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INTERNATIONAL WORKSHOP ON HUMAN GENOME PROJECT: LEGAL ASPECTS

BILBAO, BASQUE COUNTRY, SPAIN 24-26 MAY 1993

REFLECTIONS ON THE CONFERENCE

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Justice Michael Kirby

Australia

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Conference in Bilbao May 1993

Between 24-26 May 1993 a conference convened in Bilbao, Spain, concerned with the legal aspects of the Human Genome Project. The conference was organised by the BBV Foundation, a research institute established by one of Spain's largest banks. The chairman of the conference was Professor Santiago Grisolia, a distinguished Spanish biologist. He is chairman of the UNESCO Committee for the Human Genome Project. Four Nobel Laureates in relevant fields of science and medicine took part in the conference: Dr Carleton Gajdusek (Medicine, 1976); Dr Hamilton O Smith (Medicine, 1978); Dr Jean Dausset (Medicine, 1990); and Sir Aaron Klug (Chemistry, 1982). Dr Gajdusek's Nobel Prize was awarded for the study of the central nervous system diseases transmitted by lentiviruses. He was co-discoverer of Kuru's disease in New Guinea, a viral condition transmitted following cannibalism. Sir Aaron Klug is Director of the Medical Research Council Laboratory on Molecular Biology at Cambridge

University, England.

The conference in Bilbao was held at the University of Deusto in the presence of a mixed audience of scientists, administrators and lawyers. Leading papers were delivered by judges of the Constitutional Court of Spain and of the High Court of the Basque Country as well as by judges and legal academics from countries of Europe and North America. One of the most important papers was presented by Mme Noëlle Lenoir, an expert in the field, who is the only woman member of the Constitutional Council of France. Mme Lenoir was the chief architect of important new legislation adopted recently in France concerning the regulation of alteration of human genes. The legislation places limitations upon gene therapy and patenting. Amongst lawyers from common law countries attending the conference were Justice Jean-Louis Baudouin of the Court of Appeal of Québec and the writer.

The Bilbao Conference convened just forty years after the publication in *Nature* (23 April 1953) of the thesis of James Watson and Francis Crick concerning the existence of a basic life form described as the DNA (deoxyribonucleic acid) "double helix". Watson and Crick postulated that the three dimensional shapes of biological molecules could be governed by information embedded in linear one-dimensional codes. Their work gave rise to the most important development in life sciences to occur this century. Biologists interested in the mechanisms of hereditary quickly realised that genetics was to be considered henceforth in terms of large information-carrying molecules in the human cell. It is now known that almost all human cells contain genetic information about a person's entire being. Each carries an identical set of the body's estimated 100,000 genes. Egg and sperm cells ("germ cells") are exceptions, carrying only the genes that the mother and father will

contribute to their child when egg and sperm unite. DNA is the basic bearer of genetic information in the human body. If unravelled, the DNA contained in each tiny cell would stretch about a metre in length.

Most lawyers can get by with minimal acquaintance, or no acquaintance at all, with the remarkable science of molecular biology. However, it is now increasingly apparent that the events which have followed Watson and Crick's discovery have extremely large implications for the legal system and for ethical choices open to societies governed by the rule of law. Recently, the International Commission of Jurists in Geneva adopted as a major new thrust of concerns for the future of universal human rights, a study of the implications for human rights of biotechnology and gene therapy. The BBV Foundation conference in Bilbao was therefore an extremely timely one.

The conference followed two earlier meetings organised by the Foundation in 1988 and 1990, both in Valencia, Spain. These meetings dealt successively with the scientific and ethical implications of the human genome project. The 1990 meeting produced the *Valencia Declaration on the Human Genome Project* published by the Foundation. See Fundacion BBV, *Human Genome Project: Ethics*, 1990, Madrid. James Watson himself contributed to the 1990 meeting. His paper (*ibid*, 27) declared:

*"[G]enetic injustice arise through throws of the genetic dice that operate when our sperm and egg are formed. This genetic variability between humans reflects the fact that the gene distribution process is not perfect and the new genetic mutations are constantly arising. There is no way to stop this process. Moreover, this variation has been the basis of our evolution. Without the differential survival of more fit variants, we as human beings would not have our highly empowered brains that have led us to develop the languages, both written and spoken, that underlie the creation of our various civilisations. The question now faces us ... as to how we are going to deal with these differences between*

*individuals. In the past, at the time of the eugenics movement ... and during the reign of racist thoughts in Nazi Germany, there was very little genetic knowledge. Most decisions were made without solid genetic evidence. ... Now we have to face the fact that we soon will have real facts and how are we going to respond to them?"*

Since those words were written extremely important advances have occurred in identifying (by the marriage of biology and information technology) those features of human and animal DNA which cause particular diseases. Thus the cause of Huntington's chorea has been tracked down. Recently, scientists in several countries have claimed identification of the cause of the trigger for breast cancer. A report in May 1993 of research in Finland and the United States claimed to have identified a gene which serves as a marker (or warning sign) of the presence in the subject of cancer of the colon. It was asserted that early detection of the presence of this gene could promote treatment which might spare most of the subjects from death from colon cancer. Thus, a great deal of research is now being devoted to identifying the genes responsible for numerous other human and animal conditions. For example, a major target of investigation is the cause of Alzheimer's disease in humans.

#### The state of the scientific art

The genetic industry is a multi-million dollar enterprise with most present work proceeding in the United States of America. Until now, much experimentation has concentrated on animals. Pigs have been genetically designed to contain certain human growth genes in the hope of creating "super pigs" which would yield more meat. Carp, catfish and trout have also been modified with genes from humans, as have cattle and rats to increase their growth and reproduction. Chicken have recently been engineered in an attempt to delete the genetic trait causing brooding. By eliminating a mothering instinct it is hoped to make chicken more efficient "egg producers". One

prominent scientists was reported as suggesting that it would soon be possible to produce a "five tonne cow and pig 4 metres long and 1½ metres tall". The implications of such developments for the environment and for biological pollution are beginning to concern administrators and lawyers who generally prefer not to think about such complicated and unfamiliar problems.

In Canada and the United States, scientists believe that they will shortly be able to clone unlimited supplies of the "perfect" lamb, pig or cow. These developments may readily be regulated by laws on animal husbandry. But their long-term implications for the human species are obvious. If it is possible to manipulate (and use) human genes in animal production, the same will obviously be possible in respect of the human species. More likely than the creation of human giants or servant drones will be the elimination of perceived "defects" in genetic composition and the production of "designer human beings" conforming to a pre-conceived notion of desirable human height, weight, IQ, skin pigmentation, aggression/shyness mix and other genetic traits.

The problems presented by this prospect to the law is not entirely novel. The eugenic movement was extremely powerful earlier in the century, particularly in English-speaking countries and in Germany. That great jurist Oliver Wendall Holmes Jr added his authority to the movement in the majority judgment which he wrote in *Buck v Bell* 274 US 200 (1927). The decision upheld the constitutionality of a State statute which imposed compulsory eugenical sterilisation on a woman with intellectual disabilities. It was in this case that Holmes used the strong clear language of eugenics:

*"Three generations of imbeciles are enough."*

see (*ibid*, 207). The judgment of the Supreme Court lent strong authority to the eugenic movement. It resulted in the unconsensual sterilisation of thousands of Americans. See Mary L Dudziak, "Oliver Wendall Holmes as a Eugenic Reformer: Rhetoric in the Writing of Constitutional Law", 71 *Iowa L Rev* 833 (1986).

Following the explosion of world-wide research on human genes, an idea was proposed independently in a number of countries of North America and Europe that an international project should be established, known as the Human Genome Project. Its object would be to pool developments concerning techniques and advances in molecular biology and genetics and to monitor the discoveries of the connection between particular genes and identified disabilities. A Human Genome Organisation (HUGO), a non-governmental body, has been established to collect data in compatible genomic data bases and networks designed to make available world-wide information concerning the state of research and discovery. This international movement has coincided with attempts, particularly in the United States of America, to obtain intellectual property law protection for discoveries and even potential discoveries of sequences of DNA thought to be related to particular human disabilities. If a first step towards the diagnosis and possible cure of disabilities is the identification of the DNA sequence involved, and if billions of dollars of medical and scientific research turn upon the identification of such genes, it is obviously of great economic potential to "own" even for a time, the exclusive right to exploit the significance of the relevant DNA sequence.

This development in patenting of human genes and DNA sequences caused probably the major area of disputation at the Bilbao meeting. Many scientific and legal commentators from Europe expressed dismay and disagreement with the developments of the law in the United

states permitting the patenting of human genes and DNA sequences for possible future use by biotech companies in decoding the messages and patenting the products which may follow. In France, the law prepared by Mme Lenoir proposes that human genes may not be patented. Some United States commentators at the conference criticised the development of United States law. For example, Professor Neil Holtzman, Professor of Paediatrics at Johns Hopkins University contrasted the growing commercialisation of University objectives in recent times in the United States with the earlier dedication of American universities to research of value to the human family. On the other hand, several European commentators urged that it was necessary for Europe to face the realities presented by the United States developments of patent law. If the United States were the only country to be patenting genetic material deriving from Human Genome research, it could patent developments occurring in Europe. This would rob European researchers and biotech companies of effective legal protection. The course having been embarked upon, European legislation could not hold back.

#### A variety of legal problems

The sessions of the Bilbao conference addressed a remarkable collection of legal problems which so far seem to have attracted little public debate in Australia. In the opening session the ground was laid by Mr José A Sanchez Asiain, President of the BBV Foundation, who insisted that it would be essential to adapt the law to the new conditions for the human species presented by genomic research. He expressed the hope that the earlier consideration of the ethical issues presented by the Human Genome Project would provide a useful basis for the development of legal principles apt for a matter of global concern.

The Head of the Basque Government (José A Pradera), a



politician, invoked the words of Goethe:

*"The more you know, the more you have doubts."*

Professor Grisolia explained the objective of the Human Genome Project to develop a map of all of the genes of the human being. This was, in a sense, an adventure similar to that of the discovery of the New World by earlier Spanish explorers. But it had a potential for the relief of suffering and its positive aspects should never be overlooked. One in eight women living today in Western countries would suffer from breast cancer. The early detection of the gene which is associated with that condition would provide science and medicine with opportunities of prompt and life-saving intervention.

Professor José Villar Palasi of Madrid spoke on the legal implications, specifically from the point of view of EC laws. He explained the early consideration which had been given to the Human Genome Project in the European Parliament and Commission. The historical background to the project and to the creation of HUGO was described by Mr Robert Cook-Deegan of the National Academy of Sciences in the United States. He was followed by Mme Lenoir. She pointed out that the European Council of Ministers in 1989, whilst sanctioning research on the Human Genome Project, prohibited germ line therapy, ie the inclusion of genetic manipulation of future generations as distinct from treating a living patient. Mme Lenoir explained, and defended against criticisms of paternalism, the proposed French law designed to control genomic experimentation.

The foregoing background material was followed by a round table in which the Nobel Laureates Gajdusek and Smith took a leading part. In this session, Dr Charles Cantor, Director of the Centre for Advanced Research in Biotechnology in Boston, United States of

America, asserted that within the next ten to fifteen years scientists would identify the causes of most human diseases. This would present significant questions about the future preservation of human diversity. Some of the questions would have to be reflected in social and legal decisions. Dr Cantor emphasised that it was only by the marriage of information technology and biotechnology that the mapping of the human genome was possible. Until miniaturisation, it would simply not have been physically possible to store a mass of data about the variety of genes that is now feasible.

Dr Craig Venter of the Institute of Genomic Research in the United States put forward the most eloquent case for increasing the speed of research and providing just legal protection to scientists and companies to encourage and promote expenditure of the huge sums necessary to underpin the genomic activities. He painted a most optimistic picture of the medically beneficial outcome of the research of his Institute. Some European participants, however, were critical of the reported applications for intellectual property protection in what they asserted was the "common property of mankind".

It was after this general background, with several other explanations of the current state of scientific research, that the conference turned to an examination of the legal issues

#### Legal genomic issues

The introduction to the legal issues was given by Dr Frits Hondius, long-time senior official of the Council of Europe and pioneer of many European conventions on human rights topics. Dr Hondius pointed out that upon many of the problems presented by genomic research the law was presently silent. In a sense, this silence was a negation of the rule of law. It was desirable, if not essential, for organised democracies to face up to the legal problems

and to present solutions. A similar theme was struck by the writer in his intervention during the conference. The techniques of the Australian Law Reform Commission in its early work on *Human Tissue Transplants* (ALRC 7, 1976) were described as one model for addressing the legal issues now presented by gene research and therapy.

Professor Gregario Peces Barba of Madrid spoke from the perspective of the philosophy of law. He said that lawyers, politicians and indeed society had a fear of facing up to the unknown. He urged that HUGO should be linked into developments of international law, particularly with respect to human freedoms and the defence of the free consent of individuals.

Important contributions were made to the perspective of religious views about related topics such as abortion, gender selection, sexual orientation and experimentation. Professor Robert Nelson of the Institute of Religion in Houston explained the current thinking of major Christian churches. Mr Mark Frankel, Director of the American Association for the Advancement of Science said that there was a basic tension between fast moving genetics and conservative law which tended to seek stability and to preserve the status quo.

After this broad view of the basic legal and institutional issues presented by genomic research, the conference turned to a number of very specific topics of legal importance.

#### Specific legal problems

These topics included:

- \* The right to confidentiality in the use of genetic information;
- \* Genetic legacy and the culpability for criminal offences;
- \* Patents, intellectual property and the human genome;

- \* Insurance law and genetic developments;
- \* The imposition of legal limits on genetic experimentation;
- \* The identification by genetic testing and the legal aspects thereof; and
- \* Implications of genetic knowledge in labour relations.

It is beyond the purpose of this note to examine each of these sessions. In each of them, the organisers maintained a careful balance between scientists and lawyers. Understandably, a large contribution was made by speakers from Spain and Europe. But many scientists and lawyers from North America contributed, because that is where, at the moment, a great deal of the action in human genomic research is taking place and legal reflection occurring.

On the right to confidentiality, Ms Paula Kokkonen of Finland pointed to the paradox of detailed human gene mapping at the very time of heightened demands for respect for privacy. The reconciliation of greater knowledge about the individual with demands for respect of that individual's control over such information would require legal attention. This point was taken up by Mr José Elizalde, Adviser for Legal Affairs of the European Commission in Brussels. Professor Fernando Falla of Madrid likened the problems presented by human genomic research to the earlier challenge of nuclear fission. He said that humanity should learn from the earlier mistakes made in *Buck v Bell* and in Nazi Germany. An ethical and legal stamp must be put upon the use and consequences of genomic research. Science, he implied, was too important to be left exclusively to scientists.

Professor Harold Edgar of Columbia Law School, New York, presented many of the problems that would follow from the intensive knowledge which human genomic research would provide to individuals. Would it become an obligation (moral or legal) to tell a future

spouse of genomic "defects" from which the subject suffered and which might be passed onto progeny? The risk of genetic discrimination was raised by Mr Michael Yesley of Los Alamos. Several speakers pointed out that many individuals may not wish to know their own genetic information, still less to have it known by others without very strong reason, individual consent or express authority of law.

The session on culpability explored the old problem of free will. If it were shown that, even to some extent, violence were the product of genetic inheritance, would it still be just for the legal system to hold the subject personally criminally responsible? This discussion was led by Professors Otto Triffterer of Salzburg and José Braun of Madrid. The latter suggested that the courts would not wish to change the fundamental assumption of individual responsibility for behaviour in a particular case. But what use might be made of the genetic predisposition which genomic research would present? It was in this session that an important intervention was offered by Judge Amnon Carmi of Israel. Responsibility in law, he pointed out, was an arbitrary concept imposed by the human needs of any organised society. Because individuals are afforded freedom of choice they were obliged to shoulder the burden of responsibility when they chose to harm their neighbours. The general consensus of this session was that human genomic research would not have a great impact upon the theory of individual responsibility for criminal action at least in the foreseeable future.

The session on patents and intellectual property law was extremely lively, being chaired by Dr Craig Venter who surveyed the debate in the United States. He pointed out that over 35,000 relevant applications for patents of biological material had already been lodged in the United States compared with about 13,000 in Europe. Mr John Collins, an experienced patent lawyer from Kansas

explained developments in United States and European patent law. He suggested the need to study advances in Australian intellectual property law which, he said, provided a possible model to other countries. Several speakers stressed their view that intellectual property law had not kept pace with the nature of the problems being presented. What was needed was a new concept which afforded a measure of protection but for a shorter period and under different conditions more apt for beneficial human genomic breakthrough.

The mood of many participants at this point was reflected by Mr Salvador Bergel, Director of the Inter-Disciplinary Centre, Buenos Aires, Argentina. He pointed out that Watson had refused to patent his major discovery. He had said that it should be available for all humanity. Mr Bergel regarded the way in which market laws were overriding the basic needs of humanity as completely immoral. The species and its genes did not belong to American corporations, he declared. This point was also taken up by Professor Holtzman. He deplored the commercialisation of university research. He regarded it as very short-sighted and, in part, a result of current pressure upon the economy of the United States. These themes were reflected in the audience. Several members described the patenting of the products of human genomic research as a new form of legal "neo-colonialism". It would probably result in gross delays in the spread of knowledge relevant to medicine and the curing of disease for the benefit of people in developing countries. One of the Nobel Laureates, Professor Dausset lent his support to his expression of concern.

The session on insurance was led by Professor Alexander Capron of the University of Southern California in the United States. He spoke to the important new report *Genetic Information and Health Insurance* produced by a task force of the United States National Institute of Health. It reached the view that it was inappropriate

to place limits on the use of genomic information. However, a moratorium was needed on such use until lawyers could differentiate between use which would be regarded as legitimate and lawful and that use which would be illegal because unacceptable. Some of the debates in this session reflected earlier discussion in the context of HIV status and insurance. This point was made by Ms Bronwer Loder of the EC Commission. Insurance being about actuarial risk, the facility of precise identification of risk would afford insurers, unless checked, much more scientific data upon which to judge the acceptance of insurance and the fixing of premiums to spread risks amongst insureds.

The session on the legal limits on genetic information was extremely interesting. The lead paper was given by Justice J-L Baudouin of Quebec, Canada. He explored the rôle of the law in setting the limits for genetic experimentation following the shock of the Nazi abuses. He also outlined the different methods available to achieve regulation both in national and international law. He presented three levels of regulation, viz criminal law (which might be apt to prohibit, for example, cross-fertilisation of humans and animals and possibly human cloning); internal controls of research institutes; and individual self-regulation and peer review. A recent text by Australian lawyer Paul M McNeill, *The Ethics and Politics of Human Experimentation*, Cambridge Uni Press, 1993 examines, analyses and criticises the various forms of institutional and individual self-regulation. The book explains the distinct limits upon the effectiveness of enthusiastic scientists controlling the experiments of their colleagues. The need for the introduction of a healthy component of community superintendence is stressed by McNeill. That was also a recurring theme in the session on genetic engineering in Bilbao.

On the last day of the conference very particular topics were examined including identification evidence and the use of genetic information by employers in circumstances of labour relations. In the former debate an important contribution was made by Judge Luis Martinez-Calcerrada of the Supreme Court of Spain.

#### Closing ceremony and Declaration

As befitted a conference in the historic city of Bilbao, participants were entertained to musical and ceremonial occasions and culinary delights. On the last evening, a ceremony took place in the Town Hall of Bilbao. The four Nobel Laureates were honoured as a symbol of the tribute which the community, and all participants, paid to the advances of human understanding and the basic makeup of the human body which molecular biology makes possible.

The closing ceremony heard important reflections by the Nobel Laureates, Sir Aaron Klug and Professor Jean Dausset. Each of them expressed optimism about the utility for the species of the cartography of human genes. But each also expressed anxiety about manipulation of the human germinal cells and the view that such experimentation should not take place at all in the current state of scientific knowledge. Such caution on the part of distinguished scientists was all that was required to make most of the lawyers present (particularly those from Europe), often conservative by instinct, determined to ensure that the law should respond effectively to the challenges identified in the conference.

Closing speeches were offered by Judge Rafael de Mendizabal Allende of the Constitutional Court of Spain and Judge Juan Bautista Pardo Garcia of the High Court of the Basque Country. Each emphasised the need for an effective legal response which would be in harmony with the important and beneficial developments in the protection of human rights seen in Spain, in Europe and indeed in the



world generally. Judge Pardo Garcia urged "We should be cautious of the elimination of all difference. We should be fearful of the 'monsters of perfection'. Let us leave man stepping forward, with all his imperfections, striving through truth to beauty". He said that this was an area fertile for dialogue. It behoved lawyers to call for social dialogue since society is the ultimate source of law and since this subject will undoubtedly require legal regulation.

The conference accepted the *Declaration of Bilbao* as proposed by Professor Grisolia. That Declaration is an annex to this report. It contains some of the key ideas considered at the Bilbao conference. Naturally enough, in such a novel and experimental area with so many controversial ethical and legal problems exact consensus could not be secured upon all topics opened for examination. That the topic of the Human Genome Project is of the greatest importance for the future of humanity and carries with it important implications for international and nation legal régimes is beyond doubt. The Bilbao meeting, and the succession of conferences organised by the BBV Foundation, represent an important and novel contribution to enliven ethicists and lawyers to a critically important and little-known development in human genomic research that will certainly shape a large number of legal problems in the 21st century and beyond.

Perhaps, from the perspective of history, the most important scientific breakthrough of this century may be seen in time to be neither nuclear fission, nor interplanetary flight nor even informatics but the fundamental and basal mollecular biology which permits the human species to look into itself and find, at last, the basic building blocks of human and other life. Who knows where this discovery will lead the imaginative human mind? Lawyers and indeed citizens everywhere should begin thinking about the issue. In its resolution may lie the very future of our species.