EUROPEAN COMMISSION

Brussels, 7 October 2013
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TO THE PRESIDENT AND MEMBERS OF THE COURT OF JUSTICE OF THE EUROPEAN UNION

WRITTEN OBSERVATIONS

submitted pursuant to Article 23 of the Statute of the Court of Justice by the European Commission represented by Mr Friedrich Wenzel Bulst and Ms Julie Samnadda, members of its Legal Service, acting as agents with an address for service in Luxembourg at the office of Ms Merete Clausen also a member of the Commission's Legal Service, Bureau F3/907, Bâtiment BECH, 5 Rue A Weicker, L-2721 Luxembourg, who consent to service by e-Curia

in Case C-364/13

a request for a preliminary ruling by the High Court of Justice (Chancery Division) (Patents) (United Kingdom) pursuant to Article 267 of the TFEU in proceedings between

International Stem Cell Corporation

Appellant

and

Comptroller General of Patents

Respondent

regarding the interpretation of Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions *OJ L 213, 30.7.1998, p. 13–21.*

THE COMMISSION HAS THE HONOUR TO SUBMIT THE FOLLOWING OBSERVATIONS:

1. THE MAIN PROCEEDINGS AND THE REFERENCE FOR A PRELIMINARY RULING

1. The present case concerns the notion of "human embryo" within the meaning of Article 6(2) (c) of Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions OJ L213 30.7.1998, p 13-21 ("the Directive") when read in the light of this Court's judgment of 18 October 2011 in Case C-34/10 Oliver Brüstle v Greenpeace eV [2012]ECR *("Brüstle")*.

2. The dispute before the High Court of Justice ("the Referring Court") is an appeal by International Stem Cell Cooperation ("the Appellant") against a decision of the Comptroller General of Patents ("the Comptroller") whereby the Comptroller refused to grant two patent applications in the name of the Appellant ("the Decision"). In the Decision of 16 August 2012, the Comptroller refused to grant the patent applications on the grounds that the inventions disclosed in the applications were excluded from patentability under paragraph 3(d) of Schedule A2 to the Patents Act 1977, which implements Article 6(2) (c) of the Directive. The Comptroller had decided that he was bound to reject the patent applications in the light of *Brüstle*.

2. THE LEGAL CONTEXT

The Directive

3. For present purposes, the following provisions and recitals of the Directive are of direct relevance: Article 5 and Article 6(2) (c) of the Directive and Recitals 16 and 38 of the preamble.

4. Article 5 and 6 (2) (c) of the Directive provide:

Article 5

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.

2. 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.

Article 6

1. Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation.

2. On the basis of paragraph 1, the following, in particular, shall be considered unpatentable:

...

(c) uses of human embryos for industrial or commercial purposes;

5. Recitals 16 and 38 of the Directive state:

(16) Whereas patent law must be applied so as to respect the fundamental principles safeguarding the dignity and integrity of the person; whereas it is important to assert the principle that the human body, at any stage in its formation or development, including germ cells, and the simple discovery of one of its elements or one of its products, including the sequence or partial sequence of a human gene, cannot be patented; whereas these principles are in line with the criteria of patentability proper to patent law, whereby a mere discovery cannot be patented;

...'

(38) Whereas the operative part of this Directive should also include an illustrative list of inventions excluded from patentability so as to provide referring courts and patent offices with a general guide to interpreting the reference to ordre public and morality; whereas this list obviously cannot presume to be exhaustive; whereas processes, the use of which offend against human dignity, such as processes to produce chimeras from germ cells or totipotent cells of humans and animals, are obviously also excluded from patentability;

...'

<u>*The Brustle judgment*</u>

6. In *Brüstle,* the Court interpreted Article 5 and Article 6(2) (c), stated as follows at paragraphs 32-36:

"(34) The context and aim of the Directive thus show that the European Union legislature intended to exclude any possibility of patentability where respect for human dignity could thereby be affected. It follows that the concept of 'human embryo' within the meaning of Article 6(2)(c) of the Directive must be understood in a wide sense.

(35) Accordingly, any human ovum must, as soon as fertilised, be regarded as a 'human embryo' within the meaning and for the purposes of the application of Article 6(2)(c) of the Directive, since that fertilisation is such as to commence the process of development of a human being.

(36) That classification must also apply to a non-fertilised human ovum into which the cell nucleus from a mature human cell has been transplanted and a non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis. Although those organisms have not, strictly speaking, been the object of fertilisation, due to the effect of the technique used to obtain them they are, as is apparent from the written observations presented to the Court, capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do so."

7. This reasoning in paragraphs 34-36, as applied by the Court to a fertilised and a non-fertilised ovum respectively, led the Court to rule in the operative part of its judgment that "any human ovum after fertilisation, any non-fertilised human ovum into which the cell nucleus from a mature human cell has been transplanted, and any non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis constitute a 'human embryo'".

The patent applications in question

8. The patent applications in question both relate to methods of obtaining human stem cell lines and corneal tissue from the parthenogenetic activation of an unfertilised ovum. The applications are more specifically:

   (1) GB0621068.6 entitled *"Parthenogenetic activation of oocytes for the production of human embryonic stem cells"*. Claims 1-29 as proposed to be amended are for methods of producing pluripotent human stem cell lines from parthenogenetically-activated oocytes. Claim 30 and 31 are for stem cell lines produced according to the claimed methods and claim 32 is an omnibus claim relating to a stem cell line.

   (2) GB0621069.4 entitled *"Synthetic cornea from retinal stem cells"*. As with GB0621068.6, there are method claims (all of which involve the isolation of pluripotent stem cells from parthenogenetically-activated oocytes), product-by-process claims and an omnibus claim.

9. In its Decision, the Comptroller held that the applications concerned uses of "human embryos" and were therefore excluded from patentability. This is because the Comptroller considered that the methods or techniques in the applications were "capable of commencing the process of development of a human being" as set out by the Court at paragraph 36 of *Brüstle*, and should be considered "human embryos" within the meaning of Article 6(2) (c).

The arguments before the Referring Court

10. The Appellants contest this interpretation of "human embryo" before the Referring Court. In essence, the Appellants submit that the current state of scientific knowledge would support their assertion that the methods or techniques which they seek to patent would not be "capable of commencing the process of development of a human being" and therefore should not excluded from patentability. Expert evidence was heard before the Referring Court.

11. In its summary of the technical background including the expert evidence presented to it, the Referring Court made certain findings of fact pertaining to parthenotes which are set out at paragraph 17 (a) –(d) of the Order for Reference. The Referring Court states at paragraphs 14 et seq of the Order for Reference that "[i]n contrast to the fertilised ovum and its early stage descendants, the cells of a parthenogenetically-activated oocyte are pluripotent, not totipotent, even in the first few cell divisions after activation. The same is true of the cells in a parthenogenetic blastocyst-like structure. [...] Human parthenotes have thus far been shown to develop only to the blastocyst stage, over about five days."

12. In the light of those findings of fact as they apply to parthenotes, it was further argued before the Referring Court that paragraph 36 of *Brüstle* which purports to establish a test for determining whether the definition of "human embryo" in paragraph 35 of the Court's judgment also applies to a non-fertilised ovum to which the technique of parthenogenesis is applied, the Court's ruling that such a technique is *"capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do so" (*emphasis added*)* is based on the factual scientific situation, as it applied at the time. In particular, the Appellants argued that the Court's assessment at paragraph 36 is based on the written observations of the parties and the Member States that intervened in the proceedings before this Court in *Brüstle.* These written observations had been specifically referred to by the Court in its reasoning at paragraph 36 of *Brüstle.*

13. These written observations in *Brüstle* were adduced before the Referring Court, in argument by the Appellants. The Appellants pointed to an inconsistency between the observations submitted to the Court in *Brüstle* at the time, and the present state of scientific development.

14. As regards the scientific assessment or technical background, before the Referring Court, it appears to be common ground before the Referring Court that parthenogenesis, the method which is the subject of each patent application referred to above, insofar as it is concerns parthenotes, allows a distinction to be made between pluripotent and totipotent cells in a way in which it is possible to conclude that as a matter of fact, the process is incapable of commencing the development of a human being. The Referring Court expresses the preliminary view that there is a distinction to be made between pluripotent and totipotent cells:totipotent cells should continue to be excluded from patentability and this is consistent with Recital 38 but it could not have been the intention of the Directive to exclude pluripotent as well.

15. Nevertheless, the Referring Court agreed that the issue of how parthenotes are to be dealt with in the context of Article 6(2) (c) of the Directive is not *acte clair* in the light of the current state of scientific development and should, therefore, be referred.

16. Accordingly, the Referring Court referred the matter by way of order dated 17 April 2013. The preliminary view of the Referring Court is set out at paragraphs 33-36 to the order for reference. The Court's attention is also drawn to the full judgment of the Referring Court particular [2013]EWHC 807 (Ch) where the facts are more fully set out.

3. THE QUESTION REFERRED

Are unfertilised human ova whose division and further development have been stimulated by parthenogenesis, and which, in contrast to fertilised ova, contain only pluripotent cells and are incapable of developing into human beings, included in the term "human embryos" in Article 6(2)(c) of Directive 98/44/EC on the Legal Protection of Biotechnological Inventions?

17. The Referring Court seeks clarification of the expression "capable of commencing the process of development of a human being" as used by the Court in *Brüstle,* paragraph 36. In particular, the reference raises, in the context of an interpretation of Article 6(2)(c) of the Directive, the issue of how the Court's notion of what constitutes a "human embryo" applies to unfertilised human ova.

18. The Commission would like to remark that the Reference itself would appear to be a consequence of the progress of scientific knowledge as regards stem cell technology

compared to the situation that prevailed at the time of the written procedure in 2010 which led to the judgment in *Brüstle.*

19. In essence, the Referring Court is asking, did the Court intend and it follows would it be the correct interpretation of the Directive to:

a) treat a non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis" as an embryo independently of what kind of development this stimulation commences or

b) treat a non-fertilised human ovum as an embryo *insofar as* the effect of the technique of stimulation by parthenogenesis is capable of commencing the development of a human being.

20. In the view of the Commission, the drafting of paragraph 36 of *Brüstle* and the Court's reference to the written observations before it in the same context supports a reading of paragraph 36 along the lines of alternative b). Such a reading suggests that the Court intended to include within the notion of "human embryo", ova which are subjected to a process of stimulation, which is capable of commencing the development of a human being. It would appear that the Court was drawn to make the assessment that parthenogenesis constitutes such a process on the basis of the written submissions made to the Court in *Brüstle*. In particular, the Commission refers to the following observations submitted to the Court:

Paragraph 52 of the United Kingdom's observations:

"*(52) In the view of the UK, the organisms contemplated in Question 1(b) would also fall within this definition of "human embryo".*

- Question 1(b)(1) refers to so-called somatic ceil nuclear transfer (SCNT). This is a laboratory technique by which the nucleus of the unfertilised ovum is removed and replaced with a donor nucleus (normally from a mature human cell). Any embryo derived from the ovum will have the same genetic material as the donor. However, since the manipulated ovum is capable of resulting in an embryo, it is a "human embryo" within a broad definition. This view is supported by the reasoning of the Bundesgerichtshof at page 9, paragraph (c)(aa).

- Question 1(b)(2) refers to parthogenesis, a process by which the unfertilised ovum is stimulated by electrical or chemical techniques, causing it to undergo at least the initial stages of embryonic development as if it had been fertilised. The process can result in a parthenogenetic 20 human embryo30, and therefore also falls within a broad definition. Once again, the reasoning of the Bundesgertichtshof supports this view."

Paragraph 16 of Portugal's observations:

"(16) Cependant, bien que la viabilité des embryons jusqu'à la naissance ne soit pas encore définitivement démontrée, le développement par voie [Or. 7] parthénogénétique se déroule en suivant toutes les phases du processus de développement biologiquement normal d'un embryon."

Paragraph 44 of the Bundesgerichtshof's order for reference:

"(bb) As a further way of obtaining human embryonic stem cells, the defendant refers to parthenogenesis, which is to say the division and further development of an unfertilised ovum without fertilisation and without transplantation of a foreign cell nucleus. There is no conclusive scientific evidence to show that this method is in fact practicable and that a cell of this kind would be capable of developing into a complete individual. Irrespective of this, support for qualification as an embryo within the meaning of Article 6(2)(c) of the Directive might be found in the fact that, in the initial stages of division at least, such cells undergo the same development as fertilised ova and therefore seem worthy of protection in the same way."

21. The Referring Court appears to share the Commission's understanding of paragraph 36 in *Brüstle*.

22. The Commission is of the view that the systematic and purposive interpretation that the Court has given to the term "human embryo" [which has resulted in a broad notion of that term], does appear convincing for the reasons given in *Brüstle*, at paragraphs 32-33 in particular.

23. The Court did not take up the distinction between pluripotent and totipotent cells which was suggested by the Advocate-General in his opinion at paragraph 115 and 116 respectively where he refers to "[b]y contrast, taken individually, pluripotent embryonic stem cells are not included in that concept because they do not in themselves have the capacity to develop into a human being".

24. Rather the Court came up with a more abstract position as advocated by Greenpeace in their written observations. The Court's attention is drawn to paragraph 40 of Greenpeace's written observations in *Brüstle* where it is stated:

"(40) c) Le demandeur estime donc dans ce contexte que l'article 6, paragraphe 2, sous c), de la directive doit être interprété en ce sens que l'interdiction de brevetabilité qui y est inscrite couvre toutes les cellules qui peuvent servir de point de départ au développement d'un embryon humain (voir aussi: Denker H.W., Die Potenz von menschlichen ES Zellen, aïs Argument gegen ihre Patentierbarkeit, S. 367, dans: L. Honnefelder und C. Streffer (éd.) Jahrbuch fur Wissenschaft und Ethik, Vol. 9,2004)."

25. However, the Court included a reference to a particular technique ("parthenogenesis") when treating a non fertilised ovum, which in the Court's assessment, with the application of that technique, leads to the same result as a fertilised ovum. This reference to a particular technique is at odds with an abstract approach. For the blastocyst, which was addressed in question 1(c) referred in *Brüstle*, the Court maintained its abstract approach and left it to the national courts to apply its definition "in the light of scientific developments". It appears now that there have been scientific developments – of the kind the Court foresaw for the blastocyst stage – regarding parthenogenesis. These may lead to a re-assessment of what the Court stated at the second sentence of paragraph 36 of its judgment in *Brüstle* as regards parthenogenesis.

26. Against that background, the Commission would urge caution in two respects. First, it may now be appropriate for the Court to re-examine whether there is any merit in still relying on the written observations submitted at the time of the proceedings in *Brüstle* which reflect the state of scientific development as it applied at the time. Second, and related to the first aspect, the Commission also considers that it would be prudent to refrain from including within the notion of "human embryo" in the case of an unfertilised ovum, specific stages of development and techniques which in the case of stem cell technology may be subject to rapid biotechnological developments and superseded in time. Such an approach to the notion of "human embryo" might not only prove obsolete in a short space of time..

27. Rather, the Commission is of the view that the assessment of scientific advances in the field of biotechnology especially the effect of any particular techniques, should instead be left to the national courts to apply in the light of scientific developments. These techniques should not form part of the definition of "human embryo" itself– as the Court held for stem cells derived from blastocysts in *Brüstle.*

28. The Commission agrees with the Referring Court that the Court should clarify its definition of "human embryo" as regards a non-fertilised ovum. In the view of the Commission, the Court should retain the definition insofar as it remains abstract and to that extent can apply to a variety of circumstances for the reasons the Commission has set out above.

29. In the present case, such an approach as advocated by the Commission would allow the Referring Court, on the basis of the available scientific evidence before it, to form a view as to whether or not the techniques in question in the case before it when applied to a non fertilised human ovum, are capable or not of commencing the process of development of a human being.

30. It follows that the definition which flows from the Court's purposive and systematic interpretation of the Directive in *Brüstle* would allow the Commission to propose that the Court reply to the question of the Referring Court as follows:

"For the purposes of Article 6 (2) (c) of the Directive, a human embryo is

– *any human ovum as soon as fertilised as well as*

– *a non-fertilised human ovum capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can."*

4. CONCLUSION

31. Therefore, the Commission submits that the Court should answer the question of the Referring Court as follows:

"For the purposes of Article 6 (2) (c) of the Directive, a human embryo is

– *any human ovum as soon as fertilised as well as*

– *a non-fertilised human ovum capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can."*

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