For centuries inventors have been granted exclusive rights to their inventions as a reward for their contribution to society. However, balancing public good with private reward is always arduous. The area of intellectual property in biomedical research has witnessed a marked change in the IP scenario due to the pressure exerted on governments by the industry. This paper strives to trace some of the changes witnessed in the West against the backdrop of the Indian patent regimen and argues that the law is transiting in an industry-responsive manner. A few suggestions are also made to adequately respond to these changes.

A surgeon at the University of California, Los Angeles (UCLA), removed the spleen of a leukaemia patient in an effort to save him. The patient survived and the surgeon went on to develop and patent a T-lymphocyte cell-line from the excised spleen (US patent 4,438,032) without informing or obtaining the consent of the patient. Some pharmaceutical companies obtained licences from UCLA to use the cell-line. Everything was fine until one day the patient sued the physician, the licensees and UCLA for damages (Moore vs Regents, University of California, California Supreme Court, 1990). Ironically, John Moore sued on the grounds of violation of confidentiality between the physician and the patient and thereby left the much larger issues of intellectual property ownership out of the decision.

The court’s interpretation of the case is of interest. The law saw cell-lines, as 'tangible' property distinct from the 'intangible' or 'intellectual'. The court conceded John Moore’s right to recover his tangible property as also derive any profits made from its misappropriation. The court, however, was also reluctant to recognize cell-lines as personal property to a point where it would inhibit research. By merely donating an organ, a person must not have intellectual property on anything derived from it, to foreclose further research.
The Moore case reflects the rapidly changing concept of property in a technology-dominant global environment. Governments are variously committed to their priorities—to balance individual reward with its societal obligations and consequently respond to these issues differently.

The article will predominantly examine patents, even to the exclusion of other forms of intellectual property that can be available for biomedical inventions. Dearth of Indian examples of biomedical patents has necessitated, perforce though, to borrow cases from the West. This category of inventions could include immunobiologics, novel microbial expression vectors, therapeutic methods, diagnostics, cell-lines and the like.

Inventors have traditionally been rewarded by grant of exclusivity rights over their inventions for a limited duration. Recent developments, however, question the very wisdom of the effectivity of such a system to promote innovation. NIH's patenting of expressed sequence tags (ESTs) without an ascribable function to their credit, the Sandoz patent to all methods of ex vivo gene therapy, etc. are examples of very broad patents stifling research. Patenting has made research costlier—the oncomouse is a case in point. With the need to protect inventions in several countries simultaneously and the mounting costs of prosecution and/or litigation, it is hardly surprising that the inventor rarely profits from his invention!

Why must we patent? Patents are potent instruments to secure finance. In countries such as China, intellectual property is valued as any other fixed asset. A patent is a negative right enabling the inventor to exclude unauthorized persons from exploiting his/her invention. A patent is only worth the paper it is printed on if it is not commercially exploited. With a secure patent, the inventor can license, sell, lease or barter his invention on his own terms. A protected technology attracts buyers. Thus, it makes commercial sense to protect one's invention before going to the negotiating table for fund raising or industrial exploitation. Let us examine what kinds of biotechnology inventions can be patented.

**Patentable Biotechnology Inventions**

Process, product, product-by-process and method of use patents are well-known for vaccines, therapeutics and diagnostics. In many countries, diagnostics and therapeutic methods are not granted patents. For instance, the European Patent Convention's (EPC) Article 52(4) states that "methods of treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application within the meaning of ......[Article 52(4)EPC].

Thus drugs and other compositions or implements used in surgical or therapeutic treatment of humans or animals can be patented but such methods of treatments *per se* are not patentable, although they could be so if carried out externally.

In contrast, in USA, "whoever invents or discovers any new and useful process, machine, manufacture, a composition of matter, or any new and useful improvement thereof, may obtain a patent therefor subject to the conditions and requirements of this title: (35 USC : 101). Therefore, novel and non-obvious medical and diagnostic methods and the use of compounds or compositions in diag-
nosis and therapy would be patentable in USA.

The Indian Patents Act, 1970 describes in its section 3, subsection (i) that any process for the medicinal, surgical, curative, prophylactic or other treatment of human beings or any process for a similar treatment of animals or plants to render them free of disease or to increase their economic value or that of their products are not eligible for grant of a patent. Thus in India, only processes for the manufacture of vaccines and immunotherapeutics can be patented at present.

A vaccine, recombinant therapeutic protein or an immunodiagnostic has not been clearly defined in Indian patent law.

These are circumscribed by the terms 'medicines and drugs' which include 'all substances intended to be used for or in the diagnosis, treatment, mitigation or prevention of diseases...all substances intended to be used in the maintenance of public health, or in the prevention or control of any epidemic disease among human beings or animals [Section 2, subsection (i). Indian Patents Act, 1970].

A vaccine may be composed of a whole microorganism or a recombinant product derived from a microorganism (hepatitis antigen expressed in yeast), or parts of an organism (bacterial or viral antigens) or synthetic compositions. Case studies make it evident that with skilful articulation of specifications and claims, most prophylactic, diagnostic, and therapeutic inventions can be patented in most countries.

Diagnostics which include serological tests for the detection of diseases, DNA probes, imaging technologies, monoclonal and polyclonal antibodies and ancillary technologies for visual read-outs are also granted product or process patents in most countries. A survey of patent literature reveals that patents have been granted for novel parent myelomas that are used to make hybridomas, the family of derived hybridomas, production of monoclonal antibodies as well as applications of these in diagnostic kits. Many of the claims are directed to the method of the assay, to particular reagent compositions or to combinations of materials used in the kits.

Process patents protect the claimed process and the use of a new or an old product produced by the novel patented process. Much work in the area of natural products concerned with isolation, purification, and characterization of the active ingredients, and devising methods of their synthetic production is patentable. This was extended to a novel method of purification of recombinant antigens such as "a method of purifying recombinant Pre S1, S2, S hepatitis B virus angigen from yeast (Merck & Co.)" which in effect provides broad protection to the elements necessary for making useful vaccines against hepatitis B infections.

Methods of isolating microbial or cellular metabolites can be patented. If these metabolites are characterized, the products in effect also get patent protection. The protection provided by a process patent is limited only to the specific method disclosed or its equivalents. The Biotechnology Patent Protection Act, 1995 has considerably increased the scope of protection offered by process patents in USA.

In the "product-by-process" claims the product is described by the specific process used for its production. This route is used if the invention cannot be described otherwise, for example, when the product's structure or composition is unknown, e.g., viral vaccines.
Under the US law, the inventor has an option to seek broader product protection after detailed information about the product is furnished within two years of the issuance of the product-by-process patent.

In contrast, product patents recite inventions that fall within the statutory classes of 'machines, articles of manufacture, compositions of matter or an improvement thereof...' These may be defined by the special properties distinguishing them from other known products, for instance, "anti-gonadotropin monoclonal antibodies with hCG-binding affinity of ...,", by the function it is capable of performing, as in "cell culture capable of expressing tissue plasminogen activator obtained by transforming mammalian cells with a vector...", or as comprising a component part/parts as in "a vaccine against tuberculosis comprising of Mycobacterium w...." A product patent is the strongest in terms of protection to the owner.

Within the ambit of patentable subject matter thus can also be brought immunomodulators such as cytokines, antibodies, gene sequences encoding protective proteins, cell-lines that can express these recombinant proteins, and DNA vectors. Treatment of humans and animals are not patentable in the EPC, nor are diagnostic methods practised on the human or animal body [Art. 52(4)]. Products, substances, compositions and kits for therapeutic use, however, are patentable. In these cases, the claims are directed specifically to the product's use in the manufacture of a composition for therapeutic or diagnostic application.

The Law has Changed!

Novelty, non-obviousness, utility and now increasingly, enablement and ordre public, have gained a new meaning and determine the fate of patent applications. The terms 'microorganisms', 'essentially biological process', 'manufacture', etc have also come to be crucial pointers to the patentability of biomedical inventions. Some case laws have reversed precedents. One such pertains to the grant of process patents for biotechnology which had been difficult to obtain at the United States Patents and Trademarks Office (US PTO) because of the interpretation of 'obviousness' in the judgement In re Durden... The Durden ruling was that 'merely using a new and patentable starting material in producing a new and patentable product using an old process did not necessarily make the process itself new and patentable'. The enhancement into law of the Biotechnology Process Patent Act in November 1995 changed this. The US law now states that a biotechnology process will be deemed non-obvious if it uses or results in a composition of matter — most often a product— that is itself novel and non-obvious, and therefore patentable.

A process patentee's power to exclude others used to extend only to the claimed process in contrast to the product patentee's right which extends to the product regardless of how it is made.. Where the chemical structure of a product is not known a patent may be obtained by defining the process by which the product was derived. Here the patent is granted for the product and is not limited to the process by which it is obtained. An identical product made in a manner other than that described in the claims was no infringement. In Scripps vs Genentech, which claimed "highly purified human or porcine factor VIIIC prepared in accordance with Claim 1...", this stance was reversed. The court opined that claims must be construed the same way for validity and for infringement, that the correct way of reading of
product-by-process claims is that they are not limited to product prepared by the process set forth in the claims.

The admissibility of 'the new use of an old drug' for patents at the US PTO is another worrisome development. This would extend the patent life of any medical substance which is expected to go off-patent at the end of 17 or 20 years. Similar laws are in the offering for EPC countries as well.

The meaning of the term utility has also undergone some change in recent years. Inventions that were not able to demonstrate effectiveness in humans have been rejected at the US PTO. In Ex parte Aggarwal, the US Board of Appeals and Interferences held that in vivo data relating to tumour suppression in mice were insufficient to justify the claim for use of the compound to treat tumours. In re Krimmel, however, it was ruled that data from "standard experimental animals" or those commonly used by persons skilled in the art to establish usefulness in humans, would substitute for data for in vivo utility in humans. The 1995 US PTO guidelines state that a qualified expert's affidavit evidence can substitute for human test data.

A significant departure from the norm of diagnostics being treated as a subject ineligible for patent, comes from Canada. All other conditions being satisfied, a diagnostic method relating to the human body will be patentable if it can be performed without the use of professional medical skills, would give reproducible and claimed results when used by a normally skilled practitioner, which is non-invasive and produce only diagnostic information. Patent examiners will go easy on diagnostics in the coming years. It therefore becomes evident that universally, patent laws are increasingly becoming "liberal" in an industry-responsive manner.

The question of morality and ordre public in determining the patentability of inventions, especially in connection with living matter, still remains to be resolved satisfactorily. The patent authorities in Europe and USA appear to favour the view that technical correctness of the application is only what they should adjudicate on and that the issue of morality and public order be left to other institutions created for that function.

How Do We Respond to the Changed IP Climate?

When we contrast the Indian scenario against the global backdrop, several inadequacies are visible. Our patent laws have outlived their use. The Patents (Amendment) Ordinance, 31 December 1994 (Sub-section 1(2) enumerating inventions not patentable, stated "notwithstanding.....a claim for patent of an invention for a substance itself intended for use or capable of being used as medicine or drug may be made and shall be dealt, without prejudice to other provisions of this Act,......" This was an attempt at introducing product patents in the food and drugs sector. However, the ordinance lapsed and consequently, the old 1970 Act with its attendant provisions is still in place. Secondly, conforming to even minimum provisions of the TRIPS which is mandated, would mean recognizing microorganisms as patent eligible and protection of plant varieties by either a sui generis system, patent or a combination thereof [Art. 27 (3 b)]. The duration of patent would also be twenty years!

The following action points can be considered in response to the IPR changes:

- The cost of filing for patents in India is far cheaper than elsewhere. However, most bio-medical inventions are not granted
patents in India. The laws need to be suitably modified to treat these inventions as patent eligible subject matter to enable Indian inventors get an early filing date for their inventions at lower cost.

- The Patent Cooperation Treaty (PCT) and the Budapest Treaty must be signed. The former will enable for a single application and payment of a one-time search fee for patenting in several designated countries. At the time of writing this, a move to accede to Paris Convention and the PCT was underway. A recognized repository in India will surely help in reducing the cost of depositing and maintaining biological samples, as against doing so in repositories in other countries.

- For the present, we should go along with only the minimal provisions of the TRIPS. In an environment where we can be pressurized for international scrutiny, and can be the target of trade sanctions, it is imperative that we play by their rules. And win! It does not mean that we rush out to define microorganisms. There is safety in ambivalent definitions when your case is weak. We need strong laws only if we have a strong industry. Perhaps when we have a good indigenous biotechnology industry, we must consider having strong IP laws. In the meantime we must avail the transitional period granted by the Treaty completely and utilize the period in modernizing our patent offices and including a patent culture in academia and the industry.

- There must be insistence on submission with the patent application, where required, of certified statements as to the geographical origins of a microbial sample for scrutiny by the patent examiner. This should alert us of any erosion of germplasm.

- Fostering patent awareness and patent literacy amongst the research community through easy access to information not only regarding granted patents but also about those pending at the Patent Office will help update Indian researchers to the state-of-the-art in a given area and avoid possible patent infringement. Organizations such as the Department of Biotechnology and the Department of Science and Technology may be able to help here.

- Project proposals for government funding should be mandated to carry a current patent search report before they are evaluated. This would prevent squandering precious resources in duplicating research for which eventually someone else would claim ownership.

Let us stand back to get the view in perspective. The last two years have witnessed a blind rush for filing patent applications either in India or overseas. The pursuit of numbers only negates the very objective, as it did with the family planning programme. Trivial and commercially worthless patents can be obtained by careful drafting of a specification around a granted patent. Such patents even if granted is of not much use to anybody, save perhaps to embellish the biodata of the applicant. I am afraid that many of the patent applications emerging are of such nature. What is needed is truly innovative inventions. It is such kind of innovative inventions whose commercial and intellectual worth needs to be recognized and protected. Otherwise we would be frittering away our meagre resources on trivia. A patent should be commercially valuable. In fact securing a patent and maintaining it costs a
lot of money. What is a patent worth if it does not fetch anything?

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