Opinion on a preliminary draft law incorporating transposition into the Code of intellectual property, of a European Parliament and Council Directive 98/44/CE, dated July 6, 1998, on the legal protection of biotechnological inventions.

N°64 - June 8, 2000

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The request dated February 11, 2000, from the Secretary of State for Industry, bears essentially on problems concerning limitations to patentability, as set out by articles 5 and 6 of the Directive.

The matter is presently regulated by article 611-17 of the Code of intellectual property, which had been modified in 1994 when the "bioethics" laws as they were called, were adopted with the express purpose of excluding from patentability anything related to the human body. It reads "the human body, its elements, and its products, as well as knowledge of the total or partial structure of a human gene, cannot as such be the subject of a patent". On this specific point, the draft law proposes to replace this text by the following clauses.

Article 611-10-1 "The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.

An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element".

A complement to Article 611-15 reads "When the invention bears on a sequence or partial sequence of a gene, the industrial application must be disclosed in the patent application, in particular as regards the precise function which the sequence provides".

Finally, according to Article 611-17, cannot be patented, because they are on a list of inventions which are excluded, and whose publication, implementation, or commercial exploitation would be contrary to *ordre public* (law and order)

a) processes for cloning human beings

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

c) uses of human embryos for industrial or commercial purposes...etc

These modifications follow exactly the wording of Articles 5 and 6 of the Directive ; the only addition proposed bears on the need to specify the precise function provided by the sequence, in Article 611-15.

1) A context in which patentability is expanding

As it is called upon to consider, once again, ethical issues which could arise as a result of the development of the rules of intellectual property when they apply, not to inventions, but to knowledge itself, CCNE is well aware of the context in which its opinion is situated.
Knowledge of the genome is growing explosively. Hopes raised as regards both understanding human life and therapeutic advances are considerable. Rules governing intellectual property have extended to the living and accompany the progress of science. Acquiring patents plays a particularly significant role in the financing of such new and highly competitive research activities, which are particularly supported by sectors, both public and private, in which financial considerations are of the first importance.
Because of the considerable investment required in the area of genetics, researchers and sponsors justifiably seek to protect their inventions. In this domain as in others, a patent encourages research. European harmonisation is needed. There is no good reason why biotechnology should be an exception to these considerations.
These developments are taking place in an international environment which researchers cannot escape from. In the particular case of patents, their rules are in the hands of authorities whose mission stems from sophisticated law which was **elaborated at a time when genetic engineering did not exist and inventions were not concerned with living material, in particular the human body and its elements** . They apply methods and doctrines of their own, which enjoy international recognition. Thus, it is informative to state that, whatever the Government decides to do regarding the introduction of the directive into national law, the European Patents Office has already decided to apply the criteria of the Directive to its examination of incoming applications; these patents will naturally apply in France.
In this context, issues and interests involved and the way in which they are viewed, change from day to day. Genetic knowledge and applications for patents in this field evolve simultaneously and it is not always possible to discover in good time what ethical issues are at stake and who is conducting developments.

2) Ethical principles

These ethical issues do exist.
They exist, because all the institutions which have given thought to the consequences of this development in patent law in a field related to knowledge and to the human body, recognise that legal protection of inventors cannot be devoid of ethical references which CCNE intends to recall.
Genetic research touches upon the status of the human body. However it forces us to adopt a new conceptual approach. The gene, which is a fragment of DNA, is a chemical molecule, but the gene which codes a protein is the bearer of information the decoding of which is the main aim of this research.
To access it, researchers use computerised and formal language, and create a body of theoretical data which is detached from physical reality.
Three ethical principles are at stake :
- the principle of not making commercial use of the human body.
- free access to knowledge of the gene.
- sharing this knowledge.
The first guarantee at stake is the principle of not making commercial use of the human body. This is one of the cornerstones of the laws on "bioethics". It is consecrated by the *Code Civil* , in articles 16-1 and 16-5. "The human body, its elements, and its products cannot be the object of any rights of patrimony" and "conventions with a view to confer rights of patrimony to the human body, its elements, or its products, are null and void". The *Conseil Constitutionnel* confirmed this principle. Individuals are prohibited from engaging in the trade of their own bodies or of its elements, and this rule is of considerable

importance as regards the gift of organs and tissues. This is one of the main instruments to combat the risk of the human body being made into an **instrument** .
This principle which has been constantly advanced by CCNE in its opinions regarding the patentability of the living, does not imply that CCNE believes, wrongly, that benefit of an industrial patent is synonymous with a right of ownership over the reality which is patented. However, the inventor's rights must take this context into account.
It is true that genes or gene sequences raise new issues as d to organs, tissues, cells, or other "parts of the human body". With the gene, we enter the molecular level where to identify as human the reality in question is fairly meaningless. **However, the human gene carries, inscribed in its sequence fundamental elementary determinants of the human being; its relationship to the human body is therefore of a very different kind than is the case for other molecules. Decoding the information carried by the gene opens the door onto an understanding of life, and if this life is human, such understanding is fundamental for mankind.**
If we decided to treat the gene as though it was an ordinary product, is it conceivable that this notion would not extend to cells, organs, or transactions concerning reproduction ? CCNE therefore persists in its belief that what is seen as acceptable for the gene in the context of intellectual property, could lead, unless care is taken, to undermining the rule which excludes the human body from commercial use, and that this should be avoided.
Current developments in scientific research have demonstrated, with an intensity which CCNE feels bound to emphasise, a second principle. **Understanding the human genome is so connected to the nature of human beings, is so fundamental and necessary to their future welfare, that this knowledge cannot be appropriated. It must remain open to the scientific community and available for mankind as a whole.** This is the principle that UNESCO's Universal Declaration on the Human Genome sought to express, which France supported until it was adopted and taken into account by the United Nations. It is said here of the genome that in a symbolic sense, it is the heritage of humanity.
Finally, the potentialities which genetic science opens up are so vast, that in itself this supports the idea of a **knowledge sharing principle.** Understanding of the gene cannot be jealously guarded by the richer countries, and all the more so because it can be based on "plundering" genetic material from the poorest countries. It belongs to everyone, simply because it opens up revolutionary prospects for understanding life itself, and diseases.

3) Discovery and invention, as regards the genome

In CCNE's opinion, reconciling the principles of not making commercial use of the human body, of free access and sharing, and the patentability of living material, remains possible as long as also remains open to everyone the field of knowledge of discovery.
3-1 At first glance, achieving this condition should not be a problem since everyone agrees that protection of the inventor does not extend to the discovery of what exists in its natural state. This distinction between discovery and invention is enshrined in patent law itself. There were vigorous reminders of it when bioethics ventured onto this ground. It is on this undisputed basis that the present legislation excludes not just patenting the human body, its elements, and its products, but also and significantly, knowledge of the total or partial structure of the human gene "as such". The Directive, in one of its clauses does not diverge from this : "The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions". It therefore appears to be impossible for anyone to claim, in order to obtain protection from a patent, that they have invented a gene, a gene sequence, a mutation or any polymorphism of a gene, or even that knowing its structure is anything more than a discovery.
It is clear to CCNE, that the importance of knowledge concerning the genome and the precautions suggested by respect for ethical issues, should lead to viewing the field of discovery in terms which are ample, open, generous, and comprehensible for everyone.

3-2 Now as regards genetics, and in the present state of scientific progress and practice, it appears to be particularly difficult to distinguish discovery, which no one seeks to patent, from invention, which falls within the rules of patentability.
Knowledge of genetic information, be it borne by a gene, a gene sequence, a polymorphism, or a whole gene, is therefore obviously not patentable and remains a discovery, since it is information about the natural world. In this way, blood cannot be subject of a patent. But monoclonal antibodies, stabilised products or blood derivatives, which involve innovative processes, may be patented. This could also apply to a cloned gene with specific characteristics for the production of a recombinant protein with demonstrated biological efficacy.
What of the intermediate steps, and particularly the moment **when the gene is isolated** It has been argued that isolating by cloning a particular gene, so that it can be characterised, makes available to researchers material which contains an invention. This is disputable ; automated cloning of a DNA fragment does not involve any inventive activity. Such processes have become very common, and if isolating a gene sufficed to emerge from discovery and enter the world of patentable invention, there would already no longer be any scope for discovery in the field of genetics.
Difficulties also arise as soon as one attempts to identify a gene function and its relationship with structure. It is hardly surprising that solving legal and ethical issues is troublesome, since it is precisely here that scientific research enters into a zone of uncertainty. Is this the revelation of a characteristic of the natural element discovered, or is it a property linked to the use intended for the product or the process for which a patent is sought ?
3-3 These difficulties are apparent in the present state of scientific progress when the simple sequencing of genes is far ahead of an understanding of their functions. Using a computerised analysis of a gene sequence, it is possible to claim a very broad, but virtual, field of application. Quite frequently, this industrial application is deduced by making computerised comparisons between elements of the gene sequence for which a patent is requested and sequences of other genes or of the genes of model organisms for which the function is already identified. DNA sequencing companies already have software which automatically makes such sequence comparisons using all accessible data bases, thereby inferring fields of industrial application which are then effectively "disclosed in the patent application". This practice confers industrial protection which covers any total or partial gene sequence. The effects of this approach have recently been demonstrated by the example of the CCR5 gene. It was obtained by systematic random sequencing of DNA code messengers, and it encodes a membrane receptor of a particular type. The sequence was integrated into a patent which claims to cover any use of this receptor. Years later, academics demonstrated that protein CCR5 was a co-receptor for the HIV virus and essential to its intracellular penetration. In spite of the fundamental nature of this latter work, any therapeutic development based on the use of CCR5 as target for a drug could infringe the initial patent.
There is strong industrial and scientific pressure to interpret broadly the scope of patentability , thus working back to knowledge acquired by fundamental science; for that matter, the expression "to patent genes" is frequently used in scientific publications in the English language.
3-4 **At this time, filings for patent applications are incessant, despite the fact that the scientific community has not made a clear choice between this competition and the risk of seeing access to fundamental science entangled in a mesh of temporary exclusive ownerships or dependence on existing patents.** Furthermore, patents are an ambiguous legal instrument, since they always have **two** relatively contradictory **functions** . On the one hand, they protect intellectual property, but on the other, they are an economic instrument This dual role does not play too much havoc in areas where scientific, ethical, technical and economic interests are well defined. In areas where everything is still relatively open-ended and ambiguous, such as the genome, things are more difficult. In this case, legal simplicity is not sufficient to encompass the complexity of the scientific stakes and their relationship with the economy. **This complexity-reducing role played by the patent may in certain situations produce disadvantages of which we must be aware now in order to avoid finding later on that it generates more problems than it solves.**

As far as the genome is concerned, conventional scientific reasoning does not provide any boundary line recognised by the scientific community between what is patentable and what should not be. Such uncertainty is natural but is aggravated by external factors. It so happens that the financing of this research is particularly dependent on industrial expectations; fundamental research which is financed by public funds is more indifferent to this competitive process, and does not benefit from the same level of investment. There is certainly no reason to pick an unfair quarrel with patent law, and clearly the existence of a patent does not remove the patented reality from any possibility of research. Furthermore, the competent authorities will doubtless develop in time more adequate case-law and develop practices such as compulsory licensing for more appropriate sharing of scientific knowledge. However, a certain amount of time is bound to elapse before this can be done. Current disorderly competition to patent such research without the benefit of comprehensive reflection leads to a dangerous situation. To safeguard all their chances in a situation of patentability with no clear rules, investors ask researchers they are funding to refrain from providing too much information. This is an uncomfortable situation for researchers who know well enough that the field of discovery, already inclined to secrecy for the usual reasons based on competition, will be even further restricted. It sometimes happens that privatisation without regulation of a knowledge-seeking activity endangers the process of innovation.
To further the cause of ethics, there is therefore very good reason for trying to avoid these lapses. CCNE is convinced that the cause of sustainable economic efficacy is also at issue, and this implies that exchange of information be facilitated.

4) Modification of national legislation to align it with the Directive will not help those who seek to control these lapses.

Its wording conveys ambiguity. It is true that the first paragraph of Article 5 seems to make it clear that, as was outlined above, the simple discovery of the sequence or partial sequence of a gene does not constitute a patentable invention. However, in the second paragraph, it goes on to say that "An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element". This wording in fact says that any gene or sequence would be patentable, on the condition of it being cloned. This gives a determining role to cloning techniques which do not meet any criteria of novelty, thereby almost totally cancelling the point made by the previous paragraph.
A third point is added to this part of the text : "When the invention bears on a sequence or partial sequence of a gene, the industrial application must be disclosed in the patent application". At this point, the text ceases to be at all demanding as regards the reality of the proposed application, and so the door is left wide open to censurable, because unsupported, claims. The draft law tries to go one step further by requiring a description of the gene's function, but this description is essentially supported by fundamental science and is not in itself any guarantee of the merits of the application.
Finally, it seeks to reassure by adding, in order to exclude them from patentability, a list of inventions judged by their very nature to be contrary to human dignity. It goes without saying that it would be contrary to ethical principles to protect by law human cloning or modification of germ cell identity. However, apart from the fact that it is impossible to imagine in advance all the ways in which genetic research might assault human dignity, this form of drafting based on a list of prohibitions does not address the principal problem, which is to give free access to discovery.
The fact that the text is still so ambiguous shows that it is not possible to rely entirely on patent law to solve all the ethical issues arising from these developments. These issues should not be divorced from the democratic debate ensuing from the revision of the laws on bioethics.

5) In fact, the scrutiny of patent law which the enquiry led to, shows that this displeasing situation is not to be attributed solely to the system of industrial property. The status of the human genome holds many other unsolved problems.

The disorderly way in which genetic data banks have been set up, including the question of consent from those concerned, and confusing rules for accessing the data, reveals the seriousness of ethical issues involved. These issues, which are connected to the appropriation of genetic knowledge without any invention, its retention or its use disregarding the principle of not making commercial use of the human body, raise even more ominous problems.

In an international context, where future agreements are made, there is even more cause for concern.

6) In conclusion, CCNE considers that to insert into French law modifications based on the Directive would at this time convey an ambiguous message and would not clarify the position of research workers.

It is in their own interest and that of society as a whole to retain control over the emerging evolution. It is not suggested that genetics should be excluded from the scope of patent law, but the result must not constitute a threat over free access to the field of discovery, a drift in the direction of treating the human body like an instrument, or refusing to share the benefits expected from these scientific advances. And above all, this evolution must not take place without debate. This is not the sole concern of the scientific community and debate must be democratic It exceeds the borders of our own country and even the scope of the European Directive.

Before this debate can take place, CCNE sees no reason to diverge from the principles which presided over the formulation of the law dated July 29, 1994 : knowledge of a gene sequence cannot in any way be considered an invented product, and is therefore not patentable. Its use, as is the case for all knowledge, which is the common heritage of mankind, cannot be limited by the existence of patents invoking industrial property rights, which seek to confer exclusive ownership of that knowledge. However, inventions providing free access to this knowledge may be protected by patents.

This analysis applies regardless of whether genes sequences are of human or non-human origin.

The demand for excluding genetic knowledge from the benefit of patentability is based on two other ethical considerations : keeping the human body, its elements, and its products out of the grasp of commercial transactions, and the emergence of aspirations to share the benefits expected from exploration of the genome.

CCNE can only emphasise that at this time, genetic research is in a state of fluctuation. Access to research results which are inextricably related to man's quest for self-knowledge and therefore to ethics must remain generously open.

By adopting this position for ethical motives, CCNE is convinced that it is also arguing for an authentic economic logic, where early integration of ethical preoccupations is a major condition for sustainable economic efficacy.

CCNE considers that the principles it has sought to uphold and the difficulties it has identified should be taken up in the revision of the 1994 laws and in a review of industrial property rights which cannot take place without the benefit of this reflection. Since such changes can only take place in an international framework, CCNE would be in favour of a proposal by France to re-initiate discussion of the Directive. CCNE also calls for simultaneous international discussion on industrial property issues as regards the human genome and of all living organisms **. Such debate should lead to the creation of an organisation authorised to reconcile, as regards the genome, the necessary protection of biotechnological inventions with ethical principles, to which responds the Universal Declaration on the Human Genome and Human Rights which was adopted by UNESCO and taken into consideration by the UN, following an initiative by France.**

June 8, 2000

This text was approved by the members of the Committee with the exception of three members, who expressed disagreement.