Annex I: The Patent System, Biotechnology and Synthetic Biology

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1. INTRODUCTION

A very detailed examination of the patent system, including an introduction to patent law in Europe and in the United States and an examination of many cases that involve the patenting of life forms, was produced for the EGE by Geertrui van Overwalle in 2002 ([1]). There is therefore no attempt to provide the detailed examination of the patent system in this current paper.

2. INNOVATION

'The last half of the 19th century and the first years of the 20th century saw the development of technologies that would create the basis of wealth generation by means of major new industries – principally petrochemical, automotive, aviation and electronics. These developments helped create the modern world.' ([2]). During the latter part of the 20th Century and the beginning of this century electronics and biotechnology have been leading the revolution in providing ever-increasing sophistication to our lives. Amongst the new technologies are those involving the manipulation (and commercialization) of biology. The range of applications to which new uses of biology are becoming available is extensive, reaching far beyond the provision of medicines, food and fibre. Synthetic biology provides a new set of tools for using biology, and may either be for the purpose of pure research with an intention to understand the manner in which living systems have developed including their interactions, or for producing new processes or products. An argument has developed as to whether all or some of the fruits of synthetic biology should be patentable, for the commercial benefit of those that 'invent' the processes or products.

The 'bioeconomy' is primarily growing in developed countries. The United States originated 40.6% of biotechnology patents in 2005, with the European Union at 25.1% and Japan at 17%. Brazil, China, India, Indonesia, the Russian Federation and South Africa combined provided 2.7% of the total patents in biotechnology ([3]). Developing countries may not have the infrastructure to support the use of modern technologies and hence lack the capacity to innovate in areas (like biotechnology) where infrastructure is essential. The same problem exists for nanotechnology (US 41.8, EU 25.4, Japan 16.7).

It is believed that for the 'bioeconomy' to grow, Intellectual Property, primarily in the form of patents, will play an important role – this includes the manner in which they are recognised, traded and managed. IP will have an impact on where the bioeconomy will flourish, the form it takes and to whom the principal benefits will accrue. ([4])

([1]) EGE (2002) Study on the patenting of inventions related to human stem cell research. Luxembourg Office for Official Publications of the European Communities. ISBN 92-894-1987-3

([2]) The Royal Academy of Engineering (May 2009) 'Synthetic Biology: scope, applications and implications' ISBN: 1-903496-44-6

([3]) OECD (2008) Compendium of Patent Statistics

([4]) Herder M and Gold ER 'Intellectual Property Issues in Biotechnology: Health and Industry' Report prepared for the OECD International Futures project on the Bioeconomy to 2030: Designing a Policy Agenda (OECD, 2008)

Many argue that patenting is an essential part of the protection of scientific endeavour. A recent paper on 'Inventing Biological Organisms: A Reader of Selected Articles' states the case succinctly: 'The ability to patent biological inventions is central to protecting scientists' work… What can be patented, for how long, and the extent of global protection are critical issues. However, patenting biological organisms, particularly human genes and other human parts, is controversial. Economists question whether patenting is the quickest and best way to diffuse new knowledge throughout the marketplace. Some bioethicists question whether genetic information is the common heritage of mankind, making gene patenting inappropriate' ([5]). The debate about gene patenting has been dealt with in detail in the previous EGE paper (footnote 1). The concern has shifted to the role of the patent system as technology moves towards a 'knowledge economy'. It has always been assumed that there is an important balance between private and public interests in the manner in which the patent system has been designed – limited rights for a limited time. This balance has shifted towards the private interest, particularly when examined from the perspective of the developing world. ([6])

There is an assumption within governments and judicial reasoning that IP rights (Patent rights in particular) 'are crucial if not absolutely necessary to foster innovation' ([7]) 'Should some biological inventions be kept in the public domain and not be patentable? Would this slow or speed the development of socially important products? Conversely, does patenting new biotechnology products (agricultural seeds that are resistant to pesticides, for example) accelerate the development of products that have high social utility?' Gold has argued that the evidence for assumptions about patents having a positive effect on innovation is relatively weak. ([8])

Gold explains:

'More recent work has… cast doubt on this conclusion. The international economics literature considers cross-country differences in patent systems and the implications of these differences for economic behavior. The link between patents and innovation in the multi-country (open economy) is less clear.

Even within a closed economy, patents on initial innovations may deter later discoveries that build on patented innovations. There are also structural reasons to believe that one can never know, in fact, whether patents actually encourage or discourage innovation. First, […] while patent law takes a 'one-size-fits-all' approach to innovation, the markets for different products and knowledge assets differ significantly from one another. Second, the empirical study of the effects of patents on innovation suffers from the lack of control. Given that innovation is driven by many factors (including access to capital, access to skilled managers, first mover advantage, curiosity, *etc.*), cross-jurisdictional comparisons are difficult. Since countries rarely radically change their patent systems without changing fundamental aspects of their economies, single jurisdiction controls are usually lacking. Several studies that examine changes within a single jurisdiction – the semi-conductor industry in the US between the 1970s and 1980s and the strengthening of the Japanese patent system in the 1980s – indicate that patents either reduced innovation or had no effect. Third, […] industry rarely relies solely on a single patent to secure its inventions. Normally, firms use a

([5]) California Research Bureau (1998) http://www.library.ca.gov/crb/98/reader/reader01.pdf

([6]) Walker, Simon. 2001. The TRIPS Agreement, Sustainable Development and the Public Interest: Discussion Paper. IUCN, Gland, Switzerland and Cambridge, UK and CIEL, Geneva, Switzerland ISBN 2-8317-0604-1

([7]) Herder M and Gold ER 'Intellectual Property Issues in Biotechnology: Health and Industry' Report prepared for the OECD International Futures project on the Bioeconomy to 2030: Designing a Policy Agenda (OECD, 2008) page 5

([8]) E. Richard Gold et al., 'The Unexamined Assumptions of Intellectual Property: Adopting an evaluative Approach to Patenting Biotechnological Innovation' (2004) 18 Public Affairs Quarterly 299

combination of patents, trade secrets, and even trademarks to protect their innovations. In addition, firms also use other mechanisms such as complementary asset management (by forming alliances) and innovation lead-time to gain advantage over competitors.

All of these intellectual property management mechanisms make it difficult, if not impossible, to isolate the effect of patents on innovation.' ([9]) The vast majority of drugs produced (and patented) by the pharmaceutical companies never reach commercialization, as they fail during the various processes, including trials on patients, to meet the criteria for an effective drug. These patents would then count as not 'used' although they may be kept to ensure that when other companies produce similar products they can be relied on to block anything that might be competitively efficacious.

A distinction between pure science, not for commercial gain and technology has become blurred during the last 20 years. The goal of biological research during the first part of the 20th century was primarily to understand the mechanisms of biology; products were spin-off results of the research. Pressure from government and industry during the latter part of the 20th century moved the goal of research towards a conscious search for commercial products from the information available from biological research. Very often commercialization now occurs before a full understanding of the biology has been achieved. On 27 April 2009 President Obama spoke at a meeting of the National Academy of Science in New York. He addressed the relationship between primary basic research and technology:

> 'The fact is an investigation into a particular physical, chemical, or biological process might not pay off for a year, or a decade, or at all. And when it does, the rewards are often broadly shared, enjoyed by those who bore its costs but also by those who did not.
>
> And that's why the private sector generally under-invests in basic science, and why the public sector must invest in this kind of research – because while the risks may be large, so are the rewards for our economy and our society.'

This paper does not attempt to address the rationale for using the patent system to allow the bio-economy to grow, rather it asks the question what discoveries and inventions should be capable of being patented, and hence available directly for commercial exploitation, and which of these should not be (if any). It has been argued that some discoveries or inventions should be considered as the common heritage of mankind, and this argument is developed and considered later in this paper. Perhaps common heritage is not a necessary concept, rather that these would be in the common ownership – to the benefit of all. There is a general appreciation in Europe that there are some discoveries or inventions that should never result in commercialisation for profit. For example, processes the use of which offend human dignity such as the production of chimeras from germ-cells, or totipotent cells from plants and animals; process for cloning a human being, modified germ-line cells etc. Article 6, paragraph 2 of Directive 98/44/EC on the legal protection of biotechnological inventions provides a non-exclusive list of those products and processes considered to be not patentable due to their commercial exploitation being contrary to morality or *ordre public*. This may provide a conceptual framework for other inventions that may be unpatentable, but there are no criteria provided.

Article 7 of the Directive provides '[t]he Commission's European Group on Ethics in Science and New Technologies evaluates all ethical aspects of biotechnology.' It gives no advice on how to implement the Article, which is the only one not implemented by any of the European Patent Offices in their rules.

([9]) ibid

It may be that 'inventions' in biology in general and in synthetic biology in particular should be placed in one of three categories:

a. That which is common to all humankind, and should not be patentable or directly exploited for commercial gain.

b. That which, for a variety of reasons, should be placed in the public domain for all to use and exploit (the 'commons'). It may be that the process or product is so expensive to produce or require a vast range of expertise not available to any one organisation, or that the placing of the information in the public domain enables open standards that allow for the effective commercialisation and use of a number of products that use the technology or product.

c. That which may, at the inventor's discretion, be protected through an intellectual property rights system to encourage innovation.

3. THE PATENT SYSTEM

Most nations of the world are party to the World Trade Organisation. As part of their agreement to join the organisation, they agreed and in general ratified all the component treaties of the General Agreements on Tariffs and Trade (GATT). The last successful round of trade negotiations culminated in all ratifying Member States endorsing all agreements in the WTO package under the so-called 'single undertaking'. No opting out of individual treaties (over 17 in total) was allowed as they were to be ratified all at once. One of these is the TRIPS Agreement (Agreement on Trade-Related Aspects of Intellectual Property Rights). TRIPS provides for each country to institute a minimum set of laws protecting intellectual property, so that where inventors so wish they may protect that which they have created or invented in any jurisdiction. Countries may not discriminate between domestic and international 'creations'. ([10])

It is patently obvious that a business has a competitive advantage if it develops, maintains and exploits its assets appropriately. These have to include its intellectual property where it has an advantage over its competitors if it has information which it has not shared (secrecy) or where it has asserted rights that permit it to assure that others cannot use or copy without permission. A relatively new concept is that the portfolio of intellectual property constitutes a currency that is negotiable for use in (commercial or research?) interactions with others. Patents may then be used as such, without the intention to use them in advancing technology.

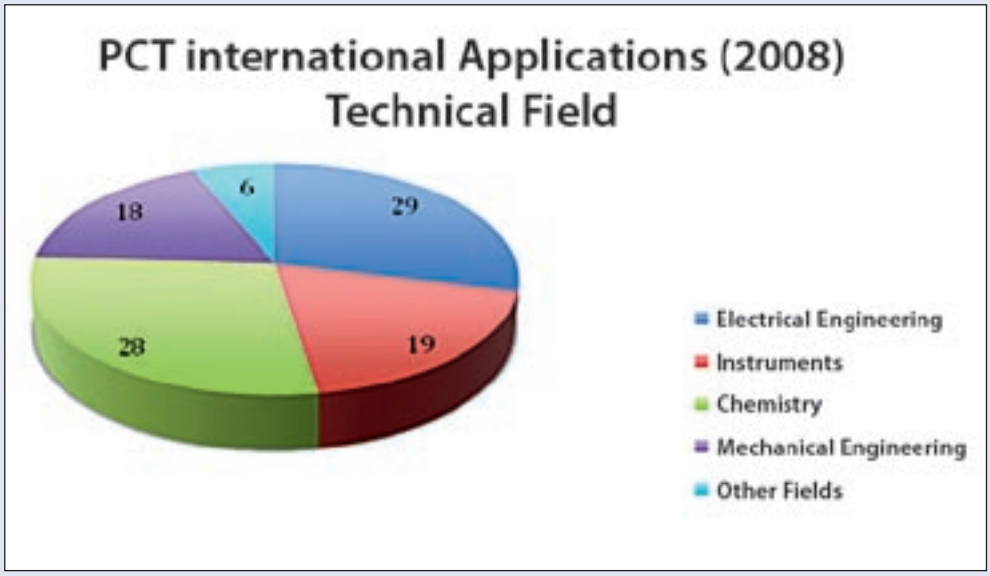
A patent is a limited 'negative' national right given to an inventor for a short period of time (usually 20 years from date of filing) in exchange for a publication of a full specification that allows anyone reading the patent to replicate the invention. In practice descriptions are often published a (relatively) long time after application, and due to careful patent drafting can be difficult to replicate. The patent specifies a set of claims by the inventor that permits the exclusion of others from making, using, offering for sale, selling, or importing that which is claimed, but only in the jurisdiction to which it applies. This relatively old system has worked extremely well for inventions in many fields in engineering, including modern electric and electronic engineering. The patent system is thought to be extremely important in the pharmaceutical industry, where the companies argue that it has enabled the expensive innovation of modern drugs and devices. Gold quotes studies conducted by Levin et al. and Cohen et al. over the last twenty years to have shown that

([10]) TRIPS Article 27.1 provides that '…patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced.'

R&D managers in pharmaceutical companies attributed significantly more importance to patent rights relative to their counterparts in other sectors. ([11]), ([12])

In the last few years there appears to have been a "patent gold gush,' in which 'inventions long thought unpatentable —everything from gene sequences of unknown function to one-step purchasing over the Internet— are now being claimed as property.' These developments are of particular concern because they tend to allow patents on subject matter that is both further 'upstream' in the innovation process and further afield from traditional industrial products and processes than has ever before been the case. ([13]) Does this expansion of the patent system encourage or discourage innovation and is the incentive really necessary to achieve innovation? The Canadian Supreme Court, in deciding against permitting the patenting of an altered mouse, stated succinctly that 'The massive private sector investment in biotechnological research is exactly the sort of research and innovation that the Patent Act was intended to promote. Healthcare is the major beneficiary of biotechnology. At the same time, vast amounts of money must be found to finance biomedical research. The Patent Act embodies the public policy that those who directly benefit from an invention should be asked, through the patent system, to pay for it, at least in part.' ([14])

The diagram below indicates the range of patent applications in all fields in 2008 at WIPO (Patent Cooperation Treaty applications) ([15]). It indicates that traditional applications still predominate, although applications for pharmaceuticals and biotechnology are increasing. The largest proportions of PCT applications related to the medical technology (12%), computer technology (8.5%) and pharmaceuticals (7.9%) sectors. Between 2003 and 2005 medicine and biotechnology accounted for 14.8% of nanotechnology filings. ([16])



([11]) Richard D. Levin et al., 'Appropriating the Returns from Industrial Research and Development' (1987) Brookings Papers on Economic Activity 783

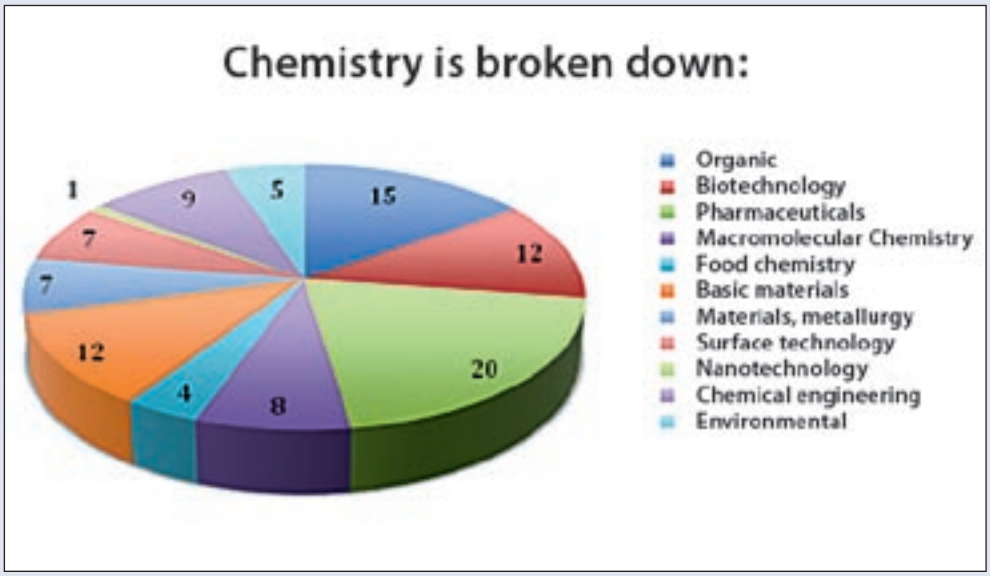
([12]) W. Cohen et al., 'Appropriability Conditions and Why Firms Patent and Why They Do Not in the American Manufacturing Sector' Working Paper (Pittsburgh: Carnegie-Mellon University 1997).

([13]) McManis C 'Re-Engineering Patent Law: The Challenge of New Technologies' Washington University Journal of Law and Policy http://law.wustl.edu/journal/2/p1mcmanis.pdf

([14]) Harvard College v. Canada (Commissioner of Patents), [2002] 4 S.C.R. 45, 2002 SCC 76

([15]) WIPO - The International Patent System in 2008 http://www.wipo.int/pct/en/activity/pct_2008.html

([16]) OECD Compendium of Patent Statistics 2008



The numbers in the diagram are the percentage of the total for each sector. The numbers in the chemistry segment can be broken down further:

There is, however, a question as to whether the system is efficient in 2 areas:

a. Modern technologies, specifically biotechnologies, personalised medicine and biologics where a specification that allows specific claims to be made may be difficult.

b. The ability to replicate an invention from its specification requires a basic infrastructure to be in place in the country in which a copy is to be used for further innovation. The system therefore favours economies that are advanced enough to replicate an invention and hence allow for innovation. The US patent office alludes to this as follows:

> 'The patentee is not required to disclose all possible uses, but promoting the subsequent discovery of other uses is one of the benefits of the patent system. When patents for genes are treated the same as for other chemicals, progress is promoted because the original inventor has the possibility to recoup research costs, because others are motivated to invent around the original patent, and because a new chemical is made available as a basis for future research. Other inventors who develop new and non-obvious methods of using the patented compound have the opportunity to patent those methods.'

In most jurisdictions, as defined in the TRIPS Agreement patents may only be granted if they meet specific criteria. They must be new, involve an inventive step and be of industrial application.

i. 'An invention shall be considered to be new if it does not form part of the state of the art' ([17]), which includes that which has been communicated to the 'public' by oral or written means.

([17]) European Patent Convention, Article 54

ii. 'An invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art.' ([18]) There has been controversy over whether uses for genes are not obvious to scientists 'skilled in the art'. The meaning of invention may be different in different jurisdictions. For example, the distinction between inventions and discoveries is not entirely clear. In the United States an inventor may patent a discovery if the invention satisfies the statutory requirements. The US Constitution (Article 1 (8)) provides for Congress to have the obligation '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' 35USC 101 provides for patents for those who 'invent or discover'.

iii. 'An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture.' ([19]) If a patent application specifies only the DNA or RNA structure without specifying a utility for a particular sequence, the claimed invention is not patentable in the US or under the European Patent Convention. Under US law, if an invention discloses a 'specific substantial and credible utility for the claimed isolated and purified gene, the isolated and purified gene composition may be patentable.' ([20]) US Patent law stipulates that 'a patent must be granted when at least one specific, substantial and credible utility has been disclosed, and the application satisfies the other statutory requirements.' Similar rulings have been made in Europe.

iv. 'Biotechnological inventions' in Europe are inventions which concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used. ([21]) They are patentable if they are

   (a) biological material which is isolated from its natural environment or produced by means of a technical process even if it previously occurred in nature;

   (b) plants or animals if the technical feasibility of the invention is not confined to a particular plant or animal variety;

   (c) a microbiological or other technical process, or a product obtained by means of such a process other than a plant or animal variety. ([22])

v. 'Synthetic DNA preparations are eligible for patents in the US because their purified state is different from the naturally occurring compound.'[20] In an early patent for adrenaline, the court explained that compounds isolated from nature are patentable: 'even if it were merely an extracted product without change, there is no rule that such products are not patentable'. (is there therefore (in the US) no conceptual difference between a synthesized purified DNA preparation and one found in the state of nature and which is subsequently purified? Are they hence interchangeable as end products for the purpose of patenting etc, and should we therefore not go any further in distinguishing between them in terms of origin of initial creation?) The same condition applies in Europe.

([18]) European Patent Convention, Article 56

([19]) European Patent Convention, Article 57

([20]) USPTO (2001) Utility Examination Guidelines Federal Register (2001) Vol 66 Page 1093.

([21]) European Patent Convention, Rule 26(2)

([22]) European Patent Convention, Rule 27

vi. A patent on a gene covers the isolated and purified gene but does not cover the gene as it occurs in nature.

vii. The US has no clauses that require a decision on whether a product or process is not patentable when its commercial exploitation may be contrary to morality or *ordre public*. European patent law does have these clauses, and the biotechnology directive ([23]) specifies a non-exclusive list of inventions that are not patentable:

a. processes for cloning human beings;

b. processes for modifying the germ line genetic identity of human beings;

c. uses of human embryos for industrial or commercial purposes

d. processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.

4. GENOMES & PATENTS

An enormous amount of data has been generated in determining the sequences of the genomes of living systems. At the time of collection of the data for the human genome project the US National Institutes of Health claimed ownership of the data, triggering many to attempt to patent DNA sequences (initially even where a use could not have been known). Many scientists were concerned with this approach – not only because of a lack of utility of the naked DNA sequences in question. ([24])

Many international organizations asserted that the human genome (and by extension other genomes) are 'the common heritage of mankind'. These include the Human Genome Organization (HUGO) Ethics Committee (2000) ([25]), the Council on Responsible Genetics (CRG 2000)([26]), and the International Federation of Gynaecology and Obstetrics (1997)([27]). The Parliamentary Assembly of the Council of Europe (Council of Europe 2001) asserted that it was 'of the opinion that the results of this grandiose research effort – in which the United States has the lead over Europe – must be made available to all, genetic information being a common human heritage, as set out in Article 1 of the Universal Declaration on the Human Genome and Human Rights, adopted at UNESCO in Paris on 11 November 1997. The Assembly in particular refers in this context to the Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine – Convention on Human Rights and Biomedicine (ETS No. 164) as well as its own Recommendations 1425 (1999) on biotechnology and intellectual property and 1468 (2000) on biotechnologies', ([28]) as well

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([23]) DIRECTIVE 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions

([24]) HUGO Statement on the Patenting of DNA Sequences and Rebecca S. Eisenberg & Robert P. Merges, *Opinion Letter as to the Patentability of Certain Inventions Associated with the Identification of Partial CDNA Sequences*, 23 AIPLA Q.J. 1 (1995)

([25]) Human Genome Organization Ethics Committee, 2000. Genetic benefit sharing. Science, 290 (5489), 49.

([26]) CRG, 2000. The genetic bill of rights. Council for Responsible Genetics CRG, Cambridge. [http://www.gene-watch.org/programs/bill-of-rights/bill-of-rights-text.html]

([27]) International Federation of Gynecology and Obstetrics, 1997. *Patenting human genes*. http://www.figo.org/]

([28]) Council of Europe, 2001. *Recommendation 1512: Protection of the human genome*. [http://assembly.coe.int/Documents/AdoptedText/ta01/EREC1512.htm]

as that of UNESCO in its Universal Declaration on the Human Genome and Human Rights ([29]). UNESCO's Declaration states that, 'The human genome underlies that fundamental unity of all members of the human family...in a symbolic sense, it (the human genome) is the heritage of humanity...The human genome in its natural state shall not give rise to financial gain.'

What exactly is the 'common heritage of mankind'? Bartha Knoppers has described it as that which 'argues against private appropriation in favor of sharing, administration in the common interest, benefits and burdens equitably distributed, equitable access, peaceful use and preservation for future generations' ([30])

When the US Patent Office considered its guidelines for utility patents in 2001 it addressed the question of whether there should be patents on genes 'as the nature of the human genome is at the core of what it means to be human, and no person should be able to own/control something so basic.' They decided that 'patents do not confer ownership of genes, genetic information or sequences. The patent system promotes progress by securing a complete disclosure of an invention to the public, in exchange for the inventor's legal right to exclude other people from making, using, offering for sale, selling, or importing the composition for a limited time. That is, a patent owner can stop infringing activity by others for a limited time.'[20]

Jasper Bovenberg has argued that we should not simply focus on the criteria for patentability when examining whether the claim of ownership should be entertained. In focussing on utility, novelty, non-obviousness and even the requirement to ensure disclosure of a patented object, we detract from the question of whether or not such sequences should be patentable at all. ([31])

The United Nations has endorsed the UNESCO Universal Declaration 'stating, in a symbolic sense, that the human genome is the heritage of humanity. The Declaration stipulates that the human genome, in its natural state, shall not give rise to financial gains and that an international framework be established to make the benefits of research on the genome available to all.' ([32])

Bovenberg argues that the prohibition on financial gain is that the common heritage principle bars private appropriation. In addition, there is a need to apply this concept in practice. He addresses the first through the medium of the arguments of Grotius in relation to the legal status of the sea. Is the genome the property of an individual, *res nullius*, the property of nobody, *res communis* – common property, or *res publicae* – public property. In his arguments Grotius traced the origin of these terms, and hence the use to which each of these could be put. Grotius reached two conclusions from these definitions of property. '[F]irst, that which cannot be occupied, or which never has been occupied, cannot be the property of anyone, because all property has arisen from occupation.' Second, 'all that which has been so constituted by nature that although serving some one person it still suffices for the common use of all other persons, is today and ought in perpetuity to remain in the same condition as when it was first created by nature.' Based on these conclusions, Grotius then listed many objects that by nature were open

([29]) UNESCO, 1997. Universal declaration on the human genome and human rights., Geneva. [http://www.unesco.org/shs/human_rights/hrbc.htm]

([30]) quoted in De Jonge, B and Korthals M (2006), 'vicissitudes of benefit sharing of crop genetic resources: Downstream and upstream' Developing World Bioethics 6 144-157

([31]) Bovenberg JA (2006) 'Mining The Common Heritage of our Dna: Lessons learned from Grotius and Pardo' Duke Law & Technology Review 8

([32]) Universal Declaration on the Human Genome and Human Rights, UNESCO Gen. Conf. Res. 29 C/Res.16, reprinted in Records of the General Conference, UNESCO, 29th Sess., 29 C/Resolution 19, at 41 (1997) (adopted by the UN General Assembly, G.A. res. 152, U.N. GAOR, 53rd Sess., U.N. Doc. A/RES/53/152 (1999)

to the use of all; the water, the sun, the air and the waves. All of these were not susceptible to occupation, and their common use was destined for all. ([33]) This argument is not sufficient, however, for although the 'sea' is *res omnium communes*, that which is in the sea, including minerals and fish, can be owned by an individual. This argument, when applied to the genome, provides that the genome itself is common property but derived inventions or discoveries could in theory be owned. In relation to synthetic biology, it is conceivable that the genome and much of that which is used to produce a synthetic product is common to all, but the product itself could be owned, and therefore patentable. The use of genes to produce pharmaceuticals or probes for disease remains a commercial activity, therefore patentable if the criteria are met.

Grotius' argument about the sea and its contents could conceivably be extended to ownership of all that falls within the high and low water marks. Many countries provide for common ownership of land within these borders, with rights similar to those on common land.

Resnik ([34]) has argued very differently. In his article, *The human genome: common resource but not common heritage*, he states that '[T]hose who oppose proprietary control of DNA have voiced a variety of objections to the patenting of DNA sequences, including the claim that patenting DNA violates human dignity, the assertion that patenting DNA violates the sacredness of nature, and the hypothesis that patenting DNA will have adverse effects on the progress of science, medicine and agriculture'. The article quoted does not address these issues directly, but rather the idea that the human genome is the common heritage of mankind – to which Resnik takes exception. The article reminds the reader that 'The common-heritage idea has influenced ethical and policy debates concerning the commercialization of the human genome' for some time, and that this needs to be considered carefully. He argues that the 'main ethical and policy rationale for granting patents is utilitarian: patents promote scientific and technological progress by giving financial incentives to inventors, investors and entrepreneurs' The argument is reiterated that '[u]nder a theory known as the patent 'bargain', the government grants an inventor a private right in exchange for public disclosure of information in the patent application.' ([35])

Resnik's primary argument is that

'A moment's reflection on the nature of DNA is sufficient to show that there are some significant problems with regarding the human genome as mankind's common heritage. The first problem is that there is not a single, identifiable thing (or set of things) that constitute(s) the human genome. There is a significant amount of genetic variation among members of the species *Homo sapiens*. Although human beings share most of their DNA, there are thousands of single-nucleotide polymorphisms (SNPs), which vary from person to person (Venter et al. 2001). Human beings also exhibit a great deal of variation in haplotypes (or patterns of sequence variation). The second problem is that there is not a single, identifiable set of people who inherit the human genome. Human beings share 98.5% of the DNA with chimpanzees, 95% with other primates, a great percentage of their DNA with other species, including fruit flies and yeast (Venter et al. 2001). So, only 1.5% of the human genome is actually 'our' common heritage; the

([33]) Bovenberg JA (2006) 'Mining The Common Heritage of our DNA: Lessons learned from Grotius and Pardo' Duke Law & Technology Review 8 paragraph 12

([34]) http://library.wur.nl/frontis/ethics/13_resnik.pdf

([35]) Miller, A.R. and Davis, M.H., 2000. Intellectual property: patents, trademarks, and copyright in a nutshell. West Group, St. Paul.

other 98.5% of the genome is the heritage of other species. ([36]) Should we say that the human genome is also the common heritage of the chimpanzees, the primates, all mammals, or even yeast? Does it make sense to say that non-human species can have property interests? ([37]) The third problem is that we cannot identify the persons or set of persons who have bequeathed our DNA to us. Did our ancestors ever intend to bequeath their DNA to all of humanity? These three problems show that is does not make much sense to regard the human genome as literally our common heritage. The common heritage idea may have symbolic importance, but it is an empirical fiction.' ([38]) In essence Resnik argues 'the human genome is not literally our common heritage. ([39]) If the human genome were literally our common heritage, the patenting of human DNA would be morally unacceptable because it would require the consent of every human being, a practical impossibility. ([40]) Even though the human genome is not literally our common heritage, it is still a very important common resource, and we have moral duties of stewardship and justice vis-à-vis the human genome. Our duties of stewardship include duties to refrain from harming the human genome but not duties to benefit the genome actively, because the idea of 'benefiting' or 'improving' the genome has clear eugenics implication. Our duties of justice imply obligations to share benefits fairly in genetics research and development. …. Finally, global benefit sharing may occur as products and services developed by companies become less expensive and more widely available. Short-term problems with access to genetic technology can be justified on the grounds that the system that allows such inequities, i.e. the patent system, promotes the interests of all members of society, especially the worst-off members, in the long run.' This argument runs counter to Lincoln's Gettysburg address, where he declared that "government of the people, by the people, for the people' is the essence of US democracy, yet there is no requirement for a referendum on every issue voted on by congress or decided by the President of the USA. Another counter-argument could be that as stewardship of the human genome does not necessarily involve active intentional improvement (other than through deliberate or capricious selective gene breeding, i.e., in the pairing and matching of sexual partners), it shall be made clear that the human genome can only be subject to the

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([36]) Substantively, it would appear that Resnik is questioning that there is such a thing as the human genome at all. If in agreement, one would need to ask then what it is that teams of scientists all over the world have spent billions of dollars and years sequencing; was the project misguided from the start, or is knowing the basis of human chemical life composition not an important research question? As President Clinton said at the conclusion and publication of the public sequencing effort in June 2000: 'Today we are learning the language in which God created life', of course it is understood that he meant human life.

([37]) The debate in fact might be broader than that. Again, given the huge sums and money and most often the collaborative research effort put toward sequencing the genome of living organisms, including that of humans, should there not be a social return regardless? Is the ownership/property discursive paradigm the most appropriate analytical and practical tool for the promotion of further innovation to increase knowledge on our species and ensure its survival onto an unseen future?

([38]) Juengst, E.T., 1998. Should we treat the human germ-line as a global human resource? In: Agius, E. and Busuttil, S. eds. Germ-line intervention and our responsibilities to future generations. Kluwer Academic Press, Dordrecht, 85-102.

([39]) A contrary view might suggest that there would seem to be some aspects in which the human genome can be understood as that which is common to humanity proper, or which forms part of its chemical (DNA) constitutive essence in parts, and including re-arrangement in a distinct chromosomal number—barring some viable anomalies. This enforces the boundaries of species. If what we take to constitute humanity in essence therefore is commonly inherited from progenitors to offspring in an unalterable chain of procreation (i.e., that no human child born of nature can fall off the species if his/her parents are 'human' from the start with respect to their genome), than it would not be far-fetched to posit that whatever the outcome of genetic permutation of sexual reproduction in the phenotypic variety of humans, there is safety in the knowledge that the genome of constitutive humans is therefore the essential non-excludable common heritage of these. No one will lose membership in a lifetime.

([40]) There are socially negotiated, acceptable and perhaps political, shortcut mechanisms for getting consent on other types of research involving human subjects, and for the disposition of research results; why not for research on the human genome and the use of its outcomes?

realm of mutational innovation which can be both fortuitous or debilitative to human health and condition, and ultimately to the human genome itself. What's more, there is no agreed global mechanism in place to ensure that the outcomes of research on the human genome are distributed equitably amongst all those who bear the essential minimum human genome sequence, i.e. Homo sapiens.

These arguments permit a return to the original questions, but in a slightly different form.

Is it only objects like the human genome that should be non-patentable as they are part of our common heritage? All the references to common ownership or heritage relate to human material; can this be extended to non-human products or processes that use material other than human tissue? The International undertaking on plant genetic resources, agreed in 1983, was based on the *'universally accepted principle that plant genetic resources are a heritage of mankind and consequently should be available without restriction'*. This was modified in 1991 when the Food and Agriculture Organisation passed resolution 3/91 that asserted that the concept of 'heritage of mankind' is subject to the sovereign rights of nations over their genetic resources ([41]) When the Convention on Biological Diversity was agreed in 1992, much of that which had been considered to be in common ownership was recognised (or reaffirmed) as within the sovereign rights of States. Article 15 addresses access to genetic resources and identifies these as sovereign rights. Decisions on their exploitation depend solely on the need to assure biological diversity, and do not presume their 'integrity' as a common resource. (would such an argument for the human genome be too premature or unrealistic given the Human Hap-Map project sequencing an ethnic diversity of genome sequences for differences etc?).

The United States Patent Office and the European Patent Office, after long deliberation have agreed that a mouse created for a particular purpose is patentable; the Canadian Supreme Court, in a divided judgement, found that under their patent law the mouse (the 'Harvard Oncomouse') could not be patented. The invention was titled transgenic animals, although it referred primarily to a mouse produced through the injection and incorporation of an oncogene into the embryo. The purpose was to provide for research into cancer. The court held that under Canadian Patent Law, a 'higher life form is not patentable because it is not a 'manufacture' or 'composition of matter' within the meaning of 'invention''. The court stated firmly that it was irrelevant whether the court believed that higher life forms such as the oncomouse ought to be patentable, the only question being addressed related to the wording of the Patent Act and whether the words 'manufacture' and 'composition of matter', within the context of the Patent Act, are sufficiently broad to include higher life forms. An important question discussed by the court related to whether it is defensible to permit the patenting of lower life forms, including bacteria whilst denying patentability to higher forms, such as a mouse. Among the arguments for a distinction is that the specific exception for plants and animals in trade agreements demonstrates that a distinction between higher and lower life forms is widely accepted as valid.

In Europe the Patent Office granted the Patent, stating: 'In the case at hand three different interests are involved and require balancing: there is a basic interest of mankind to remedy widespread and dangerous diseases, on the other hand the environment has to be protected against the uncontrolled dissemination of unwanted genes and, moreover, cruelty to animals has to be avoided. The latter two aspects may well justify regarding an invention as immoral and therefore unacceptable unless the advantages, i.e. the benefit to mankind, outweigh the negative aspects.' ([42])

([41]) FAO (2000) Multilateral Trade Negotiations on agriculture a resource manual http://www.fao.org/docrep/003/x7355e/X7355e06.htm

([42]) (Grant of European patent No. 0 169 762 (Onco-mouse/Harvard) (1992), OJ EPO 1992, 588, at pp. 591-92)

Case law in Europe, therefore, provides little evidence of any ability to decline granting of patents relating to higher life forms where other criteria are met; the only grounds would be where it is considered contrary to morality to exploit the 'invention' commercially.

An argument could be made that the information in the genome of any life form is so vast that it is in the public interest that the sequence should be placed in the public domain in order to ensure that innovation occurs. A patent would disallow others from using the information contained in the patented material for up to 20 years, and it may be that the holder is incapable of deriving the maximum benefit from the material in that time.

Hence the categories identified earlier may be confirmed as follows:

a. **That which is common to all humankind, and should not be patentable or directly exploited for commercial gain.**
   This should include the human genome and large projects such as the hap-map project ([43]) that address discoveries in the human genome. This would include artificial chromosomes introduced into human cells and would be justified under article 53(a) of the European Patent Convention (inventions for which the commercial exploitation would be contrary to morality). The International treaty on Plant Genetic Resources attempts to return some of that which was removed from the common heritage of mankind in the CBD to some crops (64) to permit free access to their genetic resources, arguing that '[n]o country is self-sufficient in plant genetic resources; all depend on genetic diversity in crops from other countries and regions. International cooperation and open exchange of genetic resources are therefore essential for food security'.

b. **That which, for a variety of reasons, should be placed in the public domain for all to use and exploit (the 'commons'). It may be that the process or product is so expensive to produce or require a vast range of expertise not available to any one organisation, or that the placing of the information in the public domain enables open standards that allow for the effective commercialisation and use of a number of products that use the technology or product.**
   This exclusion should address pre-competitive inventions, where the cost would be too great for a single organisation to bear. In addition, consideration of the compact between the private and public interest should be brought to bear. Where the range of information is so great as to make it impossible for a single organisation to develop and use during the lifetime of a patent, the basic information should be placed in the public domain or made available at minimum cost to others to use. This would ensure that information is not held so as to restrict innovation.

   As synthetic biology may involve the development of building blocks which could be assembled into a living organism, the development of open-standards that permit interaction between systems developed by the engineers needs to be explored.

c. **That which may, at the inventor's discretion, be protected through an intellectual property rights system to encourage innovation.**
   Inventors should be mindful of the choices that they may be able to make. They could choose to patent the invention, or could choose to place some or all of the information in the public domain or using some form of open licence. Importantly, where a choice is

([43]) See the HapMap website at http://www.hapmap.org/hapmappopulations.html.en. The HapMap is a catalog of common genetic variants that occur in human beings. It describes what these variants are, where they occur in our DNA, and how they are distributed among people within populations and among populations in different parts of the world.

made to patent, it should be remembered that although the rules relating to patents are almost universal, the patents themselves are national, and an inventor could choose the jurisdictions in which protection is sought. It may be that in order to encourage innovation in developing countries, inventors should be encouraged to choose not to patent their inventions in these countries. As the information regarding the invention (process or product) is disclosed in a patent application, an inventor could choose to use some sort of licence in countries where patent protection is not sought.

Patenting in biotechnology would have to serve some goal of utility (as a sub-category of equity served in purpose) in the distribution of the benefits, and perhaps also necessarily of the costs, of advanced research in biotechnology. Excluding one area of research from commercial ownership through the patent system does not mean that the benefits need necessarily have no return. Returns can bear social value for forming infrastructure for further development in research capacity or in real actual economic terms in the long run.

A second problem arises when dealing with Synthetic Biology – concern that unscrupulous individuals may attempt to use published information to synthesise dangerous DNA sequences. Due to the cost and analytical sophistication needed for synthesis, there are relatively few companies that synthesise long sequences of DNA. There have been suggestions that these companies screen all sequences for toxicity or infectivity before processing an order. That implies that databases of toxic or infective DNA sequences are available. These databases would of necessity fall within the ambit of the Database Directive ([44]). Regulation should ensure that all necessary information is readily available to these companies to permit the required searches. If the copyright protection provided for databases restricts access to the information necessary Article 6(2)(c) ([45]) or Article 9(c) ([46]) should be invoked to ensure that these companies are able to track possible dangerous sequences before synthesis.

([44]) Directive 96/9/EC of the European Parliament and of the Council of 11 March 1996 on the legal protection of databases

([45]) Article 6: Exceptions to restricted acts
2. Member States shall have the option of providing for limitations on the rights set out in Article 5 in the following cases:
(c) where there is use for the purposes of public security of for the purposes of an administrative or judicial procedure;

([46]) Article 9 : Exceptions to the sui generis right
Member States may stipulate that lawful users of a database which is made available to the public in whatever manner may, without the authorization of its maker, extract or re-utilize a substantial part of its contents:
(c) in the case of extraction and/or re-utilization for the purposes of public security or an administrative or judicial procedure.