRC) is gratefully acknowledged. The work was part of the programme of the ESRC Research Centre for Economic and Social Aspects of Genomics.

Dr. Paul Oldham is Research Associate at CESAGen, Lancaster University and member of the Development Research Group, Anthropology Department, University of Durham. The author thanks Mr. Mark Cutter who served as Research Assistant for the project for his assistance with generating the underlying patent dataset upon which this review is based and which constitutes the results of our joint work. The author thanks Professor Peter Whittaker and Professor Brian Wynne for their valuable scientific advice and comments and Mr. Michael Warburton for his valuable assistance in relation to the public trust doctrine. The author thanks the staff of the European Patent Office for their generous assistance in clarifying the characteristics of the esp@cenet patent database. The author also thanks the members of the Intellectual Property Group, Regulatory & Competition Policy Branch, Ministry of Economic Development, New Zealand/Aotearoa for their warm and generous hospitality during the completion of this review. The views expressed are exclusively those of the author and not necessarily those of the ESRC, CESAGen or any other institution or individual named above. Responsibility for any errors, omissions or misinterpretations resides solely with the author.

Executive Summary:

This paper has been prepared as a contribution to analysis and discussion of the development of an international regime on access to genetic resources and benefit-sharing under the Convention on Biological Diversity (Decision VII/19).

The paper provides a review and preliminary assessment of the implications of intellectual property claims in relation to microorganisms for the development of an international regime. The review is divided into two sections which may be read independently. Section I examines the public policy implications of intellectual property claims over microorganisms which form part of access and benefit-sharing agreements between protected area authorities and public or private bodies. Section II presents the outcomes of research on global trends in intellectual property claims over microorganisms.

Section I considers growing interest in the potential of access and benefit-sharing agreements between protected area authorities and private bodies for the promotion of conservation objectives in protected areas. The discovery of a microorganism *Thermus aquaticus* in Yellowstone National Park in the United States and identification of an enzyme Taq DNA polymerase which has proved vital in the arena of biotechnology serves as an exemplar for the potential of access and benefit-sharing arrangements involving protected areas. A review of the litigation surrounding the enzyme reveals a series of wider public policy issues that may merit further consideration. These issues include: a) the impacts of patenting of biological research tools on research and innovation; b) the implications of the commercialisation of public sector research for protected area authorities; c) risks of involvement in patent litigation and cases of inequitable conduct; d) potential conflicts between agreements permitting patenting of components of organisms within protected areas and requirements for protection of the public domain and resources covered under the common law public trust doctrine; e) a need to clarify the meaning of the public domain and the public trust doctrine in light of international human rights obligations relating to indigenous peoples and local communities and the existence of multiple overlapping ownership and/or sovereign rights.

The review recommends a deliberative, participatory and evidence based approach to the consideration of access and benefit-sharing arrangements involving protected areas including scientific and economic analysis of the potential impacts of intellectual property claims over DNA, amino acids, and proteins such as enzymes upon public welfare.

Section II of the review seeks to contribute to methodological development in tracking intellectual property claims over microorganisms and analysis of the role of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure, the agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) under the World Trade Organisation (WTO), and the Patent Cooperation Treaty under the World Intellectual Property Organisation (WIPO) as possible elements of the international regime.

The review reveals that in the period between 1980 and 2000 a total of 43,533 microorganisms were deposited with International Depositary Authorities (IDAs) for

patent disclosure purposes under the Budapest Treaty. Data on the country of origin and conditions of collection of such material is presently limited. However, the establishment of online databases by International Depositary Authorities such as the American Type Culture Collection (ATCC) offers a potential route to tracking the country of origin of deposits.

Article 27.3 (b) of the agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) under the WTO introduces a requirement for patent protection for microorganisms and microbiological processes. Additional requirements for protection of microorganisms are reported in the case of so-called "TRIPS-plus" agreements and may also feature in Bilateral Investment Agreements (BIAs).

However, a major constraint in assessing the implications of the requirements of international intellectual property agreements and trade related agreements for the development of an international regime is a lack of effective methodologies to track patent claims relating to microorganisms. As a contribution to methodological development, the review presents the results of two types of search of the European Patent Office esp@cenet "worldwide" database which incorporates approximately 36,165,421 industrial property publications from 73 national patent offices, four regional patent offices and the World Intellectual Property Organisation (for the Patent Cooperation Treaty).

The results of a key word search of patent publication titles and abstracts for the term "microorganism" suggests that international demand for patent protection (measured in terms of publications) rose to approximately 6,915 patent publications between 1990 and 2000 rising to approximately 10,024 publications if preliminary data for 2001 to 2003 is taken into account. However, the key word search methodology is confined to the titles and abstracts of patent publications available in English and does not provide an accurate indicator of international demand for patent protection. A superior approach to mapping international demand is provided by the International Patent Classification (IPC) system which provides a higher level of data capture. A search of the esp@cenet worldwide database for the main sub-class relating to microorganisms, C12N (Microorganisms or Enzymes), reveals a total of approximately 188,213 patent publications between 1990-2000 rising to approximately 299,163 publications if preliminary data for 2001-2003 is taken into account.

In considering this disparity the review highlights issues surrounding the definition of "microorganisms" under international instruments and notes that patent claims in relation to microorganisms are characterised by publications that may not generally be regarded as "microorganisms", notably plant, animal and human DNA (deoxyribonucleic acid). The review concludes by highlighting the implications of such trends for the scope of an international regime and recommends further methodological development in tracking intellectual property claims in relation to microorganisms.

Introduction:

The *Global Biodiversity Outlook* estimates that there are approximately 1,000,000 species of bacteria (Archaebacteria and Eubacteria) of which 4,000 are thought to have been described.[1] There are also approximately 600,000 species of Protoctists (algae, protozoa, etc.) of which 80,000 are thought to have been described.[2] 'Microorganisms' therefore represent a significant proportion of the world's biodiversity and are likely to represent a greater percentage of the world's biodiversity than is presently reported.

A patent is a legal certificate which awards temporary protection over a claimed invention for a period that is generally twenty years.[3] Patents are awarded in accordance with three criteria, they must be: a) new (or novel); b) involve an inventive step (be non-obvious), and; c) be capable of industrial application (be useful or of utility). A patent awards an exclusive temporary protection to its holder including the right to exclude others from "making, using, offering for sale, or selling" or "importing" the protected invention into a jurisdiction where the patent protection is in force, or to charge others for any uses or purposes involving the protected invention within such jurisdictions (i.e. through licensing).[4]

Until 1980 patents over microorganisms were confined to processes relating to microorganisms rather than microorganisms *per se* (as such). The main legal landmark in the extension of patenting to microorganisms is the well-known and widely cited 1980 Supreme Court case *Diamond v. Chakrabarty*.[5] This case established that for the purposes of the US Patent Act (U.S.C. 35), microorganisms that have been modified are not a product of nature and are eligible for patent protection. This decision also established that the status of microorganisms as living organisms is irrelevant for the purposes of patent law.[6] The extension of patent protection to microorganisms provided the foundation for the subsequent extension of patentability to living organisms and DNA (deoxyribonucleic acid).

Growth in patenting related to microorganisms reflects the importance of microorganisms as a rich and largely untapped source of DNA, amino acids, and proteins such as enzymes for the pharmaceutical, agricultural and chemical industries.[7] A specialist group of biotechnology companies have now emerged which focus on the identification and commercialisation of the properties of

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[1] Secretariat of the Convention on Biological Diversity (2001) *Global Biodiversity Outlook*. Montreal: Secretariat of the Convention on Biological Diversity (SCBD). Citation at 61.

[2] Ibid., SCBD 2001. The protoctists are also known as protists.

[3] WIPO 'Inventions (patents)'. Location: <http://www.wipo.int/about-ip/en/patents.html>.

[4] United States Patent and Trademark Office 'General Information Concerning Patents' online brochure. Citation at 'What is a patent?'. Location: <http://www.uspto.gov/web/offices/pac/doc/general/>.

[5] See Kevles, D (2002) *A history of patenting life in the United States with comparative attention to Europe and Canada*. European Group on Ethics in Science and New Technologies to the European Commission. 12 January 2002. Luxembourg: Office for Official Publications of the European Communities. Location: <http://europa.eu.int/comm/european_group_ethics/docs/study_kevles.pdf >

b) The text of the *Diamond v. Chakrabarty* judgement is available online. Location: <http://supct.law.cornell.edu/supct/cases/patent.htm>.

[6] Ibid., *Diamond v. Chakrabarty.*

[7] GRAIN (1999) 'Bacteria Become Big Business'. *Seedling*, March 1999. Location: <http://grain.org/seedling/?type=17>.

microorganisms. Microorganisms are also a particular focus of attention for public and private genome mapping projects.[8]

Concerns in connection with the rise of intellectual property protection over microorganisms can be briefly summarised as follows:

a) The ethics of patenting life-forms;
b) The eligibility of such organisms for patent protection on the grounds of whether they are new (or novel), involve an inventive step (are non-obvious) and susceptible to industrial application (utility);
c) The terms and conditions of bioprospecting arrangements between companies and developing country institutions, and indigenous peoples and local communities, and;
d) The longer term implications of the temporary enclosure of the world's microorganisms through patent grants for the promotion of research and innovation.

Bioprospecting for microorganisms and so-called "extremophiles" aided by discoveries such as "Conan the Bacterium" (*Deinococcus radiodurans*) has recently risen to scientific, public and policy attention.[9] In particular, the exploitation of microorganisms and microbial resources has drawn attention to the potential of access and benefit-sharing arrangements in protected areas to generate revenue and other potential benefits. In contrast, wider trends in the patenting of microorganisms and the public policy implications of such trends have received less attention.

The review begins by examining a bioprospecting agreement involving microorganisms within a protected area as a contribution to identifying the public policy issues surrounding access and benefit-sharing agreements involving intellectual property claims. The review then turns to the analysis of the implications of global trends in the patenting of microorganisms.

[8] See the Genomes OnLine Database (GOLD) for details of genome mapping projects related to microorganisms. Location: <http://www.genomesonline.org>.

[9] See: a) Black, H (2002) 'Extremophiles: they love living on the edge', *The Scientist*, Vol. 16, Issue 14, 8, July 8, 2002. Location: <http://www.the-scientist.com/yr2002/jul/research1_020708.html>; b) Hogan, J (2002) 'Can tough little bugs speed up computing?', *New Scientist*, 7th December 2002. Location: <http://www.newscientist.com/hottopics/quantum/quantum.jsp?id=23722000>; c) For discussion of Conan the Bacterium see, The Associated Press (2004) 'Bioprospecting in nature fuels debate: Profits and stewardship at play', The Associated Press, 7th July 2004. Location: <http://www.msnbc.msn.com/id/5295305/>.

I. Microorganisms and Protected Areas:

International attention has been drawn to the economic importance of microorganisms as a result of an historic case from Norway. In 1969 a scientist working for the Switzerland based Sandoz company collected soil samples in the Hardangervidda mountains while on holiday.[10] The samples were found to contain a fungus, *Tolypocladium inflatum* within which a compound which came to be known as Cyclosporin was identified (also known as Cyclosporine). This led to the development of a new and critically important immunosuppressant drug for preventing organ transplant rejection (Sandimmun/Neoral).[11] Following the merger of Sandoz and Ceiba Geigy to form the Novartis Group in 1996 Sandimmun/Neoral was transferred to the new company. In 2000 Novartis generated CHF 2,052 million, CHF 1,829 in 2001, CHF 1,607 in 2002 and CHF 1,020 in 2003 from sales of Sandimmun/Neoral.[12]

This historic pre-CBD example illustrates the potential economic importance of microorganisms and microbial materials as sources of potentially valuable compounds, genes, amino acids and proteins such as enzymes and has led some commentators to suggest that if 2% annual royalties had applied this would have generated revenue of US$24.3 million for Norway in 1997.[13] The Hardangervidda mountains were designated as a national park in 1981 and this has served to highlight the potential of microorganisms and microbial resources as potential sources of revenue for protected areas.[14]

More recently, companies have demonstrated growing interest in so-called "extremophiles" in countries such as Canada (among others).[15] Increasingly this extends to protected areas, marine environments, and areas governed under international treaty arrangements (notably Antarctica).[16] These trends have in part been presented as a retreat on the part of companies from the controversies which have surrounded bioprospecting activities in developing countries.[17] However, these

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[10] Svarstad, H., Dhillion, S., Bugge, H. (2000), 'From Norway to Novartis: Bioprospecting within an open access regime', *Biodiversity and Conservation*, 9(11).

[11] Heusler, K and Pletscher, A (2001) 'The controversial early history of cyclosporin', *Swiss Medical Weekly*, 2001, 131: 299-302. Location: <http://www.smw.ch>.

[12] Novartis Group 2000 – 2003 *Annual Reports*. The declines in revenue are attributed to the emergence of generic competitors following the expiry of the original patents. The original developer of Cyclosporin products (Sandoz) developed a patent portfolio of approximately 79 patents of which the first appears to have been awarded in Switzerland in 1973. Novartis presently possesses approximately 60 patents and applications related to Cyclosporin according to a search of the esp@cenet database of which the most recent application was published in April 2004. Location: <http://www.novartis.com/investors/en/sales_reports/annual_reports.shtml>.

[13] Ibid., Svarstad, Dhillion, and Bugge 2000.

[14] Norway Directorate for Nature Management, entry for Hardangervidda. Location: <http://www3.dirnat.no/nasjonalparker/engelsk/psmaler/park.asp?thisId=951914842>.

[15] Dalton, R (2002) 'Bioprospectors turn their gaze to Canada', *Nature* 419, 768, 24th of October, 2002.

[16] See: a) Lohan, D and Johnston, S (2003) *The International Regime for Bioprospecting: Existing Policies and Emerging Issues for Antarctica*. UNI/IAS Report. Tokyo: United Nations University/Institute of Advanced Study.

Location: <http://www.ias.unu.edu/binaries/UNUIAS_AntarcticaReport.pdf>; b) See also, ETC Group (2004) 'Rocking the Boat: Craig Venter's Microbial Collecting Expedition Under Fire in Latin America', ETC Group News Item, 22 July 2004. Location: <http://www.etcgroup.org/article.asp?newsid=473>.

[17] Hayden, C (2003) 'From market to market: Bioprospecting's idiom of inclusion', *American Ethnologist*, Vol. 30, No. 3 August 2003. 359-371.

trends raise wider public policy issues which can be introduced through reference to the case of the Yellowstone National Park in the United States.[18]

Bioprospecting in Yellowstone National Park:

Yellowstone National Park "…is home to an estimated eighty percent of the world's terrestrial geysers and more than half of its thermal features, including hot springs, mud pools, and fumeroles".[19] In 1966 Dr. Thomas Brock accompanied by Hudson Freeze of Indiana University discovered a microorganism *Thermus aquaticus* (a bacterium) in Mushroom Pool in Yellowstone National Park which was resistant to high temperatures.[20] The microorganism was then deposited in the American Type Culture Collection (ATCC) thus making the discovery publicly available.[21]

One of the major obstacles for the emerging arenas of biotechnology and genomics in the 1970s and early 1980s was the time consuming process involved in replicating or amplifying DNA (deoxyribonucleic acid) which had to be performed by hand. In 1983 Dr. Kary Mullis, a scientist working for Cetus corporation, conceived of the Polymerase Chain Reaction (PCR) to dramatically increase the speed of DNA replication.[22] This involves a basic three step process: a) denaturation; b) annealing of primers; c) primer extension.[23] In the first step (denaturation) an excess of primer consisting of synthetic nucleotides is mixed with the DNA to be replicated and heated to 98ºC until the two strands of DNA separate. This is then allowed to cool to 60ºC at which point the separated DNA strands begin to stick (or anneal) to the complementary sections of the primer DNA (annealing of primers). During the third step (primer extension) a thermostable enzyme is added and through repeated cycles of heating and cooling multiple copies of the target DNA are created. The strength of this technique is that a single fragment of DNA can be replicated upto one million times in merely 20 cycles of heating and cooling. Dr. Mullis was subsequently awarded the Nobel Prize for his contribution to science in 1993.[24]

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[18] For background information on the case see: a) ten Kate, K and Touche, L & Collis, A (1998) *Benefit-sharing case study: Yellowstone National Park and the Diversa Corporation.* Submission to the Executive Secretary of the Convention on Biological Diversity by the Royal Botanic Gardens, Kew, 22 April 1998. Location: <http://www.biodiv.org/doc/case-studies/abs/cs-abs-yellowstone.pdf>; b) Doremus, H (1999) 'Nature, Knowledge and Profit: The Yellowstone Bioprospecting Controversy and the Core Purposes of America's National Parks', *Ecology Law Quarterly* 26, 401; c) Wood, M (2000) 'Are National Park Resources for Sale?: Edmonds Institute v. Babbitt', *Public Land & Resources Law Review*, Vol. 21. 189-210. Location: <http://www.umt.edu/law/lawrev/pllr/v21/wood.pdf>.

[19] United States District Court for the District of Columbia *Edmonds Institute v. Babbitt* 'Memorandum Opinion', Civil Action 98-561(RCL). 24th March 1999. Location: <http://www.edmonds-institute.org/yellowstone98561.pdf.>. See also, Ibid., ten Kate, K et al. (1998).

[20] See: a) Yellowstone National Park 'Thermophiles', Location: <http://www.nps.gov/yell/nature/thermophiles/biopro.html>; b) Brock, T and Freeze, H (1969) '*Thermus aquaticus* gen. N and sp.n., a Nonsporulating Extreme Thermophile', *Journal of Bacteriology*, 1969 April 98 (1): 289-297. Location: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=249935>.

[21] American Type Culture Collection. Location: <http://www.atcc.org/>.

[22] For a detailed history see Rabinow, P (1996) *Making PCR: A Story of Biotechnology*. Chicago: University of Chicago Press.

[23] This description is taken from Raven, P and Johnson, G (2002) *Biology*. Sixth Edition. Boston: McGrawHill. Citation at 398.

[24] See: a) Nobelprize.org. Location: <http://nobelprize.org/chemistry/laureates/1993/index.html>; b) Kary Mullis's homepage. Location: <http://www.karymullis.com>; c) Ibid., Rabinow 1996.

Thermus aquaticus proved to be central to the success of PCR by providing a thermostable enzyme (Taq DNA polymerase) capable of withstanding the high temperatures required for the PCR process.[25] This technique and the enzyme derived from *Thermus aquaticus* are commonly used in DNA replication around the world: it is difficult to overstate the importance of both the technique and the enzyme in the arena of biotechnology.[26] The patent on the enzyme was reportedly sold for US$300 million in 1991 and generated an annual revenue of US$100 million for the company concerned.[27] However, Yellowstone National Park did not directly benefit from the revenue generated by the discovery. [28]

In recognition of the desirability of securing a share of benefits which may arise from research on the resources within Yellowstone National Park, in 1995 the National Park Service (NPS) entered into negotiations to establish a benefit-sharing agreement with Diversa Inc..[29] Diversa is a biotechnology company formed in 1994 which specialises in bioprospecting for extremophiles.[30] The company expresses a public commitment to the objectives of the Convention on Biological Diversity and has entered into access and benefit-sharing agreements in a number of countries and regions.[31]

In 1997 a Cooperative Research and Development Agreement (CRADA) was agreed between the National Park Service (under the Department of the Interior) and Diversa under which the parties agreed to cooperate in researching and documenting the biodiversity of the geysers, hot springs, lakes and other ecosystems within the Park.[32] Sample collection in the field would be followed by reproduction in the laboratory, isolation of nucleic acids, cloning and creation of a genetic library.[33] The genetic library would then be screened for enzymes and bioactive molecules for potential commercial development. The libraries would also reportedly be made available to Park scientists.

The Cooperative Research and Development Agreement (hereafter CRADA) is reported to award a non-exclusive license for research and development relating to microbial organisms in Yellowstone for which Diversa agreed to pay an annual fee of an estimated US$20,000.[34] Diversa also agreed to pay royalties to the Park of between

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[25] The process initially employed an enzyme from *E.coli*, see ibid., Rabinow 1996.

[26] *Thermus thermophilus* provides an alternative enzyme for the PCR process.

[27] United States District Court for the District of Columbia *Edmonds Institute v. Babbitt* 'Memorandum Opinion', Civil Action 98-561(RCL). 24th March 1999. Location:

<http://www.edmonds-institute.org/yellowstone98561.pdf>.

[28] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[29] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[30] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'

[31] Diversa's Annual Report for 2003 lists the following states, countries, and organisations as sources of material: Alaska, Antarctica, Australia, Bermuda, Costa Rica, Hawaii, Iceland, Ghana, Indonesia, Kenya, Mexico, Puerto Rico, Russia, the San Diego Zoological Society, South Africa, and Yellowstone National Park. Diversa (2003) *Diversa: Discovering and Evolving the Best from Nature*. Annual Report 2003. Citation at 15. Location: <http://www.diversa.com/inverela/Diversa_Annual_Report_2003.pdf>.

[32] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[33] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[34] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

0.5% and 10% on any future commercial development "…depending upon the nature of the raw material and final product."[35]

On the 5th of March 1998 a coalition of non-profit NGOs consisting of the Edmonds Institute, and the Alliance for the Wild Rockies, assisted by the International Center for Technology Assessment in Washington, and supported by a Mr. Philip Knight (a Yellowstone guide and activist), filed a legal challenge to the agreement on the grounds of "...violation of the Federal Technology Transfer Act of 1986, the National Park Service Organic Act, the Yellowstone National Park Organic Act, the National Environmental Policy Act, and public trust doctrine."[36]

The key focus of the case was whether the National Park Service (hereafter NPS) had engaged in public consultation and carried out the necessary environmental impact assessments required under the National Environmental Policy Act (NEPA).[37] Furthermore, the plaintiffs argued that the agreement violated the prohibition on "…sale or commercial use of natural products" under Park Service regulations and the public trust doctrine.[38]

The NPS sought to defend itself against these allegations by asserting that "…the collection of specimens under the CRADA will amount to taking samples that each contain about a teaspoon of water, sediment, and microbial life". As such any aesthetic and environmental consequences would allegedly be minimal.[39]

However, presiding Judge Royce C. Lamberth observed that "…although each sample taken from Yellowstone may be the size of a test tube, the overall impact of the specimen collection authorized by the CRADA and its corresponding permit is not teaspoon-sized."[40] Judge Lamberth went on to observe that:

> "There is an undeniable reality that commercial activity is qualitatively different than scientific and educational activity of a similar nature, due to the very different forces and motivations that drive them."[41]

Judge Lamberth concluded that the issues raised, required "…intensive deliberation by the defendants, ideally with public-input--precisely the deliberation mandated by Congress through the NEPA…" and ordered:

> "…that defendants suspend implementation of the Yellowstone-Diversa CRADA pending the completion of any and all review mandated by the National Environmental Policy Act, including but not limited to the preparation of an Environmental Assessment."[42]

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[35] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[36] Edmonds Institute et. al. (1999) 'Public Interest Wins in Yellowstone Case', Press Release, March 25th 1999. Location: <http://www.icta.org/ctanews/yellrel.htm>.

[37] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[38] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[39] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[40] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[41] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

[42] Ibid., *Edmonds Institute et. al., v. Babbitt* 'Memorandum Opinion'.

On the 12th of April 2000, Judge Lamberth issued his final judgement in the case. On this occasion Judge Lamberth found that in practice the National Park Service had correctly interpreted the relevant legislation and regulations. Specifically, he found that the company concerned would not own the organisms they collected and would be required to meet the conditions for normal research permission.[43] Judge Lamberth observed that the CRADA only applied to: "…rights and responsibilities of Yellowstone and Diversa with respect to information and inventions developed after the conclusion of research specimen collection and analysis" (original emphasis).[44] Furthermore, in the absence of such an agreement, "…Yellowstone could not share in any of the potential benefits from Diversa's research. Instead the positive gains from the research would go exclusively to Diversa."[45] On this basis Judge Lamberth concluded that the NPS had correctly interpreted the governing statutes of the Park "…because it would produce direct, concrete benefits to the Park's conservation efforts by affording greater scientific understanding of Yellowstone's wildlife, as well as monetary support for Park programs."[46]

Judge Lamberth also concluded that opposition to the proposed agreement on the grounds that this would represent "sale or commercial use" of Park resources in breach of the Park's mandate was not sustainable. In drawing this conclusion, Judge Lamberth referred to the case of *Diamond v. Chakrabarty* to support the view that the company concerned would not obtain a property right over the specimens as such (*per se*), or a right to transfer such specimens to third Parties, in contravention of Park regulations.[47] Rather, the Judge concurred with the National Park Service view that there is:

> "...a critical distinction between researchers profiting from the sale of the actual specimens themselves, which is prohibited by Section 2.1, and profiting from a future development based on scientific discoveries resulting from research on those resources, which is permitted."[48]

On this basis the case was dismissed "with prejudice". The NPS may proceed with the benefit-sharing agreement subject to the provisions of the previous order requiring action including "but not limited to" the preparation of an Environmental Assessment in accordance with the NEPA .[49]

The potential attractions of the establishment of access and benefit-sharing agreements between National Park authorities and private companies are apparently, but, as will be seen, deceptively straight-forward. Thus, it is widely recognised that the majority of protected areas around the world are under-funded: the revenue and research capacity building which may potentially result from benefit-sharing agreements with the private sector or Public Research Organisations could potentially

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[43] United States District Court for the District of Columbia *Edmonds Institute, et al., v. Babbitt.* 'Order and Final Judgement'. Civil Action No. 98-561 (RCL) April 12th 2000.

[44] Ibid., *Edmonds Institute, et al., v. Babbitt.* 'Order and Final Judgement', at 18.

[45] Ibid., *Edmonds Institute, et al., v. Babbitt.* 'Order and Final Judgement,' at 19.

[46] Ibid., *Edmonds Institute, et al., v. Babbitt.* 'Order and Final Judgement,' at 20.

[47] Ibid., Kevles 2002.

[48] Ibid., *Edmonds Institute, et al., v. Babbitt.* 'Order and Final Judgement,' at 22.

[49] Ibid., *Edmonds Institute, et al., v. Babbitt.* 'Order and Final Judgement'.

play an important role in addressing conservation objectives.[50] Furthermore, as the NPS highlighted, under the prevailing law within the United States, companies or researchers are free to engage in the commercialisation of the results of research carried out on specimens collected within national parks but the parks will receive no direct benefits in the absence of access and benefit-sharing agreements.[51] The extent to which this situation pertains elsewhere in the world is an open question.

In 2002 the delegation of the United States of America submitted a report entitled 'Access to Genetic Resources Regime of the United States National Parks' to the WIPO Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore (the IGC) as a contribution to discussion.[52] This experience may also have informed development of the new programme of work on protected areas established by the Seventh Conference of the Parties to the Convention on Biological Diversity (COP7) which includes an element relating to the third objective of the Convention.[53]

In considering this important initiative it is also necessary to consider the wider policy implications of intellectual property protection in access and benefit-sharing arrangements that may be established in protected areas. These issues are particularly important in a context in which many protected areas around the world are inhabited and in view of the promotion of protected areas managed by indigenous peoples and local communities under the programme of work on protected areas established by COP7 (Decision VII/28).[54] These implications come into focus through closer attention to the history of Taq DNA polymerase.

The case of Taq DNA Polymerase:

As noted above, the discovery of *Thermus aquaticus* and an enzyme, Taq DNA polymerase which is stable at the temperatures required for Polymerase Chain Reaction (PCR) has been fundamental to the emergence of biotechnology and genomics. As also noted Taq DNA polymerase serves as an exemplar for the potential of access and benefit-sharing arrangements to generate revenue and other benefits for conservation within national parks.

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[50] COP Decision VII/28 'Protected areas (Articles 8 (a) to (e))', para. 17. Location: <http://www.biodiv.org/decisions/default.aspx?m=COP-07&id=7765&lg=0>.

[51] See Ibid., ten Kate, K et al. (1998) for discussion of the legal background to the establishment of the CRADA agreement.

[52] WIPO (2002) 'Access to Genetic Resources Regime of the United States National Parks'. Document submitted by the Delegation of the United States of America. Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore, Fourth Session. Document WIPO/GRTKF/IC/4/13. Dated: December 6th, 2002.

Location: <http://www.wipo.int/documents/en/meetings/2002/igc/pdf/grtkf_ic_4_13.pdf>.

[53] See COP Decision VII/28 'Protected areas (Articles 8 (a) to (e))', Programme element 2, para. 2.1.6 "Establish or strengthen national policies to deal with access to genetic resources within protected areas and fair and equitable sharing of benefits arising from their utilization, drawing upon the Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilization as appropriate." Location: <http://www.biodiv.org/decisions/default.aspx?m=COP-07&id=7765&lg=0>.

[54] COP Decision VII/28 'Protected areas (Articles 8 (a) to (e))', see for example Goal 2.1 activity 2.1.3 and Goal 2.2 of the programme of work.

Location: <http://www.biodiv.org/decisions/default.aspx?m=COP-07&id=7765&lg=0>.

There are three main patents relating to the PCR process and Taq DNA polymerase (hereafter Taq). US patent 4,683,202 filed in October 1985, listing Dr. Kary Mullis as the inventor, refers to the PCR process for "amplifying nucleic acid sequences" and is followed by US patent 4,683,195 filed in February 1986 concerning a "Process for amplifying, detecting, and/or cloning nucleic acid sequences."

In June of 1987 a separate application (US 4,889,818, hereafter '818) was filed by other researchers at Cetus corporation claiming:

a) a "Purified thermostable *Thermus aquaticus* DNA polymerase";
b) the polymerase isolated from *Thermus aquaticus*, and;
c) the same polymerase isolated from a recombinant organism (a bacteria) designed to express the *Thermus aquaticus* DNA polymerase.

These three patents form the basis for the revenue generated from licensing PCR. As noted above, it is widely reported that the patents were sold to Hoffman-LaRoche Corporation (also known as Roche) for $300 million and are estimated to have generated annual revenue of upto $100 million per year. According to one recent unconfirmed report: "Roche has gained US$2 billion from control of the PCR process."[55] However, the Taq polymerase patent ('818) has also been the focus of over twelve years of ongoing litigation in multiple jurisdictions and is the subject of a US$1 billion lawsuit.[56]

Controversy surrounding the Taq polymerase patent emerged in 1992 when Hoffman –LaRoche and Roche Molecular Diagnostics (a division of Hoffman-LaRoche[57]) filed a lawsuit against the US based Promega Corporation alleging breach of contract and infringement of the Taq patent ('818) and related PCR process patents for sales of unlicensed Taq.[58] In response, Promega alleged that the original Taq patent had been obtained from the United States Patent and Trademark Office (USPTO) through "inequitable conduct" consisting of fraudulent claims. Specifically, Promega alleged that the applicants had made a series of misrepresentations to the USPTO in applying for the '818 patent relating to:

a) the molecular weight of the Taq enzyme relative to the weight reported by other researchers in the US and Russia in prior publications;
b) claims that a key experiment had been conducted at the time of the application that had not in fact been conducted;
c) technical claims relating to the distinction between previously published results surrounding Taq polymerase and the enzyme described in the patent application.

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[55] Fleisher-Black, M (2004) 'The Hydra-Headed Patent Case: Roche's fight to hold on to PCR is popping up in courtrooms all over the country', *IP Law & Business*, July 2004. Location: <http://www.ipww.com/texts/0704/os.hydra0704.html>.

[56] Promega (2003) 'Hoffmann-LaRoche charged with conspiracy and filing false, fraudulent claims in new $1 billion lawsuit filed by Promega', Press Release, November 12, 2003. Location: <http://www.promega.com/pressrelease/031113rochefraud.htm>.

[57] Roche Molecular Diagnostics, Inc is the operating name of Roche Diagnostics in the United States. Location: <http://www.roche-diagnostics.com/FPLBusiness_molecular.html>.

[58] Promega (nd.)'Taq Patent News: US Chronology', Location: <http://www.promega.com/taqlegal/lchron.htm>.

On December the 7th 1999 the United States District Court, Northern District of California held that all claims in the '818 patent for Taq are "unenforceable" due to "inequitable conduct" consisting of misrepresentations before the USPTO.[59]

This judgement was considered by the US Court of Appeals for the Federal Circuit on the 31st of March 2003 which partly affirmed and partly reversed the judgement of the lower court to which the case was again referred.[60] In a second judgement filed on the 13th of May 2004, Judge Vaughn, R Walker, confirmed the unenforcability of the Taq '818 patent due to inequitable conduct and expressed further reservations surrounding the process patents.[61] The case is now likely to move back to the Court of Appeals for the Federal Circuit.[62]

The case has also been pursued in other jurisdictions in the United States and overseas.[63] In Europe, the patent was overturned by the European Patent Office (EPO) Board of Appeals (Opposition Division) on the 30th of May 2001 but was reinstated in October 2003.[64] In Australia, the claims to the Taq polymerase were rejected in November 1997 but reportedly remain subject to appeal.[65]

The litigation surrounding the legitimacy of the patent over the Taq enzyme is complex, ongoing, and involves high stakes for the parties concerned. This review focuses on the public policy implications arising from disputes in relation to the role of patent protection in access and benefit-sharing arrangements within protected areas. Five main issues stand out.

The first of these is the impact of patents on research and innovation. As noted above, Taq is central to the PCR process. The patent on Taq signifies that Public Research Organisations and companies are required to use licensed Taq in countries where the patent is in force or risk litigation. Details of licensing costs for Taq are reported to be confidential and apparently determined by Roche Diagnostics on a case by case

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[59] United States District Court, Northern District of California *Hoffmann-LaRoche Inc. and Roche Molecular Systems Inc., v. Promega Corporation*. No C-93-1748 VRW at 67, line 16.
Location: <http://www.promega.com/taqlegal/991207/991207order.pdf>.

[60] U.S Court of Appeals for the Federal Circuit (2003) *Hoffman-La Roche Inc. v. Promega*, Docket No.00-1372. 31st of March 2003. Location: <http://www.ll.georgetown.edu/federal/judicial/fed/march2003.cfm>. See also, Brickley, P (2003) 'Promega wins *Taq* patent round', *The Scientist*, April 1, 2003.

Location: <http://www.biomedcentral.com/news/20030401/04/>.

[61] United States District Court, Northern District of California *Hoffmann-LaRoche Inc. and Roche Molecular Systems Inc., v. Promega Corporation*. No C-93-1748 VRW. Filed May 13th 2004. Location: <http://www.roche-diagnostics.com/media/pdf/ba_rmd/remedies_order.pdf>.

[62] Roche Molecular Diagnostics 'Key Events Related to the Dispute Between Roche Molecular Systems, Inc. and Promega Corporation', May 13th 2004.

Location: <http://www.roche-diagnostics.com/ba_rmd/pcr_litigation_chronology.html>.

[63] Fleisher-Black, M (2004) 'The Hydra-Headed Patent Case: Roche's fight to hold on to PCR is popping up in courtrooms all over the country', *IP Law & Business*, July 2004.

Location: <http://www.ipww.com/texts/0704/os.hydra0704.html>.

[64] Roche (2003) 'Roche Diagnostics Patent for Key PCR Enzymes Upheld in Europe: The Ruling is the Final Determination of the European Patent Office and Cannot be Appealed', Trade Press Release, Basel, 30th October 2003.

Location: <http://www.roche-diagnostics.com/media/pdf/press_release/2003/press-release_30102003-1.pdf>.

[65] Roche Diagnostics 'Key Events Regarding Australian Patent Applications',

Location: <http://www.roche-diagnostics.com/ba_rmd/pcr_litigation_chronology.html>.

basis.[66] Investigations into the cost of licensed Taq from licensees are also reported to have been met with a refusal to disclose details.[67] However, a 2001 report in *Nature* suggests that the cost of the polymerase was around 50 cents each time it was used in a single round of genotyping.[68] In contrast, non-licensed Taq was estimated to cost 20-30% less than the licensed enzyme.[69] It has been reported that the cost of unlicensed Taq has fallen to between 10 cents and 16 cents per unit.[70]

For publicly funded research organisations employing PCR such cost differentials are significant and are likely to influence the type and amount of research (i.e. genotyping) that can be conducted. This problem was highlighted in a 1996 workshop convened by the United States National Research Council where participants argued that the cost of the polymerase was inhibiting widespread use of diagnostic tests for HIV RNA. Other participants reported that "…the high cost *Taq* polymerase made many experiments impossible for them" particularly in areas of research that do not attract the levels of funding of human genetic research.[71] Small biotechnology companies were also reported to be affected by the high cost of the Taq enzyme and related PCR technology. The dependency of researchers on the Taq enzyme and other patented enzymes is reflected in the close attention that the patent dispute has received in the scientific press and concerns surrounding the implications of the case for research budgets.[72]

In addition to the price of licensed Taq concern has also been expressed about whether those using unlicensed Taq will be pursued for fees if the patent is upheld. It has commonly been assumed that a "research exemption" or "experimental use exemption" applies to non-commercial research and such measures have been introduced in a number of countries.[73] However, in the United States a 2002 decision by the Court of Appeals for the Federal Circuit in *Madey v. Duke University* held that this exemption does not apply except in the "very narrow form" determined by the court in earlier cases.[74]

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[66] Beck, S (1998) 'Do You Have A License?: Products Licensed for PCR in Research Applications,' *The Scientist*, 12 [12], 21st June 1998. Location: <http://www.the-scientist.com/yr1998/june/profile2_980608.html>.

[67] Ibid., Beck 1998.

[68] Dalton, R (2001) 'Patent ruling could cut PCR enzyme prices', *Nature* 411, 622. Location: <http://www.nature.com/cgi-taf/DynaPage.taf?file=/nature/journal/v411/n6838/full/411622a0_fs.html&content_filetype=PDF>.

[69] Ibid., Dalton, R 2001.

[70] See: a) Brickley, P (2003) 'The Trouble with Taq', *The Scientist*, Volume 17, Issue 10, May 19, 2003.

Location: <http://www.the-scientist.com/yr2003/may/prof4_030519.html>; b) New England Biolabs advertises unlicensed Taq at US$200 for 2,000 units, amounting to 10 cents per unit. Location: <http://www.neb.com/nebecomm/products/productM0267.asp>.

[71] National Research Council (1996) *Intellectual Property Rights and Research Tools in Molecular Biology*. Summary of a Workshop Held at the National Academy of Sciences, February 15-16, 1996. Section 5 Case Studies. Location: <http://books.nap.edu/html/property/>.

[72] Ibid, Brickley 2003.

[73] See McBratney, A., Nielsen, K., and McMillan, F. (2004) 'Australia experiments with 'experimental use' exemption', *Nature Biotechnology* 22: 1023-1025.

[74] See: a) Eisenberg, R (2003) 'Patent Swords and Shields,' *Science*, 14th February 2003; 299:1018-1019; b), McBratney, A., Nielsen, K., and McMillan, F. (2004) 'Australia experiments with 'experimental use' exemption', *Nature Biotechnology* 22: 1023-1025; c) the text of *Madey v. Duke University* is available at <http://cyber.law.harvard.edu/people/tfisher/2002Madeyedit.html>, see "The Experimental Use Defense" for quotation.

A second and related issue surrounds the nature of patent claims in relation to DNA, amino acids, and proteins such as enzymes. The key problem here is that in contrast with other areas of invention addressed by the patent system it is not presently possible to readily "invent around" DNA, amino acids, and proteins such as enzymes.[75] Put simply, DNA molecules and complex folded proteins such as enzymes are presently beyond the skill of human beings to actually create i.e. through synthetic chemistry.[76] Thus, the Taq enzyme was not created or invented by the researchers at Cetus: it is a highly efficient naturally occurring biological catalyst that has been artificially replicated by researchers.[77] It is becoming increasingly clear that the practical effect of permitting patent claims over artificially reproduced DNA and related amino acids, proteins or enzymes is to provide a strong monopoly over the biological make-up (or claimed components) of an organism. When seen from this perspective, in practice a non-exclusive licensing agreement between a national park and a private company which permits patent claims may provide that company with an effective monopoly over the relevant DNA and/or amino acid, protein and enzyme make-up of the organisms concerned.

This has further implications for research. Thus, court documents reveal that Park scientists will be provided with access to the genetic libraries to be developed under the agreement. It is not entirely clear whether such access is confined to scientists employed directly by the National Park Service or may extend to other researchers working within the Park. This raises questions surrounding the criteria that will be employed to determine access to collections made under access and benefit-sharing agreements, potential conflicts of interest, and wider issues surrounding the implications of the increasing commercialisation of research.

Thus, in recognising the importance of the case presented by the NGO coalition, Judge Lamberth drew attention to the critical distinction between the forces which motivate commercial activity and scientific and educational activity. Court documents suggest that all researchers who engage in research within a national park which may lead to commercial developments will be required to sign a CRADA access and benefit-sharing agreement. This raises the question of where the boundary between non-commercial and commercial research will be drawn and by whom?

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[75] This point has been widely noted. See for example: a) Nuffield Council on Bioethics (2002) *The ethics of patenting DNA: a discussion paper*. London: Nuffield Council on Bioethics, Location: <http://www.nuffieldbioethics.org/fileLibrary/pdf/theethicsofpatentingdna.pdf>; b) OECD 2002 *Genetic Inventions, Intellectual Property Rights and Licensing Practices: Evidence and Policies*. Paris: Organisation for Economic Co-operation and Development, Location: <http://www.oecd.org/dataoecd/42/21/2491084.pdf>; c) Royal Society (2003) *Keeping Science Open: The Effects of Intellectual Property Policy on the Conduct of Science*. London: Royal Society, Location: <http://www.royalsoc.ac.uk/files/statfiles/document-221.pdf>.

[76] Chemical synthesis of DNA has been possible for at least 20 years, however, this is generally confined to a couple of hundred DNA base pairs for academic experimental purposes and could not presently extend to the construction of DNA leading to the expression of an enzyme. A recent example of an attempt to create artificial DNA is provided by a team led by Dr. Steven Benner at the University of Florida who reported success in creating a DNA like molecule involving six nucleotides (as opposed to the natural four nucleotides) in February of 2004. However, Dr. Benner reported that the artificial DNA would not survive outside the laboratory. See 'Evolving Artificial DNA', *Astrobiology Magazine*, Thursday, February 26th 2004.

Location: <http://www.astrobio.net/news/article845.html>.

[77] For a detailed discussion of the role of enzymes as natural catalysts see Raven, P and Johnson, G (2002) *Biology*. Sixth Edition. Boston: McGrawHill.

It has been widely observed that in the 20th Century the boundary between commercial and non-commercial research became increasingly blurred.[78] In the case of the United States, the 1980 Bayh-Dole Act sought to promote innovation by permitting intellectual property claims over the outcomes of federally sponsored research.[79] In response, universities and other Public Research Organisations have engaged in the aggressive pursuit of intellectual property protection in order to generate revenue.[80] The application of this model is now being promoted on a wider level by organisations such as the Organisation for Economic Co-operation and Development (OECD) as part of a process of "Turning Science into Business".[81] Patent claims by Public Research Organisations (PROs), such as universities, commonly take the form of claims not to commercial products but to basic "research discoveries and research tools" such as DNA, amino acids, and proteins such as enzymes.[82] While drawn from the private sector the Taq DNA polymerase '818 patent is in fact cited as a key example of a "research tool" patent.[83]

The rise of patenting by universities in the United States has led to a situation in which universities are increasingly in competition with each other and with the private sector and is manifest in the increasing establishment of Technology Transfer Offices and the use of tools such as Material Transfer Agreements (MTAs) to regulate relationships.[84] One consequence of this competition is a lack of willingness to share or publish research results until requirements for patent submission have been met.[85] Taking into account the shared commercial contexts in which Public Research Organisations such as universities and private companies now operate, it is unclear what incentive researchers who signed CRADA agreements would possess to collaborate with others in the pursuit of the wider conservation and/or sustainable use objectives of a protected area. Any temptation to naïvely romanticise the "open" tradition of science should be resisted. However, one practical effect of the introduction of commercial competition into protected areas could be to inhibit

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[78] See for example: a) Ibid., Rabinow 1996; b) ten Kate, K and Laird, S (1999) *The Commercial Use of Biodiversity*. London: Earthscan; c) Royal Society (2003) *Keeping Science Open: The Effects of Intellectual Property Policy on the Conduct of Science*. London: Royal Society, Location: <http://www.royalsoc.ac.uk/files/statfiles/document-221.pdf>.

[79] Rai, A and Eisenberg, R (2003) 'Bayh-Dole Reform and the Progress of Biomedicine', *Law and Contemporary Social Problems*, Winter/Spring 2003, Vol. 66: 289-314. Location: <http://www.law.duke.edu/journals/66LCPRai>.

[80] This point has been widely noted, see for example, Ibid., Rai and Eisenberg 2003.

[81] OECD (2003) *Turning Science into Business: Patenting and Licensing at Public Research Organisations*. Paris: Organisation for Economic Co-operation and Development. Available from: <http://www.oecd.org/document/61/0,2340,en_2649_34797_2513917_1_1_1_1,00.html>.

[82] Ibid., Rai and Eisenberg 2003 at 292. See also NIH (1998) *Report of the National Institutes of Health (NIH) Working Group on Research Tools*. June 4 1998. Location: <http://www.nih.gov/news/researchtools/>. See also National Research Council (1996) *Intellectual Property Rights and Research Tools in Molecular Biology*. Summary of a Workshop Held at the National Academy of Sciences, February 15-16, 1996. Location: <http://books.nap.edu/html/property/>.

[83] Ibid., National Research Council 1996.

[84] See for example, Park, P (2004) 'Buffalo Case Highlights MTAs: Material transfer agreements can be misunderstood or considered an annoyance, say officials', *The Scientist*, August 9th 2004. Location: <http://www.biomedcentral.com/news/20040809/03>.

[85] See for example, Ibid., Royal Society 2003. A number of countries including the United States provide for a grace period wherein publication of research results does not destroy novelty if a patent application is submitted within the time frame established by the grace period. Grace periods for publication in relation to patent applications appear to vary significantly from country to country. See for discussion, McBratney, A. Nielsen, K and McMillan, F (2004) 'Australia experiments with 'experimental use' exemption', *Nature Biotechnology* 22: 1023-1025.

collaborative research in the pursuit of conservation and/or sustainable use objectives. Furthermore, the increasing commercialisation of publicly funded research may skew research away from important areas of research such as conservation and sustainable use in favour of research directed towards securing revenue.[86]

A fourth public policy issue surrounds the risk of involvement in patent litigation and/or claims of "inequitable conduct". Thus, if a protected area authority received revenues from a patent found to be unenforceable due to inequitable conduct the authority concerned would have benefited from fraud at the expense of the public. While conservation benefits might offset some of the negative costs to public welfare, the wider negative costs to welfare could be very significant. A further risk, in a highly competitive research environment, is that protected area authorities may face legal challenges where conflicting intellectual property claims arise between researchers. The increasing number of patent disputes involving companies and universities suggests that this risk cannot be readily dismissed and the potential costs of litigation could be considerable.[87]

A fifth policy issue surrounds the public domain and the public trust doctrine. In the United States the extension of patentability to scientific "discoveries" is commonly attributed to Article 1, Section 8, Clause 8 of the Constitution which seeks "To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries".[88] However, the public domain also enjoys constitutional protection under the First Amendment which establishes that: "Congress shall make no law respecting an establishment of religion, or prohibiting the free exercise thereof; or abridging the freedom of speech, or of the press; or the right of the people peaceably to assemble, and to petition the Government for a redress of grievances."[89]

A 1966 patent case *Graham v. John Deere Co.* led the Supreme Court to declare that, "…Congress may not authorize the issuance of patents whose effects are to remove existent knowledge from the public domain, or to restrict free access to materials already available."[90] As such, the promotion of the protection of intellectual property protection under Article 1, Section 8, Clause 8 of the Constitution must be balanced against the constitutional requirement for protection of the public domain under the First Amendment.[91]

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[86] Royal Society (2003) *Keeping Science Open: The Effects of Intellectual Property Policy on the Conduct of Science*. London: Royal Society, Location: <http://www.royalsoc.ac.uk/files/statfiles/document-221.pdf>.

[87] Eisenberg, R (2003) 'Patent Swords and Shields', *Science*, 299: 1018-1019.

[88] Benkler, Y (2003) 'Through the Looking Glass: Alice and the Constitutional Foundations of the Public Domain.' *Law and Contemporary Problems*, Winter/Spring 2003. Vol. 66: 173-224. Citation at 175. Location: <http://www.law.duke.edu/shell/cite.pl?66+Law+&+Contemp.+Probs.+173+(WinterSpring+2003)>. See also *The United States Constitution*. Location: <http://www.house.gov/Constitution/Constitution.html>.

[89] Ibid., Benkler 2003 and The United States Constitution.

[90] Boyle, J (2003) 'The Second Enclosure Movement and the Construction of the Public Domain', *Law and Contemporary Problems*, Winter/Spring 2003. Vol. 66: 33-74, citation at 58. Location: <http://www.law.duke.edu/shell/cite.pl?66+Law+&+Contemp.+Probs.+33+(WinterSpring+2003)>. For the text of the *Graham v. John Deere Co*. judgement, see <http://digital-law-online.info/cases/148PQ459.htm>.

[91] Ibid., Benkler 2003 and see also Lange, D (2003) 'Reimagining the Public Domain', *Law and Contemporary Problems*, Winter/Spring 2003. Vol 66: 463-481. Location: <http://www.law.duke.edu/shell/cite.pl?66+Law+&+Contemp.+Probs.+463+(WinterSpring+2003)>.

This constitutional requirement may also potentially be linked with the common law public trust doctrine which "Provides that submerged and submersible lands are preserved for public use in navigation, fishing and recreation and state, as trustee for the people, bears responsibility of preserving and protecting the right of the public to the use of the waters for those purposes."[92] This doctrine has been increasingly extended beyond the realm of submerged and submersible lands to wider "commons" resources and is arguably reflected in the language concerning state sovereignty over biological and genetic resources embodied in the Convention on Biological Diversity.[93]

It is notable here that the *Thermus aquaticus* specimen involved in PCR technology was acquired from the American Type Culture Collection (ATCC) and as such was already available in the public domain. Research on the Taq DNA polymerase was then carried out in Russia and the United States by publicly funded researchers which brought the enzyme to the attention of researchers in the private sector.[94] The material was then submitted for patent protection by private sector researchers: the legitimacy of this claim is a focus of ongoing litigation. Whether or not permitting patent claims over microorganisms within the pools of Yellowstone National Park and the underlying genetic components of such organisms could reasonably be classified as restricting "free access to materials already available" and the relationship with the public trust doctrine is clearly a matter for debate.

In considering this question it is useful to return to the court case surrounding the agreement between Yellowstone National Park and the private company, Diversa Inc.. In his final judgement, Judge Lamberth rejected the view that "this case necessarily involves the prohibited sale of natural materials" because:

> "…it ignores relevant precedent, which instructs that a substance occurring in nature may not be patented in that form. Diamond 447 U.S. at 313. Instead, to obtain a patent rights [sic], a researcher must bring to a naturally-occurring substance a contribution that is non-obvious, novel and demonstrably useful. See 35 U.S.C. § 101-103. Thus, in accord with these fundamental principles,

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[92] Entry for "public-trust doctrine", in Garner, B (ed.) (2004) *Black's Law Dictionary*. Eighth edition. St. Paul, MN: West Publishing. Citation at 1268.

[93] See: a) Ibid., Bray (nd); b) Sax, J (1970) 'The Public Trust Doctrine in Natural Resource Law: Effective Judicial Intervention', *Michigan Law Review* Vol. 68, 471-566; c) Althaus, H et al. (1978) *Public Trust Rights*. U.S. Department of the Interior, Office of the Solicitor, Portland Region, November 3rd 1978; d) Sax, J (1993). 'Bringing an ecological perspective to natural resources: Fulfilling the promise of the public trust', in MacDonnell, L and Bates, S (eds.) (1993) *Natural Resources Law and Policy: Trends and Directions*, Washington, DC: Island Press, 148-161; e) Bollier, D (2003) *Silent Theft: The Private Plunder of Our Common Wealth*. London: Routledge. Introduction available at location: <http://www.silenttheft.com/SilentTheft_Introduction.pdf>; f) Dunning, H (2003) 'The Public Trust: A Fundamental Doctrine of American Property Law', *Issues in Legal Scholarship*, Issue 4, Article 5. Location: <http://www.bepress.com/ils/iss4/art5>; g) Rose, C (2003) 'Joseph Sax and the Idea of the Public Trust', *Issues in Legal Scholarship*, Issue 4, Article 8. Location: <http://www.bepress.com/ils/iss4/art8>; h) Warburton, M (2004) 'The Public Trust: Cases & Inquiries', *Wild Duck Review*, September 30th 2004. Location: <http://www.wildduckreview.com/index.shtml>; i) for discussion of the Public Trust Doctrine in Africa see, Juma, C and Ojwang, J (1996) *In Land We Trust: Environment, Private Property and Constitutional Change*. London: Zed Press.

[94] See: a) Chien, A *et al*., (1976) "Deoxyribonucleic acid polymerase from the extreme thermophile *Thermus aquaticus*', *Journal of Bacteriology*, 127: 15507; b) See also, Kaledin, A. S *et al*., (1980) Isolation and properties of DNA polymerase from extremely thermophilic bacterium *Thermus aquaticus* YT-1", *Biokhimiya*, 45: 64451 also published in English translation in *Biochemistry*, 45: 494-501, 1980, cited by Steinberg, D (2000) Patent Wars: Judge voids *Taq* patent', *The Scientist*, 12 [1]: 6, January 10th 2000. Location: <http://www.the-scientist.com/yr2000/jan/steinberg_p6_000110.html>.

> the Park service has interpreted its regulations only to allow researchers to study, not sell, Park resources. The CRADA, in turn, accords with the regulations because any "commercial use" flowing from such research is limited to applications or products generated from such scientific study of the resources, not the resources themselves."[95]

This conclusion reveals the significant difficulties involved in understanding the nature of patenting in relation to biological organisms and genetic material. Specifically, as noted above, the enzyme found within *Thermus aquaticus*, and the Taq DNA polymerase enzyme used in PCR are in fact the same. The distinction is that researchers have artificially reproduced the enzyme. The enzyme is however in substantive terms the same enzyme as that which occurs within the organism. While researchers may be able to manipulate the enzyme to certain degrees, such as using the biological equivalent of a pair of scissors (restriction endonucleases) in relation to underlying DNA or other techniques, they are not able to invent it.[96]

The significance of this is that researchers who collect samples and artificially reproduce such material for "scientific study" will potentially be exposed to legitimate claims for licensing fees from patent holders. Patent claims surrounding biological and genetic material are commonly constructed using "comprising" language intended to make strong *per se* (as such) claims over DNA, amino acids and proteins such as enzymes.[97] The practical effect of such measures is to "enclose" the DNA, amino acids and proteins and potential uses of that material within the scope of the patent protection.[98] Permitting patent claims over DNA, amino acids and proteins such as enzymes as "research tools" or within research method claims introduces a requirement for public and private researchers to pay licensing fees for the use of such materials and also permits so-called "reach through" claims over products developed using such tools.[99] When viewed in light of the practical experience of public and private sector researchers with DNA and related patents, the conclusion that "commercial use" does not relate to the "resources themselves" is not convincing and merits re-evaluation.

It is also important to recognise that in contrast with modern experience within the United States, many protected areas around the world are inhabited. In particular,

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[95] Ibid., *Edmonds Institute, et al., v. Babbitt*. 'Order and Final Judgement' at 23-24.

[96] For detailed discussion of Thermophilic Enzymes see, Vieile, C and Zeikus, G (2001) 'Hyperthermophilic Enzymes: Sources, Uses, and Molecular Mechanisms for Thermostability', *Microbiology and Molecular Biology Reviews*, Mar. 2001, Vol. 65, No. 1: 1-43. Location: <http://mmbr.asm.org/cgi/content/full/65/1/1>. See also, Raven, P and Johnson, G (2002) *Biology*. Sixth Edition. Boston: McGrawHill.

[97] See Ibid., Nuffield Council on Bioethics 2002. See also the companion review in this series 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.

[98] See for example: a) Shiva, V (1998) *Biopiracy: The Plunder of Knowledge and Nature*. Totnes: Green Books/Gaia Foundation; b) Boyle, J (2003) 'The Second Enclosure Movement and the Construction of the Public Domain'. *Law and Contemporary Social Problems*, Winter/Spring 2003, Vol. 66: 33, 33-74. Location: <http://www.law.duke.edu/pd/papers/boyle.pdf>.

[99] See Eisenberg, R (2003) 'Patenting Genome research tools and the law', *Comptes Rendus Biologies*, October 2003, vol. 326, no. 10, pp. 1115-1120(6). See also NIH (1998) *Report of the National Institutes of Health (NIH) Working Group on Research Tools*. June 4 1998. Location: <http://www.nih.gov/news/researchtools/>. See also National Research Council (1996) *Intellectual Property Rights and Research Tools in Molecular Biology*. Summary of a Workshop Held at the National Academy of Sciences, February 15-16, 1996. Location: <http://books.nap.edu/html/property/>.

protected areas frequently encompass the lands and territories of indigenous peoples and local communities. The participation of indigenous peoples and local communities and respect for their rights is an important feature of the new programme of work on protected areas adopted by COP7, which:

> "*Recalls* the obligations of Parties towards indigenous and local communities in accordance with Article 8(j) and related provisions and *notes* that the establishment, management and monitoring of protected areas should take place with the full and effective participation of, and full respect for the rights of, indigenous and local communities consistent with national law and applicable international obligations."[100]

As this suggests, determination of what, if any, role intellectual property protection might play in the promotion of access and benefit-sharing arrangements within protected areas that encompass the lands, territories or waters of indigenous peoples and local communities will necessarily involve the participation of indigenous peoples and local communities and consideration of international obligations in the arena of human rights.[101] This will also logically involve clarification of the significance of the public domain and interpretation of the public trust doctrine in the context of international human rights obligations and recognition of indigenous ownership and/or sovereignty over traditional knowledge and biological and genetic materials.[102] The collection of specimens for bioprospecting or other research purposes may also impact upon the sacred sites, lands and waters of indigenous peoples and local communities.[103] These considerations may also be relevant to protected areas which were formerly inhabited, occupied, or used by indigenous peoples and local communities.[104]

These issues extend to countries where the residents of protected areas would not fall within the meaning of the term indigenous as employed within international law and the United Nations system or arguably the language of Article 8(j) of the Convention

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[100] COP7 Decision VII/28 'Protected areas (Articles 8 (a) to (e))' para.22. Location: <http://www.biodiv.org/decisions/default.aspx?m=COP-07&id=7765&lg=0>.

[101] See for example: a) CESCR (2001) Human Rights and Intellectual Property: Statement by the Committee on Economic Social and Cultural Rights. Document E/C.12/2001/15. Location: <http://www.unhchr.ch/tbs/doc.nsf/0/1e1f4514f8512432c1256ba6003b2cc6?Opendocument>; b) For other international standards relating to the rights of indigenous peoples see Office of the High Commissioner for Human Rights website 'Indigenous Peoples'. Location: <http://www.unhchr.ch/indigenous/main.html>; c) United Nations Permanent Forum on Indigenous Issues. Location: <http://www.un.org/esa/socdev/unpfii/>.

[102] Daes, E-I (2003) 'Indigenous Peoples' Permanent Sovereignty over Natural Resources'. Preliminary report of the Special Rapporteur, Erica-Irene A. Daes on Indigenous peoples' permanent sovereignty over natural resources. Commission on Human Rights: Sub-Commission on the Promotion and Protection of Human Rights. Document E/CN.4/Sub.4/2003/20.

Location: <http://ods-dds-ny.un.org/doc/UNDOC/GEN/G03/151/76/PDF/G0315176.pdf?OpenElement>.

[103] See Secretariat of the Convention on Biological Diversity 'Akwé: Kon Guidelines: Voluntary Guidelines for the conduct of cultural, environmental and social impact assessments regarding developments proposed to take place on, or which are likely to impact on, sacred sites and on lands and waters traditionally occupied or used by indigenous and local communities.' Location: <http://www.biodiv.org/doc/publications/akwe-brochure-en.pdf>.

[104] See for example Colchester, M (2003) *Salvaging Nature: Indigenous Peoples, Protected Areas and Biodiversity Conservation*. Revised and expanded edition. Montevideo/Moreton-in-Marsh: World Rainforest Movement/Forest Peoples Programme. See also, McKay, F and Caruso, E (2004) 'Indigenous Lands or National Parks?', *Cultural Survival Quarterly*, 28.1. March 15 2004. Location: <http://www.culturalsurvival.org/publications/csq/csq_article.cfm?id=89342542-7DE1-4524-AC65-D57E16124AB6&region_id=0&subregion_id=1&issue_id=5>.

concerning "local communities embodying traditional lifestyles".[105] Thus, the majority of national parks within the United Kingdom are inhabited and one of the specified purposes of the national park system is "…conserving and enhancing the natural beauty, wildlife and cultural heritage of the areas specified…".[106] These purposes also extend to fostering "…the economic and social well-being of local communities within the National Park."[107] However, UK legislation also specifies that "….if it appears that there is a conflict between those purposes, [a National Park authority] shall attach greater weight to the purpose of conserving and enhancing the natural beauty, wildlife and cultural heritage of the area comprised in the National Park."[108] In the case of the United Kingdom it is unclear where access and benefit-sharing agreements involving intellectual property claims would fall in terms of the purposes for which national parks were established.[109] Given that the national park system in the United Kingdom also plays a major role in environmental and scientific education for future generations, changes to the purposes of national parks would raise questions surrounding present and future public attitudes towards national parks if commercial scientific research was to be permitted in such areas. Further questions would arise surrounding the role of park residents and the wider public in determining any modifications to such purposes.[110]

As this suggests, growing interest in bioprospecting for microorganisms within protected areas raises wider public policy questions for governments and other participants within debates surrounding access and benefit-sharing and protected areas under the Convention on Biological Diversity. Experience within the United States provides a series of valuable insights into these wider public policy issues. Addressing these issues is likely to require a combination of: a) clarification of the relationship between the public domain and the public trust doctrine in contexts of overlapping rights in protected areas involving the lands and territories of indigenous peoples and

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[105] Daes, E-I (1996) *Working Paper by the Chairperson-Rapporteur, Mrs. Erica-Irene A. Daes, on the concept of "indigenous people"*. Sub-Commission on Prevention of Discrimination and Protection of Minorities, Working Group on Indigenous Populations, Fourteenth Session, 29 July-2 August 1996. Document: E/CN.4/Sub.2/AC.4/1996/2. Location: <http://www.unhchr.ch/Huridocda/Huridoca.nsf/(Symbol)/E.CN.4.Sub.2.AC.4.1996.2.Add.1.En?Opendocument>.

[106] UK Environment Act 1995 (c.25), Part III, National Parks, *Purposes of National Parks*. Art 61.1. Replaces Section 5.1 of National Parks and Access to the Countryside Act 1949 (National Parks) [1949 c. 97.]. Location: <http://www.legislation.hmso.gov.uk/acts/acts1995/Ukpga_19950025_en_1.htm>.

[107] UK Environment Act 1995 (c.25), Part III, National Parks, *Purposes of National Parks*. Art 62. (1), insertion at 11A of the National Parks and Access to the Countryside Act 1949 [1949 c. 97.]. Location: <http://www.legislation.hmso.gov.uk/acts/acts1995/Ukpga_19950025_en_6.htm#mdiv61>.

[108] Ibid., UK Environment Act 1995 (c.25), Art 62.(2), insertion at 11A of the National Parks and Access to the Countryside Act 1949 [1949 c. 97.]. Location: <http://www.legislation.hmso.gov.uk/acts/acts1995/Ukpga_19950025_en_6.htm#mdiv61>.

[109] Bioprospecting in the United Kingdom appears to be limited and at a preliminary stage. See: a) TRENDS in Plant Science 'Bioprospecting in Wales', Vol. 6, No. 5, May 2001, citing, Pickard, J (2001) Financial Times (London), 5 March, p. 17; b) Unconfirmed reports are emerging that English Nature (a UK statutory body) may initiate consultations to consider bioprospecting, see *Genetix Update: Newsletter of the Genetic Engineering Network*, Spring 04, Issue 26. Location: <http://www.geneticsaction.org.uk/news/XUpdate/GUissue26.pdf>; c) The UK Department for Environment Food and Rural Affairs (DEFRA) commissioned a report to examine marine bioprospecting in March 2004, see DEFRA 'Developing Marine Biotechnology in the UK: A Legal Framework', Press release, 5th of March 2004. Location: <http://www.defra.gov.uk/news/2004/040305b.htm>.

[110] House of Lords, Science and Technology Committee (2000) *Third Report: Science and Society*, 23rd February 2000. Location: <http://www.publications.parliament.uk/pa/ld199900/ldselect/ldsctech/38/3801.htm>.

local communities;[111] b) analysis of the cost and benefits involved in establishing research agreements which might permit intellectual property claims; c) public participation and consultation, and; d) exploration of potential alternatives to patent protection which might maximise long-term public welfare benefits and mitigate costs to welfare.[112] Above all, this review suggests the need for a deliberative and evidence based approach to determining what role, if any, intellectual property protection might play in access and benefit-sharing agreements with either public or private research organisations in protected areas.

In closing this discussion of the potential role of intellectual property in relation to microorganisms and access and benefit-sharing agreements involving protected areas, it is useful to recall that the Secretariat of the Convention on Biological Diversity has highlighted that a number of guidelines and policies have emerged in response to issues surrounding access to genetic resources and benefit-sharing in relation to microorganisms. These guidelines and policies include:

a) the voluntary "Micro-Organisms Sustainable Use and Access Regulation International Code of Conduct (MOSAICC)" which is supported by the European Commission DG XII (Science, Research and Development) and was developed by twelve partners from developed and developing countries, and;
b) the "*CAB International (CABI) Policy on Access to Ex Situ Genetic Resources*", developed by the intergovernmental organisation CAB for issues surrounding receipt, supply, and benefit-sharing surrounding microorganisms within *ex situ* collections.[113] The CABI policy includes a model Material Transfer Agreement (MTA).

In the private sector companies such as GlaxoSmithKline, Novo Nordisk (now Novo Nordisk and Novozymes), Xenova, Shaman Pharmaceuticals, and Bristol-Myers Squibb have developed policies or 'best practice' in connection with microorganisms.[114] The policies of companies such as Diversa (above), Amgen and Genecorp also merit closer attention.[115]

Existing policies and guidelines surrounding microorganisms adopted by Public Research Organisations (PROs), intergovernmental organisations and the private sector could usefully be examined as part of debates concerning the establishment of an international regime and debates surrounding the further development of the Bonn Guidelines. As the discussion provided above suggests a fuller understanding of

[111] These issues may perhaps best be addressed under the Working Group on Article 8(j) and related provisions which will collaborate with the Working Group on Access and Benefit-Sharing in the development of an international regime (Decision VII/19, D para. 1). Location: <http://www.biodiv.org./decisions/default.aspx?m=COP-07&id=7756&lg=0>. During COP7 Parties agreed on a potential list of elements for the development of a *sui generis* system for the protection of traditional knowledge based on the outcomes of deliberations during the 8(j) Working Group with strong participation by indigenous peoples' delegates (see Decision VII/16 H 'Development of elements of sui generis systems for the protection of traditional knowledge, innovations and practices' and Annex). Location: <http://www.biodiv.org./decisions/default.aspx?m=COP-07&id=7753&lg=0>.

[112] Ibid., Scotchmer, S 2004

[113] UNEP/CBD/WG-ABS/2/2 'Further consideration of outstanding issues related to access and benefit-sharing: Use of terms, other approaches and compliance measures: Note by the Executive Secretary'. Location: <http://www.biodiv.org/doc/meetings/abs/abswg-02/official/abswg-02-02-en.doc>.

[114] Ibid., UNEP/CBD/WG-ABS/2/2.

[115] Ibid., GRAIN 1999

markets and the research contexts within which intellectual property claims surrounding microorganisms are situated, including licensing practices, is also desirable.[116] This could usefully be linked with the exploration of alternative models directed towards recognising the rights of indigenous peoples and local communities and maximising public welfare gains in relation to conservation, sustainable use, and wider internationally agreed policy goals.

[116] Ibid., ten Kate and Laird (1999). See section 3.3.2 for discussion in relation to Microbial sources and Box 8.2, page 232, in relation to estimates of markets for enzymes.

II. Global Status and Trends in Patenting of Microorganisms:

The main international instrument concerned with patent procedure in relation to microorganisms is the 1977 Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (amended 1980).[117] As of April 2004, fifty-nine countries are Contracting Parties to the Treaty. The European Patent Office (EPO), Eurasian Patent Organisation (EAPO), and African Regional Industrial Property Organisation (ARIPO) follow the Treaty's provisions.[118]

The main feature of the Treaty is the creation of a Union of Contracting States for deposits of microorganisms and International Depositary Authorities (IDAs). This measure is intended to address concerns surrounding the disclosure of microorganisms for patent application purposes. As of April 2004, 35 International Depositary Authorities (IDAs) had been established under Article 7 of the Treaty.[119]

Table One presents the available data on trends in deposits of microorganisms for patent disclosure purposes under the Budapest Treaty based on statistics provided by WIPO.[120]

Table One: Microorganism Deposits for Patent Purposes under the Budapest Treaty 1985 – 2000

Year	New Deposits	Total Deposits
1985	1,480	4,386
1986	1,607	5,984
1987	2,065	8,466
1988	2,234	10,780
1989	2,321	13,027
1990	2,364	15,265
1991	1,317	17,724
1992	1,985	19,644
1993	2,489	22,152
1994	2,605	24,712
1995	2,454	28,445
1996	2,621	30,792
1997	2,651	29,496
1998	3,186	34,898
1999	3,414	41,292
2000	3,509	43,533
2001	3,194	43,147

[117] For the text of the Budapest Treaty see : <http://www.wipo.int/clea/docs/en/wo/wo002en.htm>.

[118] See Budapest Union 'Status on April 15, 2004'. Location: <http://www.wipo.int/treaties/en/documents/word/q-budpst.doc>.

[119] Ibid., Budapest Union 'Status on April 15, 2004'.

[120] Source WIPO, *25 Years of Industrial Property Statistics (1975 - 2000) - Micros*
Location: <http://www.wipo.int/ipstats/en/publications/25_years/index.htm>. Data for 2001 is taken from *Industrial Property Statistics Publication A: 2001 - Microorganisms*. Location: <http://www.wipo.int/ipstats/en/publications/a/index.htm>. Year on year comparability is affected by variations in reporting by IDAs in a given year. 29 IDAs reported between 1998 and 2000 and 27 reported in 2001.

Table One reveals that overall deposits for the purposes of patent disclosure have risen steadily over the fifteen years between 1985 and 2000 before apparently falling slightly in 2001 (the latest year for which data is available).[121] However, as this makes clear, overall deposits under the Budapest Treaty are a small fragment of the biodiversity represented by microorganisms.

With respect to access and benefit-sharing and biopiracy, in common with other categories of organisms and genetic material, very limited data is presently available on the country of origin of the microorganisms over which protection is sought under the Budapest Treaty. For the purposes of the present review it has not therefore been possible to reach a considered judgement on whether or to what extent:

a) patent protection is being sought over specimens from countries of origin that have decided not to extend patent protection to 'microorganisms', or;
b) microorganisms are being expropriated from countries which already permit such protection and submitted for patent protection in third countries.

In 1994 the non-governmental Rural Advancement Foundation International (RAFI - now the Action Group on Erosion, Technology and Concentration or ETC Group) published a study entitled "Microbial BioPiracy: An Initial Analysis of Microbial Genetic Resources Originating in the South and Held in the North' based on data gathered from the American Type Culture Collection (ATCC).[122]

The preliminary study identified a total of 874 specimens in the ATCC collection originating from fourteen southern countries. The results of the study are set out in Table Two. To date, as far as it has been possible to establish, such a study has not been repeated. The results of the study are also confined to deposits made prior to the entry into force of the Convention on Biological Diversity and it is unclear how many of the deposits were made under the terms of the Budapest Treaty. However, the preliminary study suggests that deposits were subject to patent grants or claims in 12% of cases.

The ATCC collection and a number of other IDAs have now established online searchable databases.[123] As a contribution to methodological development Table Two includes the results of a search of the ATCC online database using the list of countries employed in the original RAFI/ETC Group study.[124] The results of the search suggest that it is possible to identify the country of origin of deposits using the database. In the case of the countries listed the data suggests that overall deposits within the ATCC from these countries of origin increased by approximately 118% between 1994 and 2004 but varied significantly between countries. This indicative data is offered purely as a contribution to methodological development in mapping status and trends. Given

[121] Provisional data for the year 2001 suggests that overall deposits have declined. This is may reflect a slow down in patenting during this period or a lack of data from two IDAs who have not yet reported compared with the year 2000.

[122] RAFI (1994) 'Microbial BioPiracy: An Initial Analysis of Microbial Genetic Resources Originating in the South and Held in the North' Occasional Paper Series, Vol. 1 No.2, June 1994. Location: <http://www.etcgroup.org/documents/occ_vol1_2.pdf>. See also, the American Type Culture Collection website. Location: <http://www.atcc.org>

[123] In the case of the non-profit ATCC partnerships have also been developed with the private sector to provide access to ATCC holdings i.e. LGC Promochem in Europe. Location: <http://www.lgcpromochem.com/atcc/>.

[124] Search conducted on the 14th of July 2004.

the emerging importance of bioprospecting for microorganisms in 'northern' countries a balanced picture of deposits from Parties to the Convention on Biological Diversity within IDAs is likely to be desirable in the development of any future work.

Table Two: Results of RAFI/ETC Group Preliminary Study of ATCC Deposits

Country	Deposits 1994	Patents	Patent Claims	Deposits 2004
Brazil	258	23		371
Chile	67	1		86
Colombia	75	0		58
Congo	19	0		21
Costa Rica	97	5		131
Ethiopia	11	0	1	11
India	35	29	6	688
Kenya	78	2	2	118
Malaysia	87	0		79
Panama	46	12	4	120
Peru	22	3	1	32
Philippines	25	10	2	85
Venezuela	39	4		100
Zimbabwe	15	0		8
Total	**874**	**89**	**16**	**1,908**

Microorganisms, TRIPS and "TRIPS-plus" agreements:

Article 27.3 (b) of the TRIPS agreement introduces a requirement for member states of the WTO to provide patent protection for microorganisms and microbiological processes.[125] While the provisions of Article 27.3 (b) surrounding exclusions of plants and animals have been a focus of intensive and ongoing attention, the practical significance of the treatment of microorganisms and microbiological processes under TRIPS has received somewhat less attention.[126]

A number of so-called "TRIPS-plus" bilateral or regional trade agreements between developed countries and developing countries and regional bodies (i.e. the European Union) include references to the Budapest Treaty. A 2003 study of 45 "TRIPS-plus" agreements carried out by the non-governmental organisation GRAIN reveals 14

[125] Article 27.3 (b) of the TRIPS Agreement reads: "Members may also exclude from patentability: (b) plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by an effective *sui generis* system or by any combination thereof. The provisions of this subparagraph shall be reviewed four years after the date of entry into force of the WTO Agreement." Location:<http://www.wto.org/english/docs_e/legal_e/27-trips_01_e.htm>.

[126] See: a) Adcock, M and Llewelyn, M (2000) 'Micro-organisms, Definitions and Options under TRIPS and Micro-organisms, Definitions and Options under TRIPS Supplementary Thoughts'. Quaker United Nations Office Programme on The TRIPS Process: Negotiating Challenges and Opportunities, Occassional Paper 2, Location: <http://www.geneva.quno.info/pdf/OP2%20Adcock-Llewelyn%20PDF.pdf>; b) See also World Trade Organization (2000) 'Review of the Provisions of Article 27.3 (b): Further Views of the United States,' 3 October 2000, Document: IP/C/W/209; c) See also World Trade Organization (2000) 'Review of Article 27.3 (b): Communication from Brazil', 24 November 2000. Document: IP/C/W/228; d) See also Ibid, CIPR 2002 at 75-76.

agreements including specific requirements for accession to the Budapest Treaty.[127] In addition, requirements for conformity with the "…highest international standards" of intellectual property protection and "no exclusions" under other "TRIPS-plus" agreements suggest that accession to the Budapest Treaty may feature in additional agreements.[128] Requirements for protection of intellectual property in relation to microorganisms may also feature in Bilateral Investment Agreements (BIAs).[129] Further research may be desirable on the provisions of "TRIPS-plus" trade agreements and Bilateral Investment Agreements in relation to the patenting of microorganisms in the context of negotiation of an international regime on access to genetic resources and benefit-sharing.[130]

However, the key problem in assessing the potential implications of intellectual property requirements in relation to the development of an international regime is a lack of effective methodologies to track and assess international trends in demand for intellectual property protection.[131] It is with contributing to addressing this problem with which this section of the review is primarily concerned.

One emerging approach to assessing status and trends in relation to biological and genetic material is to conduct a key word search for patent publications within the online databases of the major patent offices (i.e. the European Patent Office (EPO), the Japan Patent Office (JPO) and the United States Patent and Trademark Office (USPTO)). While valuable, searches limited to these databases do not provide a full picture of the internationalisation of demand for patent protection in relation to biological organisms and genetic material. However, the European Patent Office (EPO) has developed the esp@cenet "worldwide" database which brings together patent information from 73 patent offices, four regional patent offices and the World Intellectual Property Organisation (for the Patent Cooperation Treaty). The worldwide database contains an estimated 45 million publications of which an estimated 36,165,421 million are industrial patent publications (applications and grants) (see Annex 3).[132] As such, for the purposes of analysing global status and trends in the patenting of biological and genetic material, the esp@cenet database is the single most important source of patent data on an international level. The results of the search of the esp@cenet "worldwide" database for the key words "microorganism" and "microbe" within the title or abstract of patent publications are set out in Figure One.

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[127] GRAIN (2004) 'Bilateral and regional agreements imposing TRIPS-plus standards for IPRs on life in developing countries'. GRAIN, February 2004. <http://www.grain.org/rights_files/trips-plus-table-en.pdf>. In a number of cases accession to the Budapest Treaty is a requirement of separate agreements between the United States and the European Union for agreements with the same state i.e. Mexico.

[128] Ibid., GRAIN 2004.

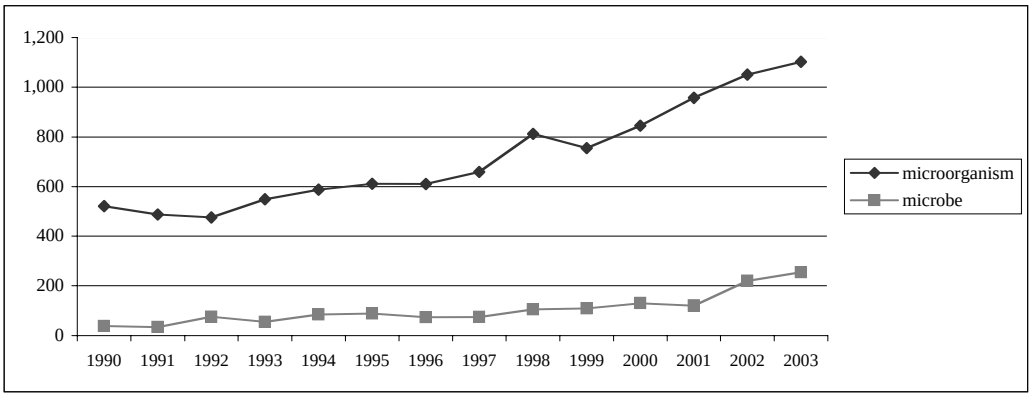
[129] Correa, C (2004) *Bilateral Investment Agreements: Agents of new global standards for protection of intellectual property rights?* An independent study for GRAIN, August 2004. Location: <http://www.grain.org/briefings/?id=186>.

[130] A website has recently been established by civil society organisations to track bilateral agreements. Location: <http://www.bilaterals.org>.

[131] The following discussion draws directly on detailed discussion in the companion review in this series 'Global Status and Trends in Intellectual Property Claims: Genomics, Proteomics and Biotechnology', *Global Status and Trends in Intellectual Property Claims*, Issue No. 1.

[132] For details of country coverage see Annex 3 and esp@cenet 'Worldwide database – detailed coverage'. Location: <http://ep.espacenet.com/espacenet/ep/en/helpV3/detailedcoverage.html>.

Figure One: esp@cenet search for 'microorganism' and 'microbe' 1990-2003[133]



This approach yielded a total of approximately 6,915 patent publications between 1990 and 2000 in which the term microorganism features in either the title or abstract rising to approximately 10,024 if preliminary data for 2001-2003 is taken into account.[134] The corresponding totals for 'microbe' are 875 for 1990 to 2000 rising to approximately 1,471 publications if preliminary data for 2001-2003 is taken into account.[135] In contrast, enzymes accounted for approximately 19,320 publications between 1990 and 2000 rising to approximately 29,105 patent publications if preliminary data for 2001-2003 is taken into account. Full data for the period is provided in Annex 1.

In considering the results of a key word search it is important to emphasise two points. First, the data generated does not provide an indicator of the number of microorganisms over which patent protection has been sought. Rather, the data provides an indicator of demand for patent protection measured in terms of publications containing key words within the title or abstract. This will also include members of "patent families" which are linked to an original (or "priority") application and thus provides an indicator of the internationalisation of demand for patent protection.

Second, the results of the search are confined to patent publications which contain the term "microorganism" or "microbe" within the title or abstract of a patent publication in English.[136] Close attention to the contents of the database reveals very significant variation in country coverage for patent publications in English ranging from zero (i.e. in the case of Brazil) to 90% or over (i.e. in the case of Canada). A review of the availability of titles and abstracts for the estimated 36,165,421 industrial patent publications within the worldwide database reveals that an average of 52% (18,806,018 publications) possess titles in English and an average of 11% (3,978,196

[133] Source: Oldham, P and Cutter, M (2004) 'Global Status and Trends in Intellectual Property Claims: Patent Dataset.' *Global Status and Trends in Intellectual Property Claims*, Issue No. 6.

[134] In the case of the USPTO a total of 5,694 references to microorganisms are located in the claims of patent publications between 1976 and August 2004.

[135] The USPTO lists 422 patent publications in which the term "microbe" features in the claims between 1976 and August 2004.

[136] The advantage of the USPTO database is that it permits a search of the claims within patent documents. However, USPTO data does not provide an adequate indicator of the internationalisation of demand for patent protection which is the key focus of this review.

publications) possess abstracts in English.[137] As this suggests, while useful, the keyword methodology possesses significant limitations in mapping international demand for patent protection and leads to an underestimation of demand.

An alternative approach to examining trends in relation to microorganisms is through use of the International Patent Classification system (IPC) (7th edition).[138] The International Patent Classification (IPC) system is a hierarchically organised classification system containing approximately 69,000 classifiers to categorise patent applications into sections, classes, sub-classes, groups and sub-groups.[139] In contrast with a key word methodology which depends on the availability of titles and abstracts in English, patent filings are generally awarded IPC codes to describe the claimed invention. Thus, in the case of Brazil, 99.3% of publications within esp@cenet contain IPC classifiers and while countries vary in the use of the IPC, coverage is generally over 90%. A detailed review of data coverage suggests that an average of 82% of the 36,165,421 industrial patent publications within the esp@cenet "worldwide" database, consisting of approximately 29,655,645 documents, possessed IPC classifiers (Annex 3).[140] This represents increased data capture compared with the keyword strategy of approximately 6,871,431 patent publications across the worldwide database. As such the IPC system provides a means to overcome translation difficulties in approaching international demand for patent protection and provides a much higher level of data capture than a key word search approach.

Microorganisms and enzymes feature in a number of International Patent Classification classes dominated by class C12 (Biochemistry; Beer; Spirits; Wine; Vinegar; Microbiology; Enzymology; Mutation or Genetic Engineering). Figure Two provides an indicator of trends in the main patent sub-classes and Table Three provides the details of C12 sub-class trends including data for 1990, 1995, 2000 and 2003 as indicator years. Preliminary data for 2001-2003 is included to provide a provisional indicator of recent trends. Data for the full period is provided in Annex 2.

In approaching this data it is important to note that an individual patent application will be assigned multiple classification codes in order to describe the claimed invention. A single application may therefore appear in the data for more than one sub-class. Any temptation to cumulate data across sub-classes should be resisted to avoid over-counting. Instead, the data provides an indicator of trends in patent claims within the relevant sub-classes relating to microorganisms and enzymes.

In summary, Table Three suggests that for the main sub-class for microorganisms (C12N) between 1990 and 2000 a total of approximately 188,213 patent claims were published rising to a provisional 299,163 claims if preliminary data for 2001-2003 is taken into account. This is followed by sub-class C12Q with approximately 72,086

[137] The database is reported to contain 45 million patent related publications, including utility models and legal documentation (XP documents). The estimates of industrial patent publications presented in this review and set out in Annex 3 exclude utility models and patent related documentation.

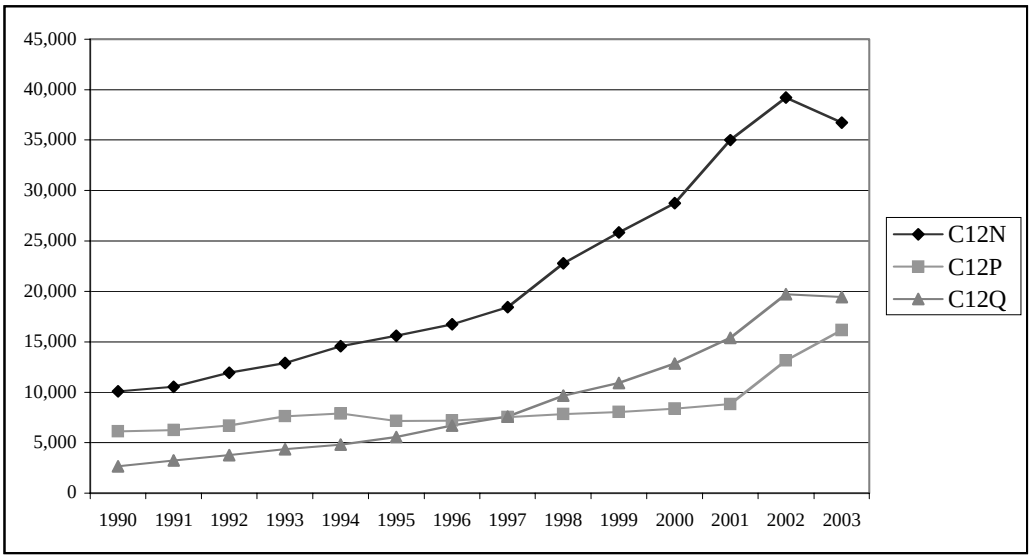
[138] See the Special Union for the International Patent Classification (IPC Union) established under the 1971 Strasbourg Agreement Concerning the International Patent Classification (amended 1979). Location: <http://www.wipo.int/classifications/ipc/en/reform/ipc_reform.html>.

[139] WIPO 'International Patent Classification (IPC)'. The present edition is the 7th edition. Location: <http://www.wipo.int/classifications/ipc/en/preface.htm>.

[140] EPO esp@cenet 'Worldwide Database – Detailed Coverage Abstracts', Table current as of 2nd of August 2004. Location: <http://ep.espacenet.com/espacenet/ep/en/helpV3/detailedcoverageab.html>. See also Annex 3.

claims between 1990 and 2000 rising to a preliminary total of 126,684 if provisional data for 2001-2003 is taken into account. This in turn is followed by C12P which focuses on fermentation or enzyme using processes to synthesise chemical compounds with approximately 80,743 patent publications between 1990 and 2000 rising to a preliminary total of 118,877 patent publications if provisional data for 2001-2003 is taken into account. Once again, this data provides an indicator of the internationalisation of demand for patent protection in multiple jurisdictions within these sub-classes rather than an indicator of the number of organisms or their components over which protection is sought.

Figure Two: Trends in Patent Publications 1990-2003 for main IPC sub-classes[141]



[141] Source: Oldham, P and Cutter, M (2004) 'Global Status and Trends in Intellectual Property Claims: Patent Dataset'. *Global Status and Trends in Intellectual Property Claims*, Issue No. 6.

Table Three: Trends in Patent Publications for Microorganisms and Enzymes[142]

Description	Category	1990	1995	2000	2003*	Total 1990-2000	Total 1990-2003*	2001-2003 +/-	2001-2003 Increase
								%	No.
Biological treatment of water/sewage using microorganisms	C02F3/34	173	337	445	452	3,675	4,945	35	1,270
Apparatus for Enzymology or Microbiology	C12M	1,255	1,310	1,648	3,612	15,016	24,273	62	9,257
Microorganisms or Enzymes; Compositions thereof	C12N	10,092	15,602	28,748	36,738	188,213	299,163	59	110,950
Plant cells or tissues	C12N5/04	139	179	518	871	2,739	4,665	70	1,926
Animal cells or tissues	C12N5/06	207	341	875	5,878	4,596	15,041	227	10,445
Human cells or tissues	C12N5/08	63	317	594	1,291	3,679	6,792	85	3,113
Fermentation or Enzyme using processes to synthesise chemical compounds	C12P	6119	7,170	8,374	16,156	80,743	118,877	47	38,134
Measuring or testing processes involving enzymes or microorganisms	C12Q	2,642	5,547	12,841	19,455	72,086	126,684	76	54,598
Processes using enzymes or microorganisms to liberate, separate or purify pre-existing compound or composition	C12S	77	345	163	206	2,633	3,165	20	532

*Data for 2001-2003 is preliminary

In considering this data, it is immediately clear that there is a dramatic disparity between the results of a patent publication search for the terms "microorganism" or "enzyme" and patent publications which are classified as involving microorganisms or enzymes. This in part reflects the significant limitations of the keyword methodology for assessing international demand compared with the use of the International Patent Classification system. However, this disparity is also linked with issues surrounding the definition of 'microorganisms' under the Budapest Treaty and within the International Patent Classification system.

As a starting point in approaching this issue, the Oxford University Press *Dictionary of Biology* offers the following definition of a microorganism:

> "microorganism (microbe). Any organism that can be observed only with the aid of a microscope. Microorganisms include bacteria, viruses, protoctists (including certain algae), and fungi."[143]

[142] Source: Oldham, P and Cutter, M (2004) 'Global Status and Trends in Intellectual Property Claims: Patent Dataset.' *Global Status and Trends in Intellectual Property Claims*, Issue No. 6.

However, the Budapest Treaty does not include a definition of a microorganism. WIPO provides the following rationale for the lack of a definition in its guide to the Treaty:

> "The term microorganism is not defined in the Treaty so that it may be interpreted in a broad sense as to the applicability of the Treaty to microorganisms to be deposited under it. Whether an entity technically is or is not a microorganism matters less in practice than whether deposit of that entity is necessary for the purposes of disclosure and whether an IDA will accept it. Thus, for example, tissue cultures and plasmids can be deposited under the terms of the Treaty, even though they are not microorganisms in the strict sense of the word."[144]

This raises the question of the criteria for the classification of biological and genetic material as a "microorganism".[145] For example, would such a classification potentially apply to human or animal tissue cultures or plasmids extracted from human or animal sources?[146] In practice, the answer to this question appears to be mixed. This is revealed in Table Four which provides an overview of the types of deposits accepted by thirty-one of thirty-five IDAs under the Budapest Treaty based on information provided by WIPO.[147]

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[143] "microorganism" *A Dictionary of Biology*. Oxford University Press, 2000. For further discussion see Ibid., Adcock, M and Llewelyn, M (2000) 'Micro-organisms, Definitions and Options under TRIPS and Micro-organisms, Definitions and Options under TRIPS Supplementary Thoughts'. Quaker United Nations Office Programme on The TRIPS Process: Negotiating Challenges and Opportunities, Occasional Paper 2, Location: <http://www.geneva.quno.info/pdf/OP2%20Adcock-Llewelyn%20PDF.pdf>.

[144] WIPO 'Introduction to the Budapest Treaty'. Paragraph 10. Location: <http://wipo.int/about-ip/en/budapest/guide/download.htm>.

[145] Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement. Location: <http://www.wto.org/english/docs_e/legal_e/27-trips_01_e.htm>.

[146] A plasmid is: "A small circular form of DNA found in bacteria which carries certain genes, such as for antibiotic resistance, and which replicates independently of the host cell." Source: University of Pennsylvania, Center for Bioethics, 'Who Owns Life? : Glossary'. Location: <http://www.med.upenn.edu/bioethic/wol/glossary.shtml>.

[147] Source WIPO 'Guide to the Deposit of Microorganisms under the Budapest Treaty, Section D: Requirements of International Depositary Authorities (IDAs)'. Location: <http://www.wipo.int/about-ip/en/budapest/guide/part_ii_text.htm>.

Table Four: Summary of IDAs Acceptance by Category of Deposit[148]

Category	Number of Accepting IDAs	Category	Number of Accepting IDAs
Algae	6	Mycoplasma	2
Animal viruses	8	Oncogenes[149]	2
Animal cell cultures	13	Plant cell cultures	7
Bacteria (pathogenic)	13	Plant viruses	7
Bacteria (non-pathogenic)	24	Plasmids (in hosts)	20
Bacteriophages	11	Plasmids (not in hosts)	9
Embryos	3	Protozoa (parasitic)	3
Eukaryotic DNA[150]	4	Protozoa (non-parasitic)	5
Fungi (pathogenic)	10	Protozoa (pathogenic)	3
Fungi (non-pathogenic)	23	RNA[151]	2
Human cell cultures	9	Seeds	4
Hybridomas	13	Yeasts (pathogenic)	11
Molds	3	Yeasts (non-pathogenic)	26
Murine embryos[152]	2		

Table Four reveals that while IDAs vary significantly in terms of the categories of material they are prepared to accept, in practice the options that appear to be available are wide ranging. This suggests that closer attention to the practices of IDAs in relation to acceptance of material as 'microorganisms' for the purposes of patent disclosure could make a useful contribution to the development of an international regime on access to genetic resources and benefit-sharing. This could also perhaps usefully include clarification of whether applicants seeking to disclose material effectively "shop" for IDAs willing to accept particular kinds of material.

Turning now to the treatment of microorganisms within the International Patent Classification (IPC) system (7th edition).[153] The main classes and sub-classes of the

[148] Source WIPO (1999) *Guide to the Deposit of Microorganisms under the Budapest Treaty*, Part II, Section D: Requirements of International Depositary Authorities. Location: <http://www.wipo.int/about-ip/en/budapest/guide/part_ii_text.htm>.

[149] Oncogenes are genes associated with cancer.

[150] Microorganisms predominantly fall in the Domain Bacteria (Eubacteria) and Archaea (Archaebacteria). In contrast eukaryotes (Domain Eukarya) fall within four kingdoms: protoctists, fungi, plants and animals. Viruses are not presently classified as organisms and thus fall outside the three domains of life. Source: Raven, P and Johnson, G (2002) *Biology*. Sixth Edition. Boston: McGrawHill.

[151] Ribonucleic acid (RNA) takes three principal forms: messenger (mRNA); transfer (tRNA), and; ribosomal (rRNA).

[152] Murine refers to members of the Muridae family such as mice and rats.

IPC are commonly prefaced by guidance notes for patent examiners. IPC patent class C12 (Biochemistry; Beer; Spirits; Wine; Vinegar; Microbiology; Enzymology; Mutation or Genetic Engineering) under which the main sub-classes concerned with microorganisms are located is prefaced by a note which states that:

> "In this class, viruses, undifferentiated human, animal or plant cells, protozoa, tissues and unicellular algae are considered as micro-organisms."[154]

The notes for sub-classes C12M to C12S highlighted in Table Three, specify that:

> "In this subclass, unless specifically provided for, undifferentiated human, animal or plant cells, protozoa, tissues and unicellular algae are classified together with micro-organisms."[155]

In practice, examination of the results of patent search results in relation to the main sub-classes of microorganisms reveals the increasing prominence of DNA and related materials within these patent sub-classes. This extends to human and animal "undifferentiated cells". Such cells include stem cells which may be collected from adults or "harvested" from embryos (either human or animal). Stem cells, particularly those derived from embryos, possess the capacity to differentiate into a wide range of other cells and are regarded as a key to the development of future therapies. In the case of human embryonic stem cells, they are also a major focus of controversy and many countries presently do not permit, or severely restrict, research involving human embryos.[156]

In the case of human stem cells, the esp@cenet database contains approximately 695 publications across all years containing the words human stem cell within the title or abstract.[157] Between 1990 and 2003 approximately 583 patent publications are recorded within the database of which 477 are classified under C12N. Approximately 173 patent publications containing the words human stem cell under C12N are Patent

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[153] WIPO (1999) *International Patent Classification.* 7th edition. Location: <http://www.wipo.int/classifications/fulltext/new_ipc/index.htm>.

[154] WIPO (1999) *International Patent Classification*. 7th edition, Section C, page 236.

Location: <http://www.wipo.int/classifications/fulltext/new_ipc/index.htm>.

[155] WIPO (1999) *International Patent Classification*. 7th edition, Section C, page 236-249.

Location: <http://www.wipo.int/classifications/fulltext/new_ipc/index.htm>.

[156] See Whittaker, P (2002) 'Stem cells, patents and ethics', for a brief and accessible discussion of the issues. Location: <http://www.ccels.cardiff.ac.uk/launch/whittakerpaper.html>. For detailed consideration, see: a) Overwalle, G (2002) *Study on the patenting of inventions related to human stem cell research*. European Group on Ethics in Science and New Technologies to the European Commission. 30 December 2001. Luxembourg: Office for Official Publications of the European Communities. Location: <http://europa.eu.int/comm/european_group_ethics/docs/stud-vanoverw.pdf>; b) European Group on Ethics in Science and New Technologies to the European Commission (2002) *Opinion on Ethical Aspects of Patenting Inventions involving Human Stem Cells*. 7th May 2002. Luxembourg: Office for Official Publications of the European Communities. Location: <http://europa.eu.int/comm/european_group_ethics/docs/avis16_en_complet.pdf>; c) see also, The Danish Council of Ethics (2004) *Patenting Human Genes and Stem Cells*. Copenhagen: The Danish Council of Ethics. Location:<http://etisk.inforce.dk/graphics/03_udgivelser/engelske_publikationer/patenting_human_genes/patents04/patenting_human_genes.pdf>.

[157] This data refers to the results of a key word combination search of titles and abstracts, that is publications containing the words human (and) stem (and) cell. Annex 2 also includes data for precise terms i.e. "human stem cell". The outcomes of searches for precise terms are lower than combination terms. Future research could usefully focus on data capture issues and refinement of the methodology.

Cooperation Treaty (PCT) publications (designated WO) which may generate applications in multiple jurisdictions.

In the case of animal stem cells a total of approximately 125 publications across the database contain the words animal stem cell within the title or abstract. In the period between 1990 and 2003, 99 publications are recorded of which 77 are classified under C12N and 35 are PCT (WO) publications which may generate applications in multiple jurisdictions.

In the case of human embryos, approximately 384 patent publications across the database contain the words human embryo of which 292 occur in the period 1990-2003.[158] The number of patent publications containing the words human embryo increased by an estimated 221% between 2001 and 2003 compared with the period 1990-2000 suggesting that this is a rapidly growing area of demand. In the case of C12N, approximately 210 publications between 1990 and 2003 contain the words human embryo of which approximately 49 publications are PCT (WO) publications which may generate applications in multiple jurisdictions.[159]

In the case of plants, materials submitted for patent protection include plant meristems which take a variety of forms (i.e. the shoot tip meristem) and are the equivalent of stem cells in animals. Approximately 112 patent publications across the database contain the term meristem of which 90 patent publications are recorded in the period between 1990 and 2003. Once again the number of patent publications increased significantly between 2001 and 2003 with an estimated 70% increase in publications relating to meristems over this period compared with 1990-2000. In the case of C12N, approximately 67 patent publications between 1990-2003 are classified under C12N of which 26 publications are PCT (WO) publications which may generate applications in multiple jurisdictions. The implications of patent claims in relation to plant meristems are considered in further detail in the companion review in this series 'Global Status and Trends in Intellectual Property Claims: Genomics, Proteomics and Biotechnology'.

In the case of DNA a key word search across the contents of the database reveals 56,736 patent publications containing the term DNA in the title or abstract. Of these, 50,025 are recorded in the period between 1990 and 2003 with publications increasing by 68% between 2001 and 2003 compared with the period 1990-2000. In the case of C12N approximately 34,309 patent publications between 1990 and 2003 contain the term DNA in the title or abstract amounting to 69% of publications between 1990-2003 and suggesting the concentration of DNA patent publications within this sub-class. Approximately 7,239 C12N publications between 1990 and 2003 are PCT (WO) publications that may generate applications in multiple jurisdictions.

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[158] It should be noted that the data does not necessarily refer to *per se* patent claims over human embryos or their components but to publications concerning embryos and/or their components and publications relating to human embryos. Further research and analysis is desirable in order to clarify the nature of patent claims in relation to human embryos.

[159] See also Overwalle, G (2002) *Study on the patenting of inventions related to human stem cell research*. European Group on Ethics in Science and New Technologies to the European Commission. 30 December 2001. Luxembourg: Office for Official Publications of the European Communities. Location: <http://europa.eu.int/comm/european_group_ethics/docs/stud-vanoverw.pdf>.

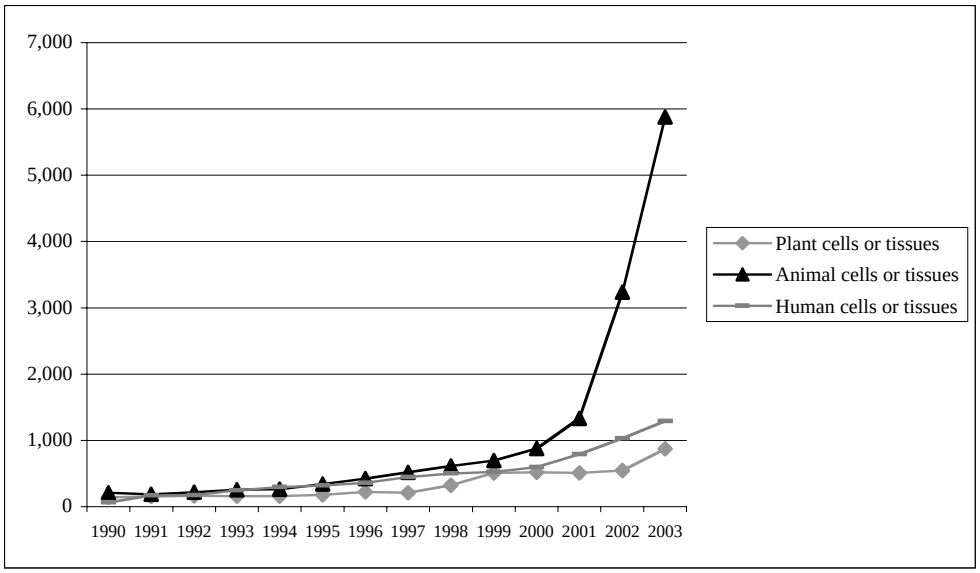
As this suggests, in practice, IPC classifier C12N concerning microorganisms and enzymes is the key IPC category under which genetic and related biological materials are classified. A wider review of trends in the biotechnology sector provided in the companion review in this series 'Global Status and Trends in Intellectual Property Claims: Genomics, Proteomics and Biotechnology', reveals that C12N publications rank first in the results of a search for biotechnology patent publications employing thirty IPC classifiers between 1990 and 2003.

The search results also serve to reveal the wider significance of the Patent Cooperation Treaty in operationalising international demand for patent protection in relation to microorganisms, genetic material and biological material such as stem cells. Thus, approximately 37,603 of an estimated 299,163 publications under C12N between 1990 and 2003 were Patent Cooperation Treaty publications and 42,279 PCT patent publications under C12N are recorded across the database as a whole. Given that a single application filed under the Patent Cooperation Treaty may generate subsequent applications in multiple jurisdictions (i.e. 109 Contracting States in 2000 rising to 123 in 2004), it appears reasonable to conclude that Patent Cooperation Treaty based applications may account for a substantial proportion, and potentially the majority, of worldwide demand for patent protection in relation to microorganisms, enzymes, genetic material and biological material such as stem cells. This is particularly likely in view of the dominance of the Patent Cooperation Treaty in relation to cumulative global demand for patent protection between 1990 and 2001.[160]

In connection with stem cells and plant meristems, as noted above the outcomes of keyword searches and keyword/IPC combination searches are limited to the availability of titles and abstracts in English and leads to an underestimation of demand. In relation to human and animal stem cells and plant meristems the IPC system also includes specific sub-groups relating to undifferentiated human, animal and plant cells or tissues under sub-class C12N. The relevant sub-groups are: a) undifferentiated plant cells or tissues (C12N5/04); b) undifferentiated animal cells or tissues (C12N5/06), and; c) undifferentiated human cells or tissues (C12N5/08). The outcomes of a search using the relevant IPC sub-groups for the period 1990-2003 are presented in Figure Three and the full dataset for this period is provided in Annex 2.

[160] EPO/JPO/USPTO (2003) *Trilateral Statistical Report 2002*. See page 18. Location: <http://www.uspto.gov/web/tws/tsr2002/>.

Figure Three: Patent Publication Trends for undifferentiated human, plant and animal cells or tissues[161]



This search revealed that between 1990 and 2000 approximately 2,739 patent publications were classified under undifferentiated plant cells or tissues (C12N5/04) rising to a provisional 4,665 if preliminary data for 2001-2003 is taken into account. This represents a provisional 70% increase in publications between 2001-2003 compared with the period 1990-2000. The most significant area of growth revealed in Figure Three concerns undifferentiated animal cells or tissues (C12N5/06) which rose to approximately 4,596 publications between 1990-2000 before increasing to a provisional 15,041 if preliminary data for 2001-2003 is taken into account. This represents a provisional increase of 227% in publications between 2001-2003 compared with 1990-2000. In the case of undifferentiated human cells or tissues, approximately 3,679 publications were classified under C12N5/08 between 1990-2000 rising to a provisional 6,792 publications if preliminary data for 2001-2003 is taken into account. This represents a provisional 85% increase in publications over the three year period 2001-2003 compared with 1990-2000.

In considering the outcomes of a search of C12N using keywords and a detailed search using IPC sub-group classifiers within C12N it becomes clear that these categories include biological and genetic material that might not generally be considered to fall within the category of "microorganism".[162] This appears to be confirmed by subsequent interrogation of the esp@cenet database using the IPC classifier C12R which is employed as an indexing classifier for microorganisms based

[161] Source: Oldham, P and Cutter, M (2004) 'Global Status and Trends in Intellectual Property Claims: Patent Dataset'. *Global Status and Trends in Intellectual Property Claims*, Issue No. 6.

[162] In light of the requirement of Article 27.3 (b) of the TRIPS agreement for patent protection over microorganisms, the UK Commission on Intellectual Property Rights has recommended that developing countries "should adopt a restrictive definition of the term "microorganism"". CIPR (2002) *Integrating Intellectual Property Rights and Development Policy*. Report of the UK Commission on Intellectual Property Rights. London, September 2002. Citation at 76. Location: <http://www.iprcommission.org/graphic/documents/final_report.htm>.

on *Bergey's Manual of Determinative Bacteriology* (1975). The outcomes of this search revealed approximately 16,427 patent publications across the database.[163]

On a wider level, as the results of a search for human embryo related patent claims under C12N reveals, this discussion may appear to be moving beyond the scope of existing measures under the Convention on Biological Diversity, notably the Bonn Guidelines.[164] However, it is important to note that advances in microbiology and genomics are increasingly transforming scientific understandings of genetic and biological relatedness between organisms and blurring the boundaries between the human and non-human.[165] Thus, in December of 1998 a researcher from the University of Wisconsin was issued patent number US5,843,780 under patent sub-group C12N5/06 entitled "Primate Embryonic Stem Cells" based on research with rhesus monkeys (*Macaca mulatta*) and the common marmoset (*Callithrix jacchus*). However, the patent claims were constructed to include all primate embryonic stem cells. Given that human beings are also primates the patent extends to human embryonic stem cells.[166] This patent grant was followed in March 2001 by the award of US patent 6,200,806 of the same title (under sub-groups C12N5/08 and C12N5/06) As this patent explains: "Because of the extremely close anatomical and physiological similarities between humans and rhesus monkeys, rhesus monkey true ES [Embryonic Stem] cell lines provide a very accurate in vitro model for human differentiation".[167] The patent goes on to make more specific claims relating to human embryonic stem cells based on the earlier patent.

These patent grants form part of a patent family consisting of a total of nine members, including Patent Cooperation Treaty number WO0622362 (International Publication Number). This application was originally filed in 1996 and designated 59 states on the national level, 6 states through ARIPO (the African Regional Industrial Property Organization), 7 states through EAPO (the Eurasian Patent Organisation), 16 states through the European Patent Office (EPO) and 14 states through OAPI (Organisation Africaine de la Propriété Intellectuelle). A review of the esp@cenet database reveals that this has led to subsequent applications under the European Patent Convention (publication no. EP07701256) and in Australia (publication no. AU4758496) and Canada (publication no. CA2190528).

Research and patenting in relation to human embryonic stem cells is a significant focus of debate and further consideration of these issues is beyond the scope of the present review. However, to recall Judge Lamberth's observation, this example serves to demonstrate that the issues surrounding the treatment of microorganisms under

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[163] Search conducted on the 2nd of December 2004.

[164] For example, Decision VI/24 para 9. establishing the scope of the Bonn Guidelines on access to genetic resources and benefit-sharing specifies that "All genetic resources and associated traditional knowledge, innovations and practices covered by the Convention on Biological Diversity and benefits arising from the commercial and other utilization of such resources should be covered by the guidelines, with the exclusion of human genetic resources." Location: <http://www.biodiv.org/decisions/default.aspx?m=cop-06&d=24>.

[165] For discussion of the emerging implications of these transformations in relation to human rights and the inherent dignity of the human person see, Motoc, I-A (2003) 'Human Rights and Bioethics', Expanded working paper submitted by Ms. Iulia-Antoanella Motoc in accordance with Sub-Commission decision 2002/114, Sub-Commission on the Promotion and Protection of Human Rights. Document E/CN.4/Sub.2/2003/36, 10th of July 2003. Location: <http://www.unhchr.ch/huridocda/huridoca.nsf/(Symbol)/E.CN.4.Sub.2.2003.36.En?Opendocument>.

[166] See: a) Ibid., Rai and Eisenberg 2003; b) Ibid., Overwalle 2002.

[167] US 6,200,806 at 40.

intellectual property instruments are "…not teaspoon-sized". In particular this example suggests that the scope of an international regime and the potential role of intellectual property instruments within access and benefit-sharing arrangements will need to be considered in light of emerging scientific understanding of the relationships between organisms and in particular the realisation that significant similarities (homologies) exist in the genetic make-up of biological organisms. Growing scientific recognition of these similarities permits intellectual property claims in relation to the biological or genetic components of an individual variety or species to be extended to encompass the homologous biological and genetic components of organisms across varieties, species, genera, and classes.

One major question that emerges in relation to intellectual property claims in relation to 'microorganisms', is whether patent claims over such materials serve to promote science and innovation i.e. through product development, increased trade in goods and services, Foreign Direct Investment (FDI) and technology transfer or instead serve as vehicles for unproductive rent extraction from public and private sector researchers which may stifle research and innovation? Further consideration of this question is also beyond the scope of the present review. However, as the OECD has recently highlighted:

> "The paucity of economic evaluation of the patent system is striking. Most of the changes to patent regimes implemented over the past two decades were not based on hard evidence or economic analysis. It is necessary to develop economic analysis in this domain that would inform the policy debate, giving governments a clearer view beyond the arguments put forward by pressure groups. Such analysis should rely notably on quantitative evidence…"[168]

This review has sought to contribute to this process of evaluation and assessment by providing quantitative indicators and analysis of international trends in demand for patent protection in relation to microorganisms as a basis for further work. The issues raised by emerging scientific understanding of genetic relatedness (homologies) between biological organisms and wider questions surrounding the economic evaluation of the patent system are considered in greater detail in the companion review in this series 'Global Status and Trends in Intellectual Property Claims: Genomics, Proteomics and Biotechnology'.

In closing this review of available data on global trends in intellectual property claims in relation to microorganisms for the development of an international regime on access to genetic resources and benefit-sharing, five main conclusions emerge:

a) Further methodological development and refinement to establish indicators on global status and trends in intellectual property claims in relation to microorganisms may be desirable in order to inform decision-making surrounding the potential role of intellectual property instruments in the development of an international regime on access to genetic resources and benefit-sharing under the Convention on Biological Diversity. In this regard it is notable that a number of organisations, such as the European Patent Office, the United States Patent and

[168] OECD (2004) *Patents and Innovation: Trends and Policy Challenges*. Paris: OECD. Citation at 26. Location: <http://www.oecd.org/dataoecd/48/12/24508541.pdf>.

Trademark Office, the Japan Patent Office (collectively the Trilateral Offices), along with WIPO and the Organisation for Economic Co-Operation and Development (OECD) possess staff with expertise in the analysis of patent trends and patent statistics. Taking into account the substantive concerns which surround the patenting of certain types of material, i.e. DNA and stem cells, the adoption of a participatory and deliberative approach to the development of indicators may be desirable in order to promote the transparency, intelligibility and utility of indicators. In approaching any future work on patent trends in this arena the European Patent Office esp@cenet database constitutes a key resource on the international level.

b) Issues surrounding the definition of microorganisms under international intellectual property instruments are not trivial and may merit closer attention in the course of the development of an international regime directed towards the pursuit of fairness and equity in relation to sharing of the benefits arising from the utilisation of genetic resources. As part of this process, the policies and practices of International Depositary Authorities (IDAs) under the Budapest Treaty could usefully be reviewed in order to clarify the criteria employed for the acceptance of material for patent disclosure purposes. This could usefully be combined with detailed analysis of the origins and trends in patent claims over material deposited with IDAs under the terms of the Budapest Treaty. Additional work may also be desirable surrounding the treatment of microorganisms in relation to other biological and genetic material within the International Patent Classification (IPC) system.

c) Limited data is presently available on trends in patenting in relation to biological and genetic material on the regional and national level. Regional and country level studies could make a valuable contribution to analysis of existing trends and the implications of intellectual property instruments for the development of an international regime across Parties to the Convention. The outcomes of the present review reveal that class C12 of the International Patent Classification system is the logical starting point for mapping trends on the regional and country level.

d) Growing scientific recognition of the significant similarities (homologies) in the biological and genetic make-up of biological organisms holds important implications for consideration of the role of intellectual property instruments in the development of an international regime on access to genetic resources and benefit-sharing. Further consideration of the significance of biological and genetic homologies between organisms across varieties, species, genera and classes may be desirable in the course of the development of the international regime. This analysis could usefully include key biological materials that extend beyond the boundaries of the lands, territories and waters of indigenous peoples and local communities, the sovereign jurisdictions of states, regions, population groups and ultimately generations, to form what may be called 'global public goods'.[169] Genes regulating biological pathways, stem cells and plant meristems may serve as potential exemplars of such 'global public goods'.

[169] Kaul, I et al. (1999) 'Why Do Global Public Goods Matter Today', in Kaul, I et al. (eds.) (1999) *Providing Global Public Goods: Managing Globalization*. Oxford: Oxford University Press. Location: <http://www.undp.org/globalpublicgoods/globalization/pdfs/Overviews.pdf>.

e) In considering the potential role of intellectual property instruments in the development of an international regime on access to genetic resources and benefit-sharing evidence based economic analysis of the costs and benefits and wider impacts of patent protection is likely to be desirable as a basis for evidence based decision-making. This analysis could potentially include consideration of the positive and negative impacts of patents in relation to science and innovation and exploration of potential alternative models to maximise research and benefit-sharing while minimising externalities.