Human genome studies and intellectual property rights: Whither national interest?

T. R. Sivaramjani and Samir K. Brahmachari

India has been acknowledged as a large reservoir of nature's random mutation, an original 'rich' source of knowledge in the context of international genome studies. Human genome knowledge and the possible understanding of the basis of uniqueness of each individual in chemical terms has presented a number of inescapable challenges to our jurisprudential philosophies and our ethical sensibilities.

Human genome: The new frontiers in science and jurisprudence

'...We really are here on a wonderful threshold of knowledge. The ascent of man is always teetering in the balance. There is always a sense of uncertainty, whether when man lifts his foot for the next step it is really going to come down pointing ahead. And what is needed for us? At last the bringing together of all that we have learned, in physics and in biology, towards an understanding of where we have come: what man is.'

Surprisingly these lines were written not in the present era of genomania but in the early 1970s (ref. 1). The spirit behind it could not ring more true for the science of human genome studies which has been hailed as the last frontier of biology and in what has now become a cliched comparison, has been likened to the Apollo space program. At last we seem to be succeeding in bringing together of all that we have learned in physics and in biology towards an understanding of what man is[1]. The Human Genome initiative is a world wide research effort with the goal of analysing the structure of the human genome at the nucleotide level. It is likely to provide in-depth understanding, and possible treatment, for more than 6000 genetic diseases that affect humankind as well as genetic alterations that increase the risk of developing some common diseases. In addition, the variability in response to pathogenic organisms and the basis of neoplastic proliferation and human behaviour are also likely to be unraveled, thus paving the path of an era of predictive medicine.

A comparison between populations in terms of physiology and susceptibility to certain diseases, whose incidence seems to result from genetic and environmental interactions, would also be of great interest to medical researchers. The vast Indian genetic pool provides a unique opportunity to discover functional significance of human genome sequences of hitherto unknown function through mutation analysis. Thus, India has been acknowledged as a large reservoir of nature's random mutation, an original 'rich' source of knowledge in the context of international genome studies. Apart from the fact that a considerable number of rare genetic disorders are likely to be found merely because of the population size, the large size of most families in India also make them ideal for genetic analysis. The large number of very competent medical practitioners with modern clinical expertise and vast network of hospitals, clinics and health centres, again, unlike in many developing countries, provide conditions conducive to the unraveling of this knowledge.

This human genome knowledge and the possible understanding of the basis of uniqueness of each individual in chemical terms has presented a number of inescapable challenges to our jurisprudential philosophies and our ethical sensibilities[2]. Illustratively, rule of law and concepts of justice are based on the fundamental assumption that all humans are equal. Jurisprudence all over the world has evolved towards taking positive action to make up for social disabilities and allow an opportunity to the socially disadvantaged to also manifest their equality. But genomic research is enabling us to understand that we are different in ways that we could never have understood before. This insight has the political and social potential to shake the very presumption of 'equality' that is the basis of the administration of justice anywhere. Thus in its potential to bring about change, in its capacity for beneficence and also in its latent potential for abuse, the Human Genome project is remarkably similar to the triumph of the splitting of the atom.

Human genome: An emerging economic issue

Although deciphering the human genome as a worldwide effort started as an intellectual and scientific endeavour, now a new generation of the biotechnology industry, the genomic companies, have put in the resources for gene hunting that the academia simply cannot match[3]. The driving force behind this boom is investment from the pharmaceutical industry. Anticipated business out of the genome analysis project and the exploitation of derived knowledge is estimated to be over US $100 billion per annum, starting 2005. Most of it will be for predictive medicine centered around DNA

T. R. Sivaramjani is in the National Law School of India University, Bangalore 560 072, India and Samir K. Brahmachari is in the Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560 012, India.

based diagnostics and therapeutics. This amount is several fold higher than the world-wide sale of pharmaceutical drugs as curative medicine today. All over the world, legal structures and policy makers have to gear up to face the demands of this new science and its commercial potential. In this context a number of imperatives for Indian scientists and the government become evident to enable the utilization of India's rich genetic wealth for economic and medical benefits for our people[4].

An issue that has come to epitomize these concerns both in terms of the inadequacy of our legal structure as well as of our philosophical discourses is the issue of patentability of the results of such research. Intellectual property rights are supposed to provide recognition and reward for intellectual creativity, and patents are the strongest form of intellectual property rights protection. Although patents have long been familiar to scientists working in the areas of chemistry and engineering, until recently they remained alien to geneticists, biologists, physicians and other academics involved in research in the life sciences. Things changed fundamentally with the advent of modern biotechnology, and especially with relation to various genetic engineering techniques, which blurred the dividing line between basic and applied research. Apart from the domestic, national legal debates that a number of western countries are going through, the issue for India has a number of peculiarities that makes it a little premature for us to talk about patenting of human genetic materials and the products or processes based on them right away.

In the context of human genome studies, patents have brought certain issues into sharp focus, which by their very nature are indicative of larger issues. It would be infructuous at best and to an extent dangerous to view patents in biotechnology as an isolated issue without understanding the trade-related development and other macro-economic issues.

IPR as a trade issue: Recent developments

Until the early 1980s, protection of intellectual property was never considered as an aspect of a trade regime. Nations both developed and developing, recognized that both as a reward and as an incentive for innovation it was necessary to make payments for intellectual property rights, particularly patents. There was much greater emphasis on using patents as a means for seeking transfer and indigenous development of technology and a tool for industrialization. Several developing nations, including India, did not adhere to the Paris convention for the protection of industrial property[5], because they thought that it would come in the way of their industrialization policy[6]. The efforts of the developing countries at trying to bring about changes in the Paris convention to reflect their development needs and priorities turned out to be an unsuccessful attempt.

Furthermore, from the beginning of the 1980s, the major developed countries, particularly the United States, seized the initiative and went about systematically reversing the direction of change from greater flexibility in the national patent systems to take care of varying needs and levels of development, towards a tightening up of such systems. The GATT related agreement on TRIPS was a culmination of this effort[7]. India being a signatory to the establishment of the World Trading Organization including the agreement on TRIPS has to honour the commitment made to the agreement. In many ways the TRIPS is a move away from the dialogue that was uptil then proceeding between the developing and the industrialized world[8]. TRIPS as an instrument of technological protectionism could freeze the present technology asymmetry between developed and the developing countries.

TRIPS seen as a product of international relations appears to hit India hardest in the field of biotechnology. The issue of harmonization of intellectual property regimes in biotechnology is extremely problematic as there is no consensus even within continental or American jurisprudence. Technical objections to the patentability of such innovations, such as the distinction between an invention and a discovery, adequacy of disclosure and obviousness, are routinely made. However, it is the ethical and moral debates about biotechnology especially human genome technological developments, which rage at national and international levels.

In view of the prospects that the progress of the human genome studies will offer for identifying proteins of interest as potential targets for intervention in disease, identifying potential therapeutic proteins and identifying genes responsible for predisposition to particular diseases, the involvement of private funds has become a crucial aspect[9]. Already at the present stage of development of somatic gene therapy and somatic cell therapy in many legal systems (e.g., US and Germany) it is undisputed that the materials involved, e.g., vectors, somatic cells as well as transformed somatic cells are to be treated either as drugs or as biological products and thus patentable under the laws currently in force[10]. It goes without saying that the necessary investment in this area will only be made if patents are able to offer sufficient security for the investors. Already in Europe the relatively lower investments in genomic studies has been taken to indicate the confused state of patentability of the results.

Patentability: The legal debate

The patent issue came to a head with the US National Institute of Health (NIH) patent claims made for cDNA

sequences which many in the scientific community felt to be unfairly broad and too numerous[11]. The argument on one side was that filing a patent application for a fully or partially sequenced gene without having the complete biologic information would be tantamount to claiming the rights to all products resulting from the use of the gene, including the products of gene expression, the antibodies to such products and any potential uses for them. While this argument would have limited weight in patent law, the genome community world wide, as well as the industry rejected the idea of having patent on cDNAs without known functions as this would represent an untenable level of monopolization of research results. This exemplifies the concern that indiscriminate patenting may also hinder product development. Patents are important to commercialization in the biomedical field because they provide the exclusivity that encourages industry to invest the resource necessary to bring an invention from the discovery stage through the stages of development, clinical trials, regulatory approvals and ultimately into commercial production. Although India has never been a major player in the International Genome community, the legal debate around patenting is of significance, as it is an acknowledged fact that supra-national patent systems are required to protect innovations of international scope.

It is generally believed that patents should not be granted for mere discovery of that which exists in nature. The leading case in this area, *Diamond vs Chakrabarty* (1980) (ref. 12) where the US supreme court held a strain of human-made, genetically engineered bacteria to be patentable subject matter is still the *locus classicus* as far as patenting of life goes. While holding that the human intervention, amounted to an 'invention' of the bacteria which did not exist in nature the court relied on the legislative history of the law and said that patentable subject matter was meant to encompass 'anything under the sun that is made by man'.

The ethical concerns expressed against genetic research *per se* at that time was a prohibitionist argument that persists to this day. The error with the prohibitionist argument is that it presupposes that all the potential products of biotechnology will carry unacceptable levels of risk. A responsiveness to the potential risk from new technologies is understandable. However a well conceived response to technological change of any kind is one which deals with the potential for risk in a fair and rational manner. Proper risk management enables humanity to reap the benefits of technological change. But the players in the human genome research, being huge multinational corporations (MNCs), which have not in the past shown themselves to be very amenable to any form of control by the nation state system, raise the fear that the rush to make profits may dilute the process of risk management. Further in the absence of any precedent to allow for the common exploitation of the products and technologies of the genome studies, corporate concerns seem to have the floor entirely to themselves. One apparently effective way to control the activities of these corporations as perceived by a number of countries is to put brakes on the patenting of the products of their research.

Even within a well defined legal system there have been discrepancies in the binding nature of various instruments. The fact that certain discoveries are not treated as inventions under the European Patent Convention (EPC)[13], nor the stringent novelty requirements under the EPC has prevented the European patent office from coming out with Examination Guidelines that are conducive to the patenting of such 'discoveries'. Thus as per the patent office guidelines, '... a substance found in nature which must first be isolated from its surroundings and can be properly characterized either by its structure, by the process by which it is obtained or by other parameters, and is "new" in the absolute sense of having had no previous existence, can be patentable *per se* provided the inventor discloses the manner in which to obtain it in a repeatable way[14]'. The patenting of genes and the knowledge based on them in Europe has culminated so far as in March 1995, the European Parliament rejected for ethical reasons the Directive on the legal protection of biotechnological inventions, primarily because under the proposal, patents on isolated human genes and human gene therapy, even germline therapy were in principle allowed[15].

Some of the arguments against patenting have chosen not to draw a distinction between the patenting of human genes and the patenting of human life, contending that the former amounts to the latter. This contention raised in the case of the patent claim for the DNA fragment encoding human H2-relaxin and its precursors[16], was met with the counter that patents covering DNA encoding do not confer on their proprietors any right whatever to individual human beings, no more than do patents directed to other human products such as proteins. It was added that DNA is not 'life' but a chemical substance which carries genetic information, and can be used as an intermediary in the production of proteins which may be useful medically. The statutory basis for an argument that patenting of human genetic material is immoral comes with Article 53(a) of the EPC, which excludes from patenting inventions the publication or exploitation of which would contradict *ordre public* or morality. Since the opposed patent did not offend widely accepted moral standards of behaviour and since there was no clear consensus amongst members of the public that patenting of human genes was immoral, the patent was upheld and arguments under article 53(a) was rejected. While the relaxin case clearly demonstrated the growing difficulties facing the European patent office, and notwithstanding the favourable outcomes for the patentee, problems persist.

The ethical issues against life forms in general often argue on an 'exceptionalism' approach to human genetic material, contending that it has characteristics that make it different from plant and animal genetic material issues for a number of reasons extraneous to the state of technology itself. For example, Switzerland recently introduced its first law regulating biotechnology, including reproductive medicine. The new law prohibits the introduction of non-human genetic material into the human genome[17]. More significantly, the first international convention on Human Rights and Biomedicine, signed by twenty European countries in early April, comprehensively links the dignity and identity of all human beings to the need to prevent abuse of application of biology and medicine[18].

From a scientific point of view it seems even questionable to distinguish genes depending on their source for, 'there is no difference between a yeast gene and a human gene if you observe it in function, if you introduce mutations and make the yeast gene a human gene there is no difference, there is no ethical issue on the human gene that is different from the yeast gene'[19].

All the same there is growing momentum to the idea that human origin is alone a sufficient cause for exclusion from patentability. The concerns reflect a moral and ethical view that borders on the theological and hence the reluctance of the legal system to incorporate such concerns. The picture of the eccentric geneticist going berserk in his lab in the mind of the public does not help either. Any absolutist approach precludes outright assessment of developments on their individual merits. Just because MNCs are the nearest beneficiaries, it will not do for mankind to cheat itself out of the responsible and regulated use of new biotechnologies. Also a prohibition on patenting will force inventors to seek other forms of protection such as trade secrets. And less disclosure can inhibit accountability and development. Obviously less accountability may well result in a greater potential for risk and not less.

Box 1

Intellectual property

It is instructive to look at the contours of intellectual property protection as incorporated into the International Bar Association (IBA), Bioethics subcommittee of the Law and Medicine Committee, DRAFT International Convention on the Human Genome (23 October 1996). Article VI of the Draft Convention, reproduced here is illustrative of the shift in the fundamental premise of intellectual property protection in the context of genetic research.

Article – VI

1. The Human Genome in its natural state is not subject to private, national or transnational ownership by claim of right, patent or otherwise.
2. Intellectual property based on the human genome may be patented or otherwise recognized in accordance with national laws and international treaties.
3. The collection, distribution and use of human genomic materials and associated information shall be undertaken on a basis which reflects an interest of the original source and of the depositor of the material to an equitable share of the economic benefit of commercialization based upon:

a) Use of the material and associated information ;
b) The relative significance and/or unique nature and/or rarity of the genomic characteristics of the material and associated information; and
c) The original source and depositor's relative contribution to the overall creation and commercial development of relevant intellectual property.

Patent law: The emerging contours

The patent law is in a state of flux, and it will take more time for human legal intellect to come to an understanding of what can be done and what cannot which has always been the concern of the law. But certain indications are clear:

- Without patent protection for investments it is going to be difficult to sustain funding in these areas of research. To that extent intellectual property rights have come a long way from providing a reward for intellectual creativity to a form of protection for investments (see Box 1).
- Rather than view patents now as a facilitator for such research, the time may have come to view the law as an essential instrument to regulate and keep such research from going underground.
- The ethical and legal concerns among the public are very real issues that cannot be brushed aside as long as they remain the subject and object of the research. Considering humanity's sake the increasing legal pluralism that is seen needs to be tackled at an international level. However, hesitation by many nations to cooperate fully in view of the moral and ethical implications of such legislation with respect to biotechnology precludes agreements of any substantive depth. While harmonization of patent laws may be inevitable, compromise at the ethical level by individual nations is going to be the major issue.
- At present, opposition to the patenting of human genetic materials is being mounted on two levels. On the first level is the opposition to the patenting

of 'life' which includes microbial, plant, animal and human life. The grounds for these are largely religious or cultural and to that extent constitute a legally pluralistic approach.

- On the second approach, patenting is opposed on the grounds that people from whom genetic material is taken are not likely to receive any financial benefits from it. The opposition arises from past experience in which large corporations have collected genetic material and knowledge from the Third World and from indigenous populations and then used these to develop and patent agricultural and pharmaceutical products without any benefits accruing to the original donors of the material or the knowledge.
- The clear interests of the nation lie in evolving ways and means to apportion the potential commercial and medical benefits to the participating nations, as contributors of genetic material both in the clinical context and in the context of human genome diversity studies.

International scenario: The Indian concerns

Patenting has become an issue in genetic studies in a clinical context. But most of the international flak has been drawn by the patenting of products derived from the genetic material of indigenous people. As of now, as pointed out in the case of *Moore vs Regents* of the University of California[20] a person who takes part in a clincial study may stand to gain nothing from whatever patents that are granted on products derived from their genetic material. In March 1995 the US department of Health and Human services and the NIH staked claim to the human T-cell line of a Papua New Guinean[21]. The patent was granted and maintained after the challenge. The ethical implications of the use of human material samples for clinical research has been the subject of very sophisticated ethical discussions. One of the first principles is the familiar moral precept that the ends do not justify the means. In clinical research, this means that human subjects cannot be seen merely as tools. On the contrary, concerns for the individual subject's welfare and autonomy must take precedence over the interests of science and society[22]. The libertarian individualist concern is manifested in the stress on effective informed consent for participation in clinical research. In cases where the participants are vulnerable groups, like indigenous people where the researcher–subject asymmetry is heightened, the ethical and hence commercial issues get exacerbated. In communal cultures, individual members of a community often do not have the necessary awareness of the implications of participation in an experiment so as to adequately give informed consent. Thus, the vulnerability to abuse of the informed consent procedure has largely rendered it inadequate as an exclusive means of protecting human rights and the welfare of research subjects. Thus in cases of human genetic studies these issues have been raised in a number of international fora by nation-states keen on protecting what they perceive as sovereign rights over their people. These developments make out a clear case for the involvement of national governments in monitoring such studies in their territory. What is required is an accurate assessment of the implication of such studies. Ideally, the vast genetic resource available in India should be used for the benefit of the entire humanity. Indeed, given the potential for benefiting humankind, the balance of the moral argument shifts to asking why human genome studies should not be carried out.

In the case of population genetics and human genome diversity studies, the sources of protest include international NGOs, the world council of churches, and the world council of indigenous people. Among the most vocal critics of the human genome diversity project are environmentalists and groups in developing countries, who are veterans of earlier campaigns to challenge the increasing control over the world's food crops exercised by a relatively small number of large, and mostly western-based agricultural and seed companies. Thus, concerns about the collection of human genetic diversity stems inevitably from similar controversies related to the collection and storage of plant genetic diversity over the past few decades. Patents on these materials will require the payment of royalties which will, in turn, severely limit the access of scientists from poor countries to research carried out by scientists in developed countries. The issue is of primary concern to third world scientists who feel that though their countries may become suppliers of genetic material for research, they may end up having to pay for the products of these research outcomes. In India with her vast scientific manpower there is no reason why such an outcome should be allowed to materialize. The issue is of special concern to the people of India as, given the potential for contributing to the worldwide effort, India is yet to control the access to and use of human genetic data. Possibly the proposed initiative of the Department of Biotechnology to catalyse and support research on the human diversity of India with a view to providing answers to a wide range of questions of biological, medical and anthropological interest[23] will usher in tighter national systems that will not impede ethical research, nor compromise the interests of the people of India.

The common heritage of humanity concept

New international instruments that have been attempted, including the UNESCO Draft and the International Bar Association (IBA) declaration on the human genome

Box 2

The UNESCO Draft declaration on the human genome and its protection in relation to human dignity and human rights:

Article 1 of which states:

The Human Genome is a fundamental component of the common heritage of humanity and needs to be protected in order to safeguard the integrity of the human species, as a value in itself, and the dignity and rights of each of its members.

The IBA DRAFT International Convention on the Human Genome (23 October 1996)

Article 1 of which states:

1. The human genome is part of the common heritage of humankind.
2. Human genome technology shall be developed and used only in full and complete consistency with the common interests of humanity.

have termed the human genome as the 'Common heritage of humanity' (CHH) (see Box 2) which is a well established juristic concept. Certain parts of the earth, sea or outer space and certain properties like the natural and cultural world heritage covered by the UNESCO Convention of 1972 are now considered by international law as to merit protection by the whole of humanity. Thus the CHH concept when applied to the human genome is regarded symbolically as representing the human species and its specific interest to be protected against the dangers created by man himself. But the use of the term is problematic. The same was used in the 1982 law of the sea convention to designate the deep seabed resources. Subsequently the 1994 agreement of the law of the sea makes a mockery of the term in relation to which nations enjoy the most of the resources. Also in the past the CHH argument has been used by the dominant countries for economic exploitation of plant genetic resources. International treaties, regarding natural resources, such as those covering seabed, outer space and Antarctica prohibit the assertion of national territorial claims. Any such 'common ownership' approach, however is objected to by both developing and developed countries because of the current possibility of asserting intellectual property rights over genetic material[24]. Some others have taken the view that the use of the concept would preclude patentability of human genes which at least in the case of the UNESCO declaration is admittedly not the intention[25]. Thus the issue of how to functionalize the concept of CHH in terms of ownership and possession rights remains open.

Institutionalizing protection: The machinery

It would appear best in the interests of the people of India that the government exercise sovereign rights over human genetic material (which to date extends only to plant and animal genetic material under the convention on biological diversity)[26] to the extent that an authority to prevent 'piracy' of genetic material can be identified. Indeed, illegal or unauthorized transfer of DNA from ethnic groups and patients have been reported in the Indian press[27]. With regard to the fact that human genetic research may well be bringing in the new 'genodollars' to the economy, the government would be well advised to identify institutions that can deal with a process of monitoring and study of the material appropriated. As suggested by a team of concerned Indian scientists, rather than simply export DNA or cell lines, a more fruitful line would be to set up modern facilities in the host country and allow exchange of DNA with other countries for standardization of techniques and comparison. Indeed the large scientific community, including geneticists, competent medical practitioners and a network of hospitals and health centres make this a workable proposition in India[28]. It has been further suggested that source material could be managed at central laboratories, and if desired made available to international collaborators with due 'protection' including intellectual property rights.

Any attempt to harmonize patent laws in India will have to be inclusive of giving an appropriate status to the original contributors of the material, which is without precedent in the law of patenting and to that extent is going to be difficult to incorporate[29]. This nonetheless has to be seen in light of what harmonization of patent laws are going to cost us in terms of the price of drugs. Thanks to this, low drug prices, the mainstay of our 'health for all' programme may soon be a thing of the past. If the particular community or the people cannot be identified, the commercial cut will have to be handed over to the government so that at least that particular therapeutic process or product can be made available at affordable price levels. There is need also to explore the possibility of allowing the indigenous group themselves to enter into well informed contracts with corporations for returns to the community not necessarily in the form of royalties or cash payments itself. This kind of a practice finds precedent in various incidents all over the world and legal backing from various soft law agreements internationally[30].

Further it would be a mistake to leave the whole issue of the developments in biotechnology to the judiciary to deal within its inimitable case by case approach. We stand to lose a lot without a clearly laid out policy. For this there is need to generate public debate at all levels. An interdisciplinary study group at the national level may be in the best position to study the developments in

various jurisprudential systems and will come out with a legislative proposal at the earliest. Though the perspectives are many and the chances of today's law getting outdated by the morrow are very high, there arise certain clearly identifiable factors that will have to be an essential part of any proposed legislative policy on the subject.

The specifics

- It has been presented that the human body (and its component parts) cannot be regarded as an asset, it cannot be marketed, and hence cannot be a source of financial gain[31]. This is also discussed in the Draft European Convention on Bioethics, Article 11, which states 'The human body and its parts shall not, as such, give rise to financial gain.' There is a crying need to come out with a broad policy statement that the human body *per se* cannot become the subject of direct financial gain. In a third world country where life already seems devalued by poverty such a statement is of the essence.
- International law allows for the identification of ownership of sovereign rights over human genetic material with the government. To functionalize this in as categorical manner as possible, an amendment to the Constitution may be neither misplaced nor mistimed.
- A positive step now is in national interest (notwithstanding the 10-year transitional period allowed by GATT) for rather than view changes in a patent law as creating an opening it should be viewed as a means to regulate the flow of human genetic material from India.
- There is need to redefine our penal laws to make the unacknowledged use of genetic material a crime beyond that of the mere ethical or moral stance.
- The exercise of any such ownership rights will have to be restrained by tenets of the public trusts doctrine. Thus the management of the 'resource' will have to be according to and within the parameters of the interests of the beneficiaries. Identification of the beneficiaries among other ways can be done by demand of detailed patent specification which is both a scientific as well as a legal document.
- The entire exercise should proceed with the full participation to the extent possible of the communities or patients contributing the material. Such 'participation' will have to be at all levels, at the planning, collection, research and commercialization stages, with scrupulous adherence to ethical behaviour and tenets of medical ethics at all times. To make such participation and informed consent truly effective, there is need to disseminate correct information as widely as possible.
- It is necessary to recognize that understanding the human genome is likely to identify some populations which will be susceptible/resistant to certain genetic and environmentally acquired diseases. Therefore, decisive measures need to be taken to prevent any discrimination, legal, social, economic or otherwise.
- The tendency to approach individuals of a particular community or patients in promise of financial gain, is to be discouraged. The gain in terms of intellectual property rights and financial profit should be channelized wherever possible through a network of medical and research centres.
- An institutional mechanism under the appropriate Department will have to be set up much on the lines of the notification of 25 January 1992 (ref. 32) wherein a nodal point for clearance of the transfer of any biological products or materials abroad was sought to be established. Such large-scale monitoring is possible only if the scientific and medical community of this country are taken into confidence and made to feel a part of the entire exercise of protecting national interests.
- To safeguard national interests, it is necessary that all genetic research involving international collaboration be undertaken after formal clearance of the national government. Such 'clearance', would include the right to monitor, and if necessary, proscribe certain types of usage/transfer of genetic material. Automatically private initiative will have to come under the scrutiny of a knowledgeable scientific body.
- In collaborative research, intellectual property rights are to be protected with a majority share of the patent, if any, being held by the collaborating Indian sites and 20% of the benefits[28] accruing from such a patent being used by the individual institutions to develop better services for the population that provided the genetic material.
- In circumstances where the above is not possible, formulation of other comprehensive methods of compensating communities or individuals for their voluntary contributions and cooperation in the research is essential. A 'people of India Fund' at various regional levels may be a possibility. For this the existing network of growing financial institutions may provide an adequate infrastructure at no additional cost. The compensation may take the form of local development work of whatever kind the community opts for.
- In the long term there is a need to catalyse a public debate on the ethical parameter of predictive and preventive genetic medicine issues like confidentiality, informed consent, right to know, and the right to refuse to know. For this pluridisciplinary bioethics committees in our centres of research as well as

our hospitals functioning under broad legislative guidelines are essential.

The problems are many and the solutions are difficult to come by. But as it is said, the only way to win the game is to play it, as per the rules. The only functional option available given the urgency of the matter is to act now in a decisive manner. Anything less would be disastrous for the people of India.

References and notes

1. Bronowski, J., *The Ascent of Man*, BBC, London 1973, p. 429.
2. Sivaramjani, T. R., Human Genetic Engineering: The John More story, *1 Law and Medicine*, 1996, pp. 96–101.
3. Starting with about $100 million in 1993, by 1996, drug companies had invested more than $1 billion in 'genomics' biotechnology. Thus 'dazzled by the commercial possibilities, venture capitalists, the big drug companies, and Wall Street are all swooning over genomics, pouring millions of dollars into start-ups, the impact of which is being felt from Boston to Beijing' Cohen, J., *Science*, 1997, **275**, 767–775.
4. Brahmachari, S. K., 26th biennial conference, Paper presented at the International Bar Association, Human Genome Treaty Symposium (medicine and the law BP179) October 21 1996, Berlin.
5. Paris Convention for the protection of industrial property (1883); amended latest in 1967. The convention is applicable to industrial property including not only inventions, trademarks, service marks and industrial designs but also utility models, tradenames, indications of source, appellations of origins and repression of unfair competition.
6. In India the question of ratification of the Paris Convention came up for consideration by the Union Cabinet several times – the last occasion being in the early 1980s and each time the Cabinet rejected the proposal for ratification, Dubey, M., *Unequal treaty*, New Age International, New Delhi, 1996.
7. The TRIPS Agreement basically universalizes the levels of intellectual Property Rights protection now prevalent in the developed countries. And the protection of IPRs provided in the agreement will be enforced through the common Dispute Settlement Mechanism of WTO, which provides for retaliation and cross-retaliation.
8. Specifically from the draft Code of Conduct on the transfer of technology negotiated in UNCTAD and the draft Code of Conduct for TNCs negotiated in the UN both of which were designed to require TNCs to transfer technology to developing countries and to function in conformity with the public interest and national development objectives and priorities of the host country.
9. Cohen, J., *Science*, 1997, **275**, 767–775.
10. Strauss, J., Patenting human genes in Europe-Past developments and prospects for the future, 1995, IIC **26** no: 6, pp. 920–950.
11. Craig Venter and colleagues at the National Institute of Health developed a technique for the rapid sequencing of cDNA, which made it possible to detect in a few months thousands of previously unknown genes and to obtain partial sequences. Although the approach to gene identification using cDNA is not new, newly developed instrumentation, powerful computers and advanced robotics have enabled NIH scientists to sequence large segments of expressed genes rapidly. Healy, B., *New Engl. J. Med.*, 1992, **327**, 664–668.
12. 447 U.S 303.
13. European Patent Convention (1977) The grant of an European patent does not result in the existence of a single unitary patent covering the whole of the territories of the designated countries, but rather leads to a bundle of national patents, each being governed by the same provision as a national patent granted directly in the countries concerned.
14. *supra n* 11.
15. The European Union Directive started in 1988 with the clear aim to introduce throughout the member states patent protection standards comparable to those applied in the USA and in Japan. The proposed directive made it clear that the human origin (of genes, proteins and cells, isolated from the body) alone was not sufficient ground for exclusion. The final Draft failed over the issue of ethics and morals linked to the patenting of human genes and human germline therapy. Strauss, J., *supra n* 11.
16. On 18 January 1995, the opposition division of the European Patent Office rejected the opposition filed by the Green Party in the European Parliament and upheld patent no: 11.2149 relating to human H2–relaxin.
17. Campbell, J. J., *Effects of International Trends and Agreements on Biotechnology Patenting*, 10 Canadian Intellectual Property Review, 1993, pp. 129–143. France amended Article 7 of its intellectual property code and declared as unpatentable the human body, its parts and products and the knowledge of the entire or partial structure of the human gene, as such,... as inventions, the publication or exploitation of which would be contrary to *ordre public* or morality.
18. The convention on human rights and biomedicine, among other things, deals with issues of consent, private life and right to information, intervention in the human genome (allows only somatic cell intervention for preventive, diagnostic or therapeutic purposes), ethics of scientific research, organ and tissue removed from living donors for transplantation purposes and prohibition of financial gain from the disposal of a part of the human body. The Convention was signed on 6 April 1997. (TOI p. 9).
19. Dr Bayreuther *supra n* 11, p. 927.
20. John Moore's doctors discovered that his spleen contained blood cells that produced an unusual blood protein that might be used to develop an anti-cancer agent. The cell line (designed the MO cell line) was made the subject of a patent application, granted in 1984. John Moore filed a law suit claiming that his cells were misappropriated and that he was entitled to profits derived from the commercial use of these cells. The potential value of the products derived from the MO cell line could reach several billion dollars, but the California Supreme court ruled in 1990 that Moore has rights to none of it.

    Although Moore had the right to sue his doctors for failing to inform him of the potential commercial value of his cell line, he did not have rights of ownership over his cells after they had been removed from his body.
21. According to the patent application, blood samples were taken from 24 people of the Hagahai. The cell line, the first of its kind from an individual from Papua New Guinea, is potentially useful in treating or diagnosing individuals infected with an HTLV-1 variant virus. Human T-lymphotropic virus type I(HTLV-1) is associated with adult leukemia and with a chronic degenerative neurologic disease. The novel cell line is of potential value in understanding the enhancement or suppression of an immune response to this virus.
22. All enlightened codes and regulations beginning with Nuremberg code and including the Helsinki Declarations and the US federal regulations, appeal to and buttress this principle. see Annas, G. J. and Grodin, M. A., *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation*, Oxford University Press, 1992. According to US Government regulations for research conducted by government agencies, the 'legally effective informed consent of the subject or the subjects' legally authorized representative' if the subject is the donor of a blood sample is a legal requirement.

23. *The Hindu*, January 1 1997.
24. see Walden, I., *Intellectual Property Rights and Biodiversity Conservation* (ed. Swanson, T.), Cambridge University Press, 1995.
25. Lenoir, N., Proceedings of 1995 MURS Japan/UNESCO IBC seminars pp. 12–22, The Eubios Ethics Institute, 1996.
26. The objectives of the Convention are stated broadly and include the conservation, biological diversity, sustainable use of its components and the equitable sharing of benefits which arise out of the utilization of genetic resources. This is to be accomplished by access to genetic resources and technology transfer, taking into account all rights over these resources and technologies. The Biodiversity Treaty will become binding on signatories when 50 states have ratified it.
27. *The Economic Times*, Bangalore, 12 February 1996.
28. Chatterji, S., Jain, S., Brahmachari, S. K, Majumdar. P. P. and Reich, T., *Nature Genetics*, 1997, **15**, 124.
29. There are a number of soft law instruments that may be helpful in working out such a space for a compensatory mechanism within the formal TRIPS arrangement itself, apart from inclusion in specific agreements for scientific collaboration. The UNESCO statement of 1996 is very pertinent in this regard. 'The great ethnic diversity and large population of India has provided and will continue to contribute to the knowledge about genomic diversity of the human species. The Indian scientists and those visiting from many nations support the concept that the developing nations and the specific ethnic groups should receive their appropriate share of the economic and commercial returns derived from medical investigations (clinical trials and genetic epidemiological studies) in and from the biological material derived from their population groups.'
30. Posey and Dutfield, *Beyond Intellectual Property: Towards Traditional Resource Rights for Indigenous Peoples and Local Communities*, International Development Research Centre, Ottawa, 1996.
31. Working group paper on population genetics, International Bioethics Committee of UNESCO, 3rd session, Sept. 1995.
32. The Ministry of Health and Family Welfare, Government of India notification dated 25 January 1992 provides general guidelines for the transfer of biological materials outside India of biological products abroad for investigations that can be carried out in India. It has been decided that all proposals for sending such products abroad should be sent to the Director General, Indian Council of Medical Research, New Delhi, who will be the nodal point to clear all such proposals.

ACKNOWLEDGEMENTS. T.R.S. thanks Prof. Madhav Gadgil, Centre for Ecological Sciences, Indian Institute of Science for project placement; Dr Joseph Strauss, Chairman, Intellectual Property Rights Committee, HUGO, Max Planck Institute for Intellectual Property Rights, Munich for sending much of the reference material used in this article; Prof. Madhava Menon, Director, National Law School of India University, Bangalore for his kind encouragement; and Ms Nagarathnam, Biodiversity Unit, Jawaharlal Nehru Institute for Advanced Scientific Research, for her help in accessing the relevant documents. S.K.B. is grateful to Dr P. P. Majumdar for critical comments and suggestions on the IBA draft document, and also thanks Drs G. Padmanabhan, Manju Sharma, R. A. Mashelkar, K. S. Singh, G. V. Satyavati and late B. K. Bachhawat for various suggestions, information and help in formulating some of the documents and ideas which have formed the basis of this paper.