Available online at www.elixirpublishers.com (Elixir International Journal)

International Law

Elixir Inter. Law 55 (2013) 12973-12977

ISSN: 2229-712X

Ethico-Legal Investigation of Patenting of Biotechnological Invention Involving Human Stem Cell

Nidhi Saxena and Nisha Saxena
Institute of Law, Nirma University, Ahmedabad - 382 481. Gujarat, India.

ARTICLE INFO

Article history:
Received: 11 December 2012;
Received in revised form:
2 February 2013;
Accepted: 8 February 2013;

Keywords
Human stem cell,
Patenting,
Ethicolegal,
Health.

ABSTRACT
Developments in the life sciences, whether in health, agriculture or the environment, have had an unexpected impact on life expectancy and the quality of life. Further, biotechnological inventions has already provided life-saving medicines such as monoclonal antibodies to treat cancer, human insulin to treat diabetes, erythropoietin to treat anaemia and cling to promise for cures for deceases currently regarded as untreatable. In the past decades biotechnology has been one of the fastest growing fields of technology among all. As the field covers a wide range of areas from micro-organisms to agriculture and medical applications, and involves publicly disputed techniques and products such as genetically modified plants, animal cloning or human embryonic stem cells, the ethical issue on patents is more heated & controversial than in other technological areas.

Introduction

Developments in the life sciences, whether in health, agriculture or the environment, have had an unexpected impact on life expectancy and the quality of life. Further, biotechnological inventions[1] has already provided life-saving medicines such as monoclonal antibodies to treat cancer, human insulin to treat diabetes, erythropoietin to treat anaemia and cling to promise for cures for deceases currently regarded as untreatable. In the past decades biotechnology has been one of the fastest growing fields of technology among all. As the field covers a wide range of areas from micro-organisms to agriculture and medical applications, and involves publicly disputed techniques and products such as genetically modified plants, animal cloning or human embryonic stem cells[2], the ethical issue on patents is more heated & controversial than in other technological areas.

Like other biotechnological inventions, stem cells may be subject to patent protection. Patents confer an exclusive right on the patentee, they can limit public access to goods, such as medicines or food crops, or hinder research by restricting access to essential research tools. On the other hand economic studies have repeatedly shown numerous of these important innovations would probably not have reached the market without patents.

Stem Cells Controversy

Human embryonic stem cells have been both isolated and cultured in the US[3], Australia, India, Singapore, Israel and Sweden, and cultured in the UK. Worldwide there have been over 2000 patent applications involving human and non human stem cells, of which one quarter refer to embryonic stem cells.

The stem cell controversy is the ethical debate cantered barely on research involving the creation, usage and destruction of human embryos. With the present state of technology, the creation of a human embryonic stem cell line requires the

[1] According to the European Patent Convention (EPC), "Biotechnological Inventions" 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. (Rule 26 (2) EPC.) This covers living organisms and DNA. Here "Biological material" means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system (Rule 26 (3) EPC).

[2] Stem cells are cells found in all vertebrate animals, including human beings. They play roles in the processes of normal development and regeneration or repair of damaged tissues. The reason for this is their properties of dividing to give cells either identical to themselves or differentiated into particular types of cells. Because of these properties, it is thought probable that stem cells will find use in the therapy of degenerative diseases or injuries.

[3] The US patent awarded to the Wisconsin Alumni Research Foundation (WARF), for human pluripotent stem cells derived from spare embryos created for infertility treatment. This broad patent covers both James Thomson's method of isolating human embryonic stem cells (ESC) and the five undifferentiated stem cell lines derived. That patent gives WARF control over who may work with its five stem cell lines and for what purpose. WARF decided to provide access against a nominal fee to academic researchers and access against a negotiable fee to other scientists. In return for its funding of James Thomson's research, the for-profit Geron Corporation was granted a licence agreement by WARF. Geron holds exclusive rights to develop the stem cell lines isolated at the University of Wisconsin into three specific differentiated stem cell lines for commercial purposes.

Tele:
E-mail addresses: nidhinriya@gmail.com

destruction of a human embryo. Most commonly, this controversy focuses on embryonic stem cells.[4]

According to the sources from which they are retrieved the stem cells are of different types. Such as Adult stem cells[5], Stem cells of foetal origin[6], stem cells of embryonic origin[7] and derived cell and stem cell lines[8]. Stem cells may possibly be also obtained by injecting stem cell or egg cytoplasm into somatic cells transforming[9] them into stem cells.

Global Legal Regime-A Comparative Overview

USA

In 1980, the US Supreme Court overturned its previous case law to allow the granting of a patent on living matter[10], since then, there is a standing practice for patenting biotechnological inventions on living matter[11].

Under US law both higher and lower life forms can be patented provided that they are genetically modified or obtained in a purified state. To be afforded patent rights, a particular stem cell invention must be judged to consist of patentable subject matter, possess utility, and to be novel and non obvious. Many stem cell inventions may be judged patentable subject matter under U.S. law.[12] Stem cell inventions would typically be classified as either a composition of matter[13]or as a process.[14]The stem cell inventions are derived from living beings does not necessarily bar their patentability. Although a patent will not be granted for inventions that merely duplicate materials found in nature, an inventor may obtain a patent for an artificially modified biotechnological product[15]. Inventions that require the isolation and purification of a stem cell line have been judged to involve a sufficient transformation of raw materials to be patentable.

A number of issued U.S. patents[16] concerns stem cell inventions, the majority of which appear to associated with "adult" or cord blood stem cell inventions. Johns Hopkins University asserted three patents[17] related to same, against Cell Pro, Inc[18]. Since none of the products or processes claimed in these patents exists in nature per se, each was considered to be patentable subject matter.

For the reason that the USPTO maintains many pending patent applications undisclosed until they are issued as granted patents,[19] the number of filed patent applications concerning stem cell inventions is uncertain. The communication between these patents and patent applications, on one hand, and stem cell lines for which federal research grants for embryonic stem cell research may be obtained, on the other, has not been determined. Several patents pertaining to an embryonic stem cell invention, on research performed by Dr. James A.[20], held by a foundation associated with the University of Wisconsin, claim both a method of isolating stem cells and the resulting stem cell line. Some observers reportedly believe that the Wisconsin patents have an extremely broad scope, in that they cover basic tools and techniques of embryonic stem cell research.

Europe

The European Patent Office (EPO) following strongly the US patent office practices[21] has granted several patents on all

[4] Not all stem cell research involves the creating, using and destroying human embryos. Stem cell research, for example adult stem cells or induced pluripotent stem cells, which do not involve creating, using or destroying human embryos is less controversial. See Stem cell controversy. From Stem cell controversy. 13,feb.,2010 <http://en.wikipedia.org/wiki/Stem_cell_controversy">

[5] Progenitor and multipotent stem cells are present in adults. Mammals appear to contain some 20 major types of somatic stem cells that can regenerate the various tissues but they are rather difficult to find and isolate and they do not seem to have the same developmental potential as embryonic or foetal stem cells.

[6]Haematopoïetic stem cells can be retrieved from the umbilical cord blood. Foetal tissue obtained after pregnancy termination can be used to derive multipotent stem cells like neural stem cells which can be isolated from foetal neural tissue and multiplied in culture, though they have a limited life span. Foetal tissue can also give rise to pluripotent EG cells isolated from the primordial germ cells of the foetus.

[7] pluripotent ES cells are those which are derived from an embryo at the blastocyst stage. Embryos could be produced either by in vitro fertilisation (IVF) or by transfer of an adult nucleus to an enucleated egg cell or oocyte (somatic cell nuclear transfer – SCNT).

[8] One should distinguish:

_ stem cells freshly derived from an organ or tissue which have not yet been subjected to any modification and which are capable of being propagated as stem cell lines,

_ unmodified stem cell lines which refer to cultured lines of cells which have been propagated originally from freshly derived stem cells and which have not been modified in any other way. When the stem cells are derived from an embryo, the undifferentiated stem cell lines which can be derived from them are pluripotent.

_ modified stem cell lines which refer to cultured lines of cells, propagated from stem cells or stem cell lines, which have been modified either by genetic manipulation, or by treatment that causes the cells to differentiate in a particular way.

[9] Such transfer is ooplasmic transfer.

[10] Diamond, the Commissioner of Patents v Chakrabarty (1980) 447 U.S. 303, 309 (US Supreme Court)

[11] For instance micro-organisms, genes, cell lines including human ones such as cancer cell lines, and there are recognised ways to patent such inventions.

[12] Under the Patent Act of 1952, patents may be granted for any "process, machine, manufacture, or composition of matter."

[13] Such as a purified suspension of stem cells.

[14] Such as a method of preparing or using stem cell products.

[15] Michael A. Sanzo, "Patenting Biotherapeutics," 20 Hofstra Law Review (1991), 387.

[16] Through August 28, 2001, a total of 168 U.S. patents with the term "stem cell" in the title had been granted.

[17] One claimed a purified suspension of stem cells; (U.S. Patent No. 4,714,680.), one more a method of creating a purified suspension of stem cells using certain antibodies; (U.S. Patent No. 5,035,994.) and an additional third patent claimed a method of using a purified suspension of stem cells in bone marrow transplants(U.S. Patent No. 5,130,144.).

[18] Johns Hopkins University v. CellPro, Inc., 152 F.3d 1342 (Fed. Cir. 1998).

[19] 35 U.S.C. § 122.

[20] *E.g.*, Sheryl Gay Stolberg, "Patent Laws May Determine Shape of Stem Cell Research," New York Times (17 Aug. 2001).

[21] European Patent Convention Articles 52 and 53 of the European Patent Convention say what can and cannot be patented.

sorts of biological materials[22]. Though not explicitly mentioned, it is generally accepted that EPC allows patent protection for microorganisms[23]. Biotechnological inventions are also patentable there, however, in contrast to the situation in the US, European patent excludes certain patentability of any invention,[24] because their commercial exploitation would offend against order public and morality.

From 1980s to July 6, 1998, a debate on biotechnology patents of clarifying the distinction between what is patentable and what is not, and harmonising EU member states' laws in this area led to the adoption of 1998 of EU Directive 98/44/EC on the legal protection of biotechnological inventions. These directive are now been implemented by all EU member states[25].

Substantive patent law and these rules now provide the basis for deciding on the patentability of biotechnology applications at the EPO. The incorporation of the EU directive into the EPC confirmed the practice of the EPO in biotechnology, whilst putting greater focus on ethical considerations[26].

An invention relating to gene sequences can be patented as long as the industrial application of the sequence is disclosed in the application and all other patentability criteria are fulfilled[27]. However, the directive rules out the patenting of the entire human body in all its developmental phases[28]. The same applies to processes for cloning human beings, processes for modifying the germ-line genetic identity of human beings and the use of human embryos for industrial or commercial purposes. Also excluded from patentability are 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 animals resulting from such processes. This catalogue of exceptions to patentability is not exhaustive.[29]

In current ruling on stem cell cultures issued in November 2008 in the WARF/Thomson case, the EBoA decided that under the EPC it is not possible to grant a patent for an invention which necessarily involves the use and destruction of human embryos. The EBoA stressed, however, that its decision did not concern the general question of human stem cell patentability.

The Directive states at Article 6 that the human body at the various stages of its formation (including the embryo and sequences or partial sequences of genes) is not patentable. However, the Directive[30] states that an element of the human body (including the sequence or partial sequence of a gene) that has been isolated from the body by means of a technical process may be patented even if the structure of the element is identical to that of a natural element. To be patentable under the Directive, as was previously true in the EU, the isolated element must still be novel, involve an inventive step and be capable of industrial application.

India

The ambiguity on the issue scratched in year 2002 after the amendment[31] in the Indian Patents Act. Currently micro-organisms can be patented provided they satisfy the other requirements.

There is dearth of judicial dicta with respect to patenting of microorganisms in India. An unreported Kolkata High Court decision[32] throws some light on this aspect. The court rejected the findings of the Indian Patent Office and held that the dictionary meaning of the word manufacture does not exclude the process of preparing a commodity which contains a living substance. Following this decision process patent was issued to the applicant from the patent office.

One former case[33] briefly touches upon the issue[34] of patenting of microorganisms in the general light of patenting of

[22] See for e.g. (1) T 162/86 'Plasmid PSGZ/HOECHSTAG (2) T 281/86 'Preprothasmatin/ UNILEVER (3) T 288/86, 'Bovine Growth Hormone/ the Regents of University of California.

[23] Article 53(b) of the European Patent Convention says that the exclusion of plants or animal varieties or essentially biological processes does not apply to products of micro-biological processes.

[24] This includes :

– any invention whose commercial exploitation would be contrary to order public or morality (Art. 53 (a) EPC)

– plant and animal varieties (Art. 53 (b) EPC)

– essentially biological processes for the production of plants and animals (Art. 53 (b) EPC), e. g. classical breeding, crossing and selection

– methods for treatment of the human or animal body by surgery or therapy, and diagnostic methods practised on the human or animal body (Art. 53 (c) EPC) Discoveries (e. g. the discovery of natural substances, such as the sequence or partial sequence of a gene) are not patentable because, without a description of the technical problem they are intended to solve and a technical teaching, they are not regarded as inventions (Art. 52 (2)(a) EPC).

[25] In 1999, the contracting states to the EPC decided to incorporate the directive as secondary legislation into the Implementing Regulations to the EPC.

[26] See for example, the directive affirmed that isolated biological material is patentable even if it has occurred previously in nature (Rule 27 (a) EPC).

[27] Rule 29 (3) EPC

[28] Rule 29 (1) EPC

[29] Rule 28 EPC

[30] These Directives directly addresses patenting life forms.

[31] Before the amendment, section 3(j) of the Act stated that plants and animals in whole or in part thereof including seeds, varieties and essentially biological process for the production of plants and animals are excluded.

[32]. In Dimminaco AG vs Controller of Patents & Design, The applicant, Dimminaco AG, had applied for a process patent involving the manufacture of a live vaccine for protecting poultry against infectious bursitis.The application was rejected by the Indian Patent Office stating that the definition of invention in the Patents Act did not include a living organism thus any process that resulted in a live vaccine would not qualify as a manner of manufacture.

[33] Vandana Shiva and Ors vs. Union of India 1995 (32) DRJ 447.

[34] The facts of the case were that four petitioners had sought a writ of mandamus restraining the Union of India from signing/ratifying the existing version of GATT Treaty, or to restrain the Union of India from, agreeing to sign and signing Art. 27.5.3 (b) of the TRIPs Agreement. They also seek a direction for exclusion of patents on life-forms including plants, animals, human beings produced through biological or microbiological processes, whether natural or modified on grounds of public morality and public order. They seek a further direction against Union of India from violating the fundamental

all living forms. The High Court of Delhi however took the view that the signing of any treaty, in this case the GATT treaty cannot be challenged if there is no infringement of fundamental rights of the citizens. The Court was of the view that it was a matter of policy which was best left to the executive, if citing British and American sources it is submitted that it was best to a non-interfering policy in this regard.

Thus court showed its reluctance to interfere with a matter of policy of the executive even if the challenge is based on the grounds of public morality and public order. Since now the matter is some what settled after the decision of the Calcutta High Court. But a call for finalising the issue towards the Supreme Court is still awaited.

Ethico-Legal Aspects

A most alarming aspect of patenting life is the patenting of human genes, cell lines and tissues. The threats involve in patenting of biotechnological invention related to human biological materials apprehends several issues.

The Universal Declaration on Bioethics and Human Rights advocates the maximum possible flow and the rapid sharing of knowledge concerning medical, scientific and technological developments over and above the patent system is required to promote the flow of timely information about new technologies. Commercialization of genetic science clearly has dejected data sharing among scientists; the world of genomics is becoming a place where people are much more reluctant to share."[35] The present patent system promotes secrecy and hinders the exchange of information.

Another concerned issue is Informed Consent. The doctrine of prior informed consent derives from medical ethics, where it reserves right to patient *i.e.* right to give consent to or refuse certain medical treatment after being informed by the practitioner about the risks and benefits of the same. This concept further extends to other fields of medical research using human tissue. With the same the consent to use certain inputs to biotechnological research has been a recurrent[36] issue with bioethical implications, which has raised questions about the need to obtain the prior consent of the human subjects concerned, in concert with the issue, whether consent extends to the patenting of outputs from research.

The Convention on Biological Diversity (CBD) makes prior informed consent a condition of access to genetic material of plant, animal or microbial origin ; UDBHR[37] sets prior informed consent[38] in the context of human dignity and autonomy; CBD links it to the sovereignty of nations over their resources, and the interests of indigenous and local communities.

Bioethics issues concerning clinical trials and informed consent questions may be relevant to the protection of test data concerning the safety and efficacy of chemical entities, because of the public interest role of this information, and concerns about duplication of trials involving human or mammal subjects.[39]

Patenting human genes would mean granting a monopoly to the patent holder, on a common human heritage. Since patents confer an exclusive right on the patentee, they can limit public access to goods, such as medicines or food crops, or hinder research by restricting access to essential research tools.[40]The CBD establishes as an international legal principle that the benefits of the use of genetic resources should be equitably shared.

Specific bioethics menace arise over the dignity of the human being, beginning-of-life and end-of-life issues, consent to medical treatment, freedom of research, the consent of the donor of human genetic material, access to health care and distribution of health resources, and equitable access to the outcomes of biological research, as well as animal protection and environmental ethics.

Patents make important health products more expensive and less accessible. Patent stacking[41] may discourage product development because of high royalty costs owed to all patent owners of that sequence; these are costs that will likely be passed on to the consumer.[42] The holder of the gene patent can charge as per his wish. Further the gene exist in one's body can be the private property of any one else.

Customarily, patents promote innovation, but that's because most patents are granted for human inventions. Genes aren't human inventions; they are features of the natural world. As a result these patents can be used to block innovation, and hurt patient care. People should not be allowed to "own" life forms or the basic chemical molecules which are fundamental to life.[43]

---

rights and ensuring their protection while signing the Treaty, the right to health and nutrition ensured by the existing Indian intellectual property regime and patent system which had ensured the exclusion of patents on life forms and patents on products in the area of health and. agriculture on grounds of morality and public order and also in respect of rights of farmers including the right to seed as owners, producers, breeders and innovators etc.

[35] L. Belkin, "Banking on Genes," The New York Times Magazine, August 23, 1998, p.59.

[36] As there have been cases where genetic materials taken from the human body have been used as inputs for research, leading to inventions, which were subsequently patented.

[37] Universal Declaration on Bioethics and Human Rights

[38] The UDBHR (Article 6 (II)) provides that "scientific research should only be carried out with the prior, free, express and informed consent of the person concerned".

[39] Id.

[40] Suman Sahai, "A mixed bag", Frontline Magzine, Volume 19 - Issue 11, May 25 - June 07, 2002.

[41] Allowing a single genomic sequence to be patented in several ways such as an EST, a gene, and a SNP.

[42] Genetics and Patenting, 14 Feb., 2010 http://www.ornl.gov/sci/techresources/Human_Genome/elsi/patents.shtml>

[43] *Supra* note 38

The UNESCO Declaration on the Protection of the Human Genome and Human Rights adopted by the UN General Assembly in 1998 recognizes the common heritage principle, at least on a symbolic level. It states that: "The human genome underlies the fundamental unity of all members of the human family, as well as the recognition of their inherent dignity and diversity. In a symbolic sense, it is the common heritage of humanity."[44] The Declaration also emphasizes that "benefits from advances in biology, genetics and medicine, concerning the genome, shall be made available to all . . . ."[45]

Allowing a market to develop in human biological material might undermine social bonds. While individuals are sometimes paid for the collection of blood or semen, such payment, from a legal perspective, is considered to be for services rendered, and not remuneration for the commodity itself.

Conclusion

IPRs for biotechnological inventions, pose challenges to access to technologies, unfair exploitation of genetic resources and fair and equitable sharing of the financial benefits. IP and bioethics have bearing on international human rights principles. The Universal Declaration of Human Rights and the International Covenant on Economic, Social and Cultural Rights provide for dignity, enjoyment of health, right to food, right to enjoy the benefits of scientific progress, right to benefit from protection of the moral and material interests resulting from one's scientific productions, but such kind of patenting may cause great harm to human rights also. Therefore Patenting of life forms can be considered unethical as it fosters bio-piracy of indigenous resources, turns life forms into commodities to be used for profit, hinders the free-flow of scientific research, destroys economic sustainability of developing nations, genetic research may pose a serious threat to the human race, the dangers are too substantial to permit such research to proceed, may spread pollution and disease, may result in a loss of genetic diversity …and depreciate the value of human life.

In order to be able to state ethical limitations, numeral problems are to be considered such as content of patents, various sources of stem cells, methods used to derive stem cells, protection of the donor, possible socio-economic consequences and philosophical implications of the patent system as applied to stem cells.

In a suggestive manner it is recommended to set up strict public control by centralised authorities on human embryo research where it is allowed, to take measures to prevent commercialisation of human embryos or cadaveric foetal tissue, as well as to ensure the respect of ethical principles through.

[44] Article 1, UNESCO (International Bioethics Committee), "Universal Declaration on the Human Genome and Human Rights." 14 Feb., 2010 http://www.unesco.org/bc/uk/genome/project/index.h

[45] Id. Article 12(a).