



Reports of Cases

OPINION OF ADVOCATE GENERAL
CRUZ VILLALÓN
delivered on 17 July 2014¹

Case C-364/13

International Stem Cell
v
Comptroller General of Patents

(Request for a preliminary ruling from the High Court of Justice of England and Wales, Chancery Division (Patents Court) (United Kingdom))

(Directive 98/44/EC — Legal protection of biotechnological inventions — Patentability — Stem cells — Stimulation by parthenogenesis of unfertilised human ova to create stem cells — Parthenotes — List of inventions excluded from patentability — Non-exhaustive character of the list — Exclusion of ‘uses of human embryos for industrial or commercial purposes’ — Notion of ‘human embryo’ — ‘Capable of commencing the process of development of a human being’)

1. These proceedings offer the Court of Justice an opportunity to consider, again, the meaning of ‘human embryos’ in 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 (‘the Directive’).²

2. In fact, the question that the High Court of Justice, Chancery Division (Patents Court) referred to the Court of Justice in the present case is, but for one difference, identical to one of the questions that the Court answered three years ago in *Brüstle*,³ at that time on reference by the Bundesgerichtshof.

3. In *Brüstle* the Bundesgerichtshof had asked, amongst others, whether ‘unfertilised human ova whose division and further development have been stimulated by parthenogenesis’ are included in the term ‘human embryos’ in the sense of Article 6(2)(c) of the Directive. The Court of Justice answered this question in the affirmative. Struggling with that answer, the referring court’s only question in the present case inquires whether the ruling in *Brüstle* applies in relation to those parthenogenetically activated unfertilised human ova even in light of the following specification: ‘which, in contrast to fertilised ova, contain only pluripotent cells and are incapable of developing into human beings’.

¹ — Original language: English.

² — OJ 1998 L 213, p. 13.

³ — Judgment in *Brüstle*, C-34/10, EU:C:2011:669.

4. The referring court is of the opinion that given the Court's reasoning in *Brüstle*, namely in paragraph 36 of the judgment,⁴ it is not possible to state with the necessary certainty whether the Court of Justice would give the same answer if confronted with the specification made in the question referred in this case.

5. A thorough analysis of the logic underlying the Court's answer in *Brüstle* will lead me to propose an 'exclusive' answer to the question referred to the Court, i.e. excluding unfertilised human ova whose division and further development have been stimulated by parthenogenesis from the notion of 'human embryos' in light of the further specifications made by the referring court.

I – Legal framework

A – *International law*

6. Article 27(1) and (2) of the TRIPS Agreement, which constitutes Annex 1 C of the Agreement establishing the World Trade Organisation, signed in Marrakech on 15 April 1994 and approved by Council Decision 94/800/EC of 22 December 1994,⁵ provides:

'1. Subject to the provisions of paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. Subject to paragraph 4 of Article 65, paragraph 8 of Article 70 and paragraph 3 of this Article, patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced.

2. Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.'

7. Article 52(1) of the Convention on the Grant of European Patents (European Patent Convention, 'EPC') of 5 October 1973,⁷ to which only the Member States, but not the European Union itself are parties, reads:

'European patents shall be granted for any inventions, in all fields of technology, provided that they are new, involve an inventive step and are susceptible of industrial application.'

8. Article 53(a) of the EPC provides:

'European patents shall not be granted in respect of:

- (a) inventions the commercial exploitation of which would be contrary to "ordre public" or morality; such exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States.'

4 — 'That classification must also apply to ... 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.'

5 — Council Decision (of 22 December 1994) concerning the conclusion on behalf of the European Community, as regards matters within its competence, of the agreements reached in the Uruguay Round multilateral negotiations (1986-1994), OJ 1994 L 336, p. 1.

6 — I deleted internal footnotes.

7 — As revised.

9. Through the rules of the Implementing Regulations to the EPC the EPC has been harmonised with the Directive.⁸ Rule 28(c) of the Implementing Regulations to the EPC states:

‘Under Article 53(a), European patents shall not be granted in respect of biotechnological inventions which, in particular, concern the following:

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

B – *European Union law*

10. Recitals 5, 16, 20, 21, 36 to 39, and 42 of the Directive read as follows:

- ‘(5) ... differences exist in the legal protection of biotechnological inventions offered by the laws and practices of the different Member States; ... such differences could create barriers to trade and hence impede the proper functioning of the internal market;
- (16) ... patent law must be applied so as to respect the fundamental principles safeguarding the dignity and integrity of the person; ... 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; ... these principles are in line with the criteria of patentability proper to patent law, whereby a mere discovery cannot be patented;
- (20) ..., therefore, it should be made clear that an invention based on an element isolated from the human body or otherwise produced by means of a technical process, which is susceptible of industrial application, is not excluded from patentability, even where the structure of that element is identical to that of a natural element, given that the rights conferred by the patent do not extend to the human body and its elements in their natural environment;
- (21) ... such an element isolated from the human body or otherwise produced is not excluded from patentability since it is, for example, the result of technical processes used to identify, purify and classify it and to reproduce it outside the human body, techniques which human beings alone are capable of putting into practice and which nature is incapable of accomplishing by itself;
- (36) ... the TRIPs Agreement provides for the possibility that members of the World Trade Organisation may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law;
- (37) ... the principle whereby inventions must be excluded from patentability where their commercial exploitation offends against *ordre public* or morality must also be stressed in this Directive;
- (38) ... the operative part of this Directive should also include an illustrative list of inventions excluded from patentability so as to provide national courts and patent offices with a general guide to interpreting the reference to *ordre public* and morality; ... this list obviously cannot presume to be exhaustive; ... 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;

⁸ — Mellulis, K.-J., ‘Article 53’ in: Ehlers, J., and Kinkeldey, U., (eds), *Benkard — Europäisches Patentübereinkommen*, Beck, München, 2nd ed. 2012, paragraph 39.

- (39) ... *ordre public* and morality correspond in particular to ethical or moral principles recognised in a Member State, respect for which is particularly important in the field of biotechnology in view of the potential scope of inventions in this field and their inherent relationship to living matter; ... such ethical or moral principles supplement the standard legal examinations under patent law regardless of the technical field of the invention;
- (42) ..., moreover, uses of human embryos for industrial or commercial purposes must also be excluded from patentability, ... in any case such exclusion does not affect inventions for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it;

11. Article 5(1) and (2) of the Directive provides:

‘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.’

12. Article 6 of the Directive states:

‘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:

- (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;
- (d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.’

C – *National law*

13. Paragraph 3(d) of Schedule A2 to the Patents Act 1977, which implements Article 6(2)(c) of the Directive, reads:

‘The following are not patentable inventions — ...

- (d) uses of human embryos for industrial or commercial purposes.’

II – Facts and the main proceedings

14. International Stem Cell Corporation ('ISC')⁹ is the applicant for two national patents at the United Kingdom Intellectual Property Office: application GB0621068.6 entitled 'Parthenogenetic activation of oocytes for the production of human embryonic stem cells', claiming methods of producing pluripotent human stem cell lines from parthenogenetically-activated oocytes and stem cell lines produced according to the claimed methods as well as application GB0621069.4 entitled 'Synthetic cornea from retinal stem cells' claiming methods of producing synthetic cornea or corneal tissue involving the isolation of pluripotent stem cells from parthenogenetically-activated oocytes as well as synthetic cornea or corneal tissue produced by these methods.

15. In the course of the patent prosecution ISC was confronted with the objection that the applications are not patentable as the inventions disclosed constitute uses of human embryos that are not patentable under the standard established by the Court of Justice in *Brüstle*. ISC argued that the holding in *Brüstle* should not apply, as the inventions in question concern parthenogenetically-activated oocytes not 'capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do so', due to the phenomenon of genomic imprinting. Confronted with research suggesting the possibility to overcome barriers of genomic imprinting in mice resulting in live-born parthenogenetic mice, ISC argued that this research did not relate to parthenogenesis alone, but included extensive genetic manipulation. ISC amended its claims to exclude any such method of manipulation (e.g. by introducing the word 'pluripotent' before 'human stem cell line' and referring to a lack of paternal imprinting).

16. In a decision dated 16 August 2012 the Hearing Officer of the UK Intellectual Property Office acting for the Comptroller held the inventions disclosed in the patent applications to concern uses of human embryos as defined by the Court of Justice in *Brüstle*, namely organisms 'capable of commencing the process of development of a human being', and hence to be excluded from patentability under paragraph 3(d) of Schedule A2 to the Patents Act 1977 implementing Article 6(2)(c) of Directive 98/44. He accordingly refused the applications.

17. ISC appealed the decision to the referring court.

18. ISC argued that the test adopted by the Court of Justice in *Brüstle* was intended to exclude from patentability only organisms capable of commencing the process of development which leads to a human being, as illustrated by the wording of the Court of Justice's test, its treatment of fertilised ova and non-fertilised ova subjected to somatic-cell nuclear transfer and as supported by the Bundesgerichtshof's final judgment after the Court of Justice's ruling in *Brüstle*. Parthenogenetically-activated oocytes hence would, in the opinion of ISC, only be excluded from patentability to the extent that they are capable of giving rise to totipotent cells.

19. The Comptroller General considered that the Court of Justice's ruling in *Brüstle* was not clear with respect to the question whether the term 'human embryo' covers organisms capable of commencing the process of development of a human being irrespective of whether the process could be completed. It is, according to the Comptroller General, equally unclear whether the Court of Justice relied on submissions reflecting an inaccurate understanding of the technical background as it stands today.

⁹ — The patents were originally filed in the name of another company, but were assigned to ISC.

20. The referring court itself is of the view that if the parthenogenetically-activated oocytes at issue are incapable of developing into a human being, they should not be regarded as human embryos. While totipotent cells should be excluded from patentability, pluripotent cells should not. A different reading would, in the opinion of the referring court, not strike the appropriate balance between encouraging biotechnological research by way of patent law and respect for the dignity and integrity of the person, which the Directive was intended to achieve.

III – Question referred for a preliminary ruling and procedure before the Court of Justice

21. In light of these considerations the referring court, by order of 17 April 2013, stayed the proceedings and referred the following question to the Court of Justice:

‘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 on the Legal Protection of Biotechnological Inventions?’

22. Written observations were submitted by ISC, France, Poland, Portugal, Sweden, the United Kingdom and the Commission.

23. On 29 April 2014 the Court held a hearing, during which ISC, the United Kingdom, France, Sweden and the Commission made observations.

IV – Assessment

A – Preliminary considerations

24. Before answering the question referred by the High Court and arguing why, in light of the Court’s ruling in *Brüstle* and of the further specifications made by the referring court, I propose to exclude unfertilised human ova whose division and further development have been stimulated by parthenogenesis from the notion of ‘human embryos’ in the sense of Article 6(2)(c) of the Directive, I shall adduce some preliminary considerations concerning firstly the scientific background of the invention at issue in the case, secondly the non-exhaustive character of the list contained in Article 6(2) of the Directive and thirdly Article 5 of the Directive.

1. Scientific background as described by the referring court and the parties

25. The case at hand concerns unfertilised human ova whose division and further development have been stimulated by parthenogenesis — organisms I will from now on refer to as ‘parthenotes’ for the sake of simplicity.¹⁰ Deciding whether parthenotes constitute human embryos requires a short scientific explanation, which I will base on the information provided by the referring court and the parties to the proceedings. The specifications provided by the referring court have already pointed to the fact that this information is not identical with the one provided in *Brüstle*, which is not the least particularity of the present case. In his opinion in *Brüstle* Advocate General Bot has rightly emphasised the difficulties in stating what the law is with a minimum degree of permanence in matters directly depending on the state of scientific knowledge in a quickly developing field.¹¹

10 — The term is not only commonly used — as evinced by its entry in the *Shorter Oxford English Dictionary* — but has even been the object of a statutory definition, namely in Article 2(d) of the Swiss Bundesgesetz über die Forschung an embryonalen Stammzellen (Federal Act concerning Research on embryonic Stem Cells, AS 2005, 947, as amended).

11 — Opinion by Advocate General Bot in Case C-34/10 *Brüstle*, EU:C:2011:138, points 47 and 48.

26. The development of a human being starts with the fertilisation of an ovum. Through cell division the fertilised ovum develops into what is referred to as a 'morula', a structure consisting of 8 to 16 cells. Within roughly five days after fertilisation, the organism develops into a so-called 'blastocyst',¹² a structure consisting of an inner cell mass, which subsequently will form all embryonic tissues, surrounded by an outer layer of cells, which will form extra-embryonic tissue such as the placenta.

27. Human embryonic stem cells are derived from human embryos in these early stages of development. Generally, scientists distinguish between 'totipotent' cells, i.e. cells that are capable of developing into all human cell types including extra-embryonic tissue and into a complete human being, and 'pluripotent' cells, which can develop into all cells that make up the body, but not into extra-embryonic tissue and hence cannot develop into a human being.¹³ Cells produced in the very first few divisions of a fertilised ovum are totipotent. Cells of the inner cell mass of a blastocyst are pluripotent.

28. The capacity of human embryonic stem cells to form various tissues has created hopes for finding therapies for numerous heretofore incurable diseases. Accordingly, research into these cells has grown exponentially since the creation of the first human stem cell line in 1998. Unsurprisingly, there are also significant economic interests at stake. However, research on human embryonic stem cells derived from embryos raises significant ethical concerns, resulting in a search for alternative sources of such cells.¹⁴

29. Scientists have found ways to initiate the process of cell division commonly connected with embryos without fertilisation of an ovum. One such method is the parthenogenetic activation of an ovum here at issue, in which the unfertilised oocyte is 'activated' by a variety of chemical and electrical techniques. Such an activated oocyte can develop into the blastocyst phase. As it was never fertilised, the oocyte contains only maternal DNA and no paternal DNA. The process of the ovum developing into a being without fertilisation is referred to as 'parthenogenesis', the organism that thus is created as a 'parthenote'.¹⁵

30. While some species produce parthenotes that develop to term,¹⁶ all participants and the referring court in the present case (in contrast to the participants and the referring court in *Brüstle*) agreed that according to current scientific knowledge a phenomenon of 'genomic imprinting' prevents human and other mammalian parthenotes from developing to term.¹⁷ Genomic imprinting means that some genes are expressed only from paternal, others only from maternal DNA. In the case of humans, some genes involved in the development of extra-embryonic tissue, for example, are only expressed from paternal DNA. Accordingly, human parthenotes — carrying only maternal DNA — cannot, for example, develop proper extra-embryonic tissue. The cells of such parthenotes are hence never totipotent, as even in the first few cell divisions they cannot develop into extra-embryonic cells. However, stem cells can be obtained from the blastocyst-like structure.¹⁸ ISC considers these cells to be a good alternative to embryo-derived human embryonic stem cells.

12 — See also Opinion of Advocate General Bot in *Brüstle*, C-34/10, EU:C:2011:138, footnote 17.

13 — The German legislator adopted a statutory definition of these terms. See Paragraph 3(1) and (4) of the Gesetz zur Sicherstellung des Embryonenschutzes im Zusammenhang mit Einfuhr und Verwendung menschlicher embryonaler Stammzellen (Stammzellengesetz; Law to ensure the protection of embryos in connection with the importation and use of human embryonic stem cells, BGBl. I, p. 2277, as amended). Advocate General Bot relied heavily on this distinction in his Opinion in *Brüstle*, EU:C:2011:138.

14 — Even where such cells are not derived from embryos, they are commonly referred to as 'human embryonic stem cells', which does not contribute to terminological clarity.

15 — See also my definition above.

16 — See Mittwoch, U., 'Parthenogenesis', *Journal of Medical Genetics* 1978 (15), p. 165.

17 — France points out that there is no consensus as to the precise reasons for cessation of development of a parthenote in mammals.

18 — While some participants consider these cells to be pluripotent, France points out that the effects of genomic imprinting are not limited to extra-embryonic tissue, but also hamper proper organogenesis and the cells cannot, hence, be regarded as pluripotent.

31. There is agreement between the referring court and participants that the barrier presented by genomic imprinting might be surmountable by genetic manipulation, even though this has so far not been proven in human beings. The Portuguese and UK Governments mentioned in this respect, for example, that in mice ‘tetraploid complementation’ was successfully used to obtain viable descendants surviving into adulthood from what originally were parthenotes.¹⁹ ISC, in the hearings, did not refute this possibility, but stated that the genetic manipulation needed to achieve this goal changes the very nature of the parthenote. The French Republic pointed out that the relevant manipulation, under French law, would be illegal. The referring court has stated as a fact that the amended claims of the patents, which are the subject of the proceedings, exclude the prospect of such manipulation.

2. The non-exhaustive character of the list contained in Article 6(2) of the Directive

32. Bearing in mind the above description of a ‘parthenote’ and before analysing the question referred by the High Court I consider it necessary to discuss the meaning and scope of the list of prohibitions of patentability that the Directive contains in its Article 6(2), among which is the exclusion that is the object of this preliminary reference.

33. The wording of Article 6(2) itself makes clear that the list of prohibitions is non-exhaustive (‘the following, *in particular*, shall be considered unpatentable’²⁰), a fact that is stressed unequivocally by recital 38 of the Directive (‘this list obviously cannot presume to be exhaustive’). The Commission agreed with this interpretation during the hearing.

34. This being so and as a matter of principle, the non-exhaustive character of the list limits the practical effect of the answer to the question referred in this case. In fact, the import of the answer of the Court of Justice differs considerably depending on whether EU law provides a ‘complete answer’ to the question of the patentability of parthenotes or just part of the answer to this question. To be aware of this issue before analysing the question referred to the Court of Justice has, in my opinion, two advantages. First of all, it provides the Court of Justice with the necessary context of the question, permitting a clearer identification of what is at stake. Secondly, it will enable the Court of Justice to give the referring court a more exact answer which might prevent further references.

35. Of course, this issue would not need to be discussed if the Court of Justice gave a, so to speak, ‘inclusive’ answer to the High Court, confirming its ruling in *Brüstle* in its entirety, namely that the Directive prohibits patenting uses of parthenotes for industrial or commercial purposes as they constitute human embryos in the sense of the Directive. This is why, in my understanding, the issue did not need to be tackled in *Brüstle*.

36. If, however, the Court were to follow my proposition and give an ‘exclusive’ answer in the sense that parthenotes are excluded from the notion of human embryos, and this is clearly the preference of the referring court, providing some further explanations as to the implications of the fact that the list of prohibitions is non-exhaustive becomes inevitable.

37. In my opinion, the non-exhaustive character of the list in Article 6(2) of the Directive implies that the exclusion of a parthenote from the concept of human embryo contained in Article 6(2)(c) of the Directive, does not prevent a Member State from excluding parthenotes from patentability based on Article 6(1) of the Directive. I shall try to explain myself in this respect as concisely as possible.

19 — Chen, Z., et al., ‘Birth of Parthenote Mice Directly from Parthenogenetic Embryonic Stem Cells’, *Stem Cells* 2009 (27), 2136.

20 — Emphasis added. The emphasised words correspond to the following terms in other language versions: ‘unter anderem’ (German); ‘notamment’ (French); ‘met name’ (Dutch).

38. The question referred indubitably belongs to the field of bioethics. However, this circumstance does not expel it from the legal sphere. In fact, we can observe, nowadays, the emergence of a ‘law of bioethics’, as is demonstrated by the legislation of Member States.²¹ The Directive, however, clearly was not intended to be a ‘law of bioethics’ as such, even though it contains some provisions in this regard. On the contrary, as indicated by its name and its legal basis,²² the Directive merely concerns the legal protection of biotechnological inventions, namely by patents, and it can be supposed that the public deliberation during the drafting process was limited accordingly rather than encompassing all the relevant aspects relating to the very complex topic of bioethics as would have been the case otherwise.

39. The biotechnological inventions that are the object of the Directive and the legal protection of which is provided by way of patents are not limited to those in the field of human biotechnology. On the contrary, they encompass the field of biotechnology in its largest sense, including the fields of biotechnology relating to animals and plants. Given the sensitivity of the topic the Directive opens up a space for ethical and moral considerations under the categories of *ordre public* and morality,²³ a space that is particularly pronounced when it comes to biotechnology relating to the species *homo sapiens*.

40. The key provision in this respect is, indubitably, Article 6 of the Directive. In its pertinent part Article 6(1) states: ‘Inventions shall be considered unpatentable where their commercial exploitation would be contrary to *ordre public* or morality’. Article 6(2) goes on to say that ‘[o]n the basis of paragraph 1, the following, in particular, shall be considered unpatentable’.²⁴

41. In my opinion and in light of the recitals these two paragraphs of Article 6 have to be interpreted jointly. Such a reading is imposed by the introductory words of Article 6(2), which clearly characterise the second paragraph as complimentary to the first. Thus, when Article 6(2) declares a list of inventions unpatentable, it does so to show, in an illustrative manner and to provide guidance to Member States, cases in which inventions offend against *ordre public* or morality. As recital 38 states, this is ‘an illustrative list of inventions excluded from patentability so as to provide national courts and patent offices with a general guide to interpreting the reference to *ordre public* and morality’.²⁵

42. Thus, it does not appear to me as though the two paragraphs of Article 6 belong to different worlds, the first to that of *ordre public* and morality and the second to that of law. On the contrary, Article 6(2) expresses a minimum, Union-wide consensus for all Member States, in legal terms, on which inventions may not be considered patentable on the basis of considerations of *ordre public* and morality. Article 6(2) is thus ancillary to Article 6(1).

21 — See explicitly in France loi No 2011-814 relative à la bioéthique du 7 juillet 2011 (law on bioethics, JORF No 157 of 8 July 2011, p. 11826), as amended; other Member States have regulated aspects of bioethics by statute such as in the United Kingdom the Human Fertilisation and Embryology Act 1990, 1990 c. 37, as amended, or in the Netherlands the Wet van 20 juni 2002, houdende regels inzake handelingen met geslachtscellen en embryo's (Emryowet, Law laying down rules for operating with gametes and embryos, Stb. 2002, 338), as amended, or the German statute already mentioned. See Hennette-Vauchez, S., ‘1994-2004: Dix ans de droit de la bioéthique’, in: Hennette-Vauchez, S. (ed.), *Bioéthique, biodroit, biopolitique*, LGDJ, Paris, 2006, p. 11.

22 — See judgment in *Netherlands v Parliament and Council*, C-377/98, EU:C:2001:523.

23 — The *ordre public* exclusion stems from Article 27(2) of the TRIPS Agreement (recitals 36 and 37 of the Directive). On the exclusion in detail: Barton, T., *Der „Ordre public“ als Grenze der Biopatentierung*, Erich Schmidt Verlag, Berlin, 2004.

24 — Emphasis added. These words read in other language versions: ‘En virtud de lo dispuesto en el apartado 1,’ (Spanish); ‘Im Sinne von Absatz 1’ (German); ‘Au titre du paragraphe 1’ (French).

25 — In Spanish: ‘una lista *orientativa* de las invenciones no patentables, con objeto de proporcionar a los jueces y a las oficinas nacionales de patentes una guía para interpretar la referencia al orden público o a la moralidad’; in French: ‘une liste *indicative* des inventions exclues de la brevetabilité afin de donner aux juges et aux offices de brevets nationaux des orientations générales aux fins de l’interprétation de la référence à l’ordre public ou aux bonnes moeurs’; in German: ‘eine *informativische* Aufzählung der von der Patentierbarkeit ausgenommenen Erfindungen ..., um so den nationalen Gerichten und Patentämtern allgemeine Leitlinien für die Auslegung der Bezugnahme auf die öffentliche Ordnung oder die guten Sitten zu geben’. (Emphasis added throughout).

43. This means that in the context of the task confided to each Member State to determine which inventions are not patentable in light of consideration of *ordre public* and morality,²⁶ the Directive establishes a nucleus of non-patentability, a kind of ‘no-go zone’ that is common for all Member States as an expression of what has to be considered unpatentable in any case. Consequently, if parthenotes are not included in the notion of human embryos in the sense of the Directive this would not imply that Member States could not prohibit their patentability on the basis of other considerations of *ordre public* or morality, all the while respecting that the notion of human embryo does not extend to parthenotes.²⁷

44. This interpretation is in conformity with the case-law of the Court, which states that Article 6(1) of the Directive allows the administrative authorities and courts of Member States a wide scope for manoeuvre and thereby allows taking into account the social and cultural context of each Member State,²⁸ whereas Article 6(2) allows for no discretion with regard to the unpatentability of the processes and uses mentioned,²⁹ the terms of which are defined autonomously under Union law.

45. The preceding comments would suffice if it were not for the particularity of the case of parthenotes, namely their external ‘resemblance’ to human embryos. This proximity might create the impression that any and all objections to the patentability of parthenotes have to be phrased in terms of their inclusion *vel non* in the notion of human embryo. In other words, the treatment of parthenotes from the perspective of *ordre public* or morality would depend solely on whether or not they are included in the concept of human embryo. Put still differently, the fact that EU law defines the notion of ‘human embryo’ in the Directive autonomously would exclude the possibility that Member States reach their own conclusions as to the patentability of parthenotes based on considerations of *ordre public* and morality.

46. I do not think this is the case.

47. It is certainly true that the Court of Justice has stated that the term ‘human embryo’ in the Directive has to be interpreted autonomously and has to ‘be understood in a wide sense’,³⁰ a ruling I will come back to later. This has led the Court to assimilate human embryos and other human organisms created by scientific and technological means with the same capacity of development as human embryos.³¹

48. Parthenotes might or might not fulfil this condition, as shall be discussed later. No matter which position one takes on this issue, given the origin of parthenotes (human ova) and the technology employed it cannot be excluded that out of the considerations involved in Article 6(1) of the Directive and completely independent from the prohibitions contained in Article 6(2) a Member State considers patents on parthenotes as contrary to *ordre public* or morality.

26 — See recital 39 of the Directive.

27 — A good example of such a decision can be provided by the case of Switzerland, which has included a provision on gene technology involving human beings in its Constitution (Article 119) and by statute prohibits the development of parthenotes, deriving stem cells from parthenotes or using such stem cells in Article 3(d) of the Bundesgesetz über die Forschung an embryonalen Stammzellen (Federal Act concerning Research on embryonic Stem Cells, AS 2005, 947, as amended) and excludes the patentability of processes of parthenogenesis using human germ cells and parthenotes created by such processes (Article 2(c) of the Bundesgesetz über die Erfindungspatente (Federal Act concerning Patents on Inventions, AS 1955, 871, as amended)). The Swiss National Advisory Commission on Biomedical Ethics invoked not only the protection of embryos as an argument in favour of this prohibition, but also concerns relating to oocyte donation, as parthenogenesis is dependent on the availability of oocytes. Swiss National Advisory Commission on Biomedical Ethics, *Research involving human embryos and foetuses*, Opinion No 11/2006, Berne, p. 15.

28 — Judgments in *Netherlands v Parliament and Council*, EU:C:2001:523, paragraphs 37 and 38, *Commission v Italy*, C-456/03, EU:C:2005:388, paragraph 78, *Brüstle*, EU:C:2011:669, paragraph 29.

29 — Judgments in *Commission v Italy*, EU:C:2005:388, paragraph 78, *Brüstle*, EU:C:2011:669, paragraph 29.

30 — Judgment in *Brüstle*, EU:C:2011:669, paragraphs 26 and 34.

31 — Judgment in *Brüstle*, EU:C:2011:669, paragraph 36.

49. Thus, when considering whether parthenotes are human embryos in the sense of the Directive in light of the further clarification made by the referring court, it has to be borne in mind that this issue relates to a prohibition of patentability that is part of a non-exhaustive list contained in Article 6(2) of the Directive, which is merely illustrative of the considerations contained in Article 6(1).

3. Article 5 of the Directive

50. A final preliminary consideration is required with respect to Article 5 of the Directive. The Court of Justice put two questions to the participants in the hearing, the second of which inquired whether a parthenote may be classified as a ‘human body’ at the initial stage of its formation and development, within the meaning of Article 5(1) of the Directive or, if not, as an ‘element isolated from the human body’ within the meaning of Article 5(2). In my opinion it is perfectly possible to answer the question referred without taking into account the content of Article 5 of the Directive.

51. According to Article 5(1) and (2) of the Directive, while the human body at the various stages of its formation and the simple discovery of one of its elements are not patentable, an element isolated from the human body or otherwise produced by means of a technical process can be patented. The distinction recalls one of the basic principles of patent law that only inventions and not discoveries are patentable.³²

52. A parthenote is neither a human body at a stage of its formation and development, nor one of its elements. Instead, parthenotes are produced by means of a technical process and hence Article 5(1) of the Directive by itself does not prevent their patentability. As the Court held in *Netherlands v Parliament and Council*, ‘inventions which combine a natural element with a technical process enabling it to be isolated or produced for an industrial application can be the subject of an application for a patent’.³³

B – *The question referred*

53. I now turn to the question whether parthenotes are human embryos under the Directive, particularly in the light of the referring court’s specifications and the Court of Justice’s judgment in *Brüstle*, in which the Court held, in the operative part of its judgment, that ‘... any non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis constitute[s] a “human embryo”’.³⁴

54. Before I undertake my own analysis, however, I will present the views of the parties.

1. Views of the parties

55. The parties to the proceedings disagree as to whether parthenotes constitute human embryos.

56. ISC, France, Sweden, the United Kingdom and the Commission consider parthenotes not to be ‘human embryos’ in the sense of Article 6(2)(c) of the Directive.

32 — See also recital 16; Opinion of Advocate General Jacobs in *Netherlands v Parliament and Council*, C-377/98, EU:C:2001:329, point 199.

33 — Judgment in *Netherlands v Parliament and Council*, EU:C:2001:523, paragraph 72. See also recitals 20 and 21, and judgment in *Commission v Italy*, EU:C:2005:388, paragraph 66.

34 — Judgment in *Brüstle*, EU:C:2011:669, operative part.

57. ISC argues that the Directive encourages research in the field of genetic engineering by granting patent incentives while limiting patentability out of respect for human dignity, by e.g. excluding the human body³⁵ as well as the use of totipotent human cells from patentability.³⁶ The interpretation of the term ‘human embryo’ would have to strike an appropriate balance between these two considerations. While human dignity and integrity of the person demand that fertilised human ova have to be regarded as embryos, an organism that is not capable of developing into a human being or at least of commencing the process which leads to a human being cannot be regarded as an embryo. As an ovum without paternal DNA can develop to the blastocyst stage, but not to term, as, in other words, the cells of a parthenote are pluripotent even in the first few cell divisions and never totipotent, thus excluding development to term, parthenotes cannot be regarded as human embryos. They are, hence, unlike fertilised ova at all stages of their development. An appropriate balance between the protection of human dignity and providing patent incentives to research can, in the opinion of ISC, only be struck if parthenotes are not excluded from patentability.

58. As to the Court’s holding in *Brüstle*, ISC argues primarily that this is not in conflict with considering parthenotes not to be human embryos. The Court’s reference to an organism ‘capable of commencing the process of development of a human being’, according to ISC, meant to establish that it is necessary to inquire whether organisms are capable of commencing the process of development that leads to a human being, leaving it to the national courts to decide whether this condition is fulfilled. ISC finds support for its argument in the Court’s focus on the development of a human being and in the fact that the Court applied the very same argument to fertilised ova and non-fertilised ova subjected to somatic-cell nuclear transfer, both of which can develop into human beings. Finally, ISC points out that in *Brüstle* the referring court and the parties submitted unclear information on whether parthenotes can develop into human beings. Should the Court’s ruling be read differently, namely as holding that parthenotes are human embryos due to the parallel character of their (initial) development with that of embryos, ISC considers a departure from *Brüstle* as justified given that the referring court in the present case has explicitly pointed out that parthenotes and fertilised ova are not identical at any stage of their development. ISC finds further confirmation for its position in the decision handed down by the Bundesgerichtshof in *Brüstle* after the preliminary reference, in which the German court considered certain non-viable organisms developed from oocytes fertilised in the course of in vitro fertilisation not to be embryos under the holding of the Court of Justice, as they are not capable of setting in motion the process of development of a human being.

59. The UK argues that the Court needs to clarify its ambiguous ruling relying on the expression ‘capable of commencing the process of development of a human being’ in *Brüstle*. It states that the technical background relating to parthenotes was not accurately reflected in the observations submitted in *Brüstle*, that the scientific understanding of parthenotes has developed since then and that parthenotes cannot, now, be considered as identical with embryos at any stage of their development. The UK points out that both the Court and the Advocate General had recognised in *Brüstle* that answers in a technological field that is still developing might change with advances in technology. The term ‘capable of commencing the process of development of a human being’ should be understood as extending only to development processes that at least have the potential to go through to completion and give rise to a viable human being, which would also achieve the required balance between the desired incentives for the biotechnology industry and dignity and integrity of the person.³⁷ France and Sweden endorse a similar understanding of the formula of the Court and consider that in light of the current state of science parthenogenesis cannot be regarded as a technique capable of commencing the process of development of a human being. The Commission holds a similar view

35 — Article 5(1) of the Directive

36 — Recital 38 of the Directive

37 — The United Kingdom also proposed to adopt the distinction between totipotent and pluripotent cells drawn in the opinion of Advocate General Bot in *Brüstle*.

and argues that the Court's assessment that parthenotes fulfil these conditions and constitute human embryos was based on written submissions which have been proved erroneous in the light of scientific developments. The Commission urges the Court to adopt criteria that are not likely to be subject to change due to the rapid developments in biotechnology.

60. Portugal also supports this reading of the formula of the Court, but emphasises the risk of further manipulation of a parthenote leading to its viability. It proposes to answer the question in the affirmative, unless it is demonstrated that parthenotes are not capable of developing into human beings through any kind of additional manipulation. It would be up to the national court to determine whether the patent application clearly demonstrates that such capability does not exist or whether the patent claims renounce a right to undertake such manipulations. The United Kingdom specifically rejects the relevancy of the possibility of such future manipulations, relying on the reasoning of the German Bundesgerichtshof in the final decision of the *Brüstle* case, which had stated that the decisive factor was the capacity of a cell itself, not its capacities after the cell had been manipulated.

61. Poland, however, would answer the question in the affirmative. It argues that in the interest of safeguarding human dignity the Court correctly relies on the capacity of *commencing* the process of development of a human being. Even though parthenotes cannot, according to our current understanding, develop into human beings, they initially undergo the same stages of development as a fertilised ovum, namely cell division and differentiation, and hence constitute human embryos.

2. Analysis

a) The judgment in *Brüstle*

62. The Court undertook to define the term 'human embryos' in Article 6(2)(c) of the Directive in *Brüstle*.³⁸ It held 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"'.³⁹ As to cells obtained in the blastocyst stage, however, the Court took a different approach: '[I]t is for the referring court to ascertain, in the light of scientific developments, whether a stem cell obtained from a human embryo at the blastocyst stage constitutes a "human embryo" within the meaning of Article 6(2)(c) of Directive 98/44.'⁴⁰

63. This wording clearly and plainly seems to include parthenotes in the definition of 'human embryos'. However, the operative part of the judgment has to be read in the light of the grounds which have led to it and constitute its essential basis.⁴¹

64. The question in *Brüstle* was referred to the Court in a proceeding concerning the validity of a German patent filed by Mr Brüstle covering 'isolated and purified neural precursor cells, processes for their production from embryonic stem cells and the use of neural precursor cells for the treatment of neural defects'.⁴² As part of its question about the meaning of 'human embryos' the Bundesgerichtshof explicitly inquired whether 'unfertilised human ova whose division and further development have been stimulated by parthenogenesis' are included in the term,⁴³ as the patent specifications named such ova as an alternative way to obtain human embryonic stem cells.

38 — Judgment in *Brüstle*, EU:C:2011:669.

39 — Judgment in *Brüstle*, EU:C:2011:669, operative part.

40 — Ibid.

41 — Judgment in *Asteris and Others v Commission*, Joined Cases 97/86, 99/86, 193/86 and 215/86, EU:C:1988:199, paragraph 27; judgment in *Bosch*, 135/77, EU:C:1978:75, paragraph 4.

42 — Judgment in *Brüstle*, EU:C:2011:669, paragraph 15.

43 — Judgment in *Brüstle*, EU:C:2011:669, paragraph 23.

65. Relying on the context and aim of the Directive, namely recitals 16 and 38, Article 5(1) and Article 6, the Court argued that the intent of the directive was to exclude any possibility of patentability where respect for human dignity could be affected, concluding that the notion of ‘human embryo’ within the meaning of Article 6(2)(c) of the Directive must hence ‘be understood in a wide sense’.⁴⁴

66. The Court then proceeded to state that 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*’.⁴⁵

67. This criterion, i.e. whether an organism is ‘capable of commencing the process of development of a human being’, is key to the Court’s argument. If an organism has this capability ‘just as an embryo created by fertilisation of an ovum’, it is the functional equivalent of an embryo and hence is included within the concept of ‘human embryo’.⁴⁶

68. The Court goes on to apply the criterion to parthenotes and non-fertilised ova after somatic-cell nuclear transfer and considers both of these organisms to be capable of commencing the process of development of a human being.⁴⁷ With respect to stem cells obtained from a human embryo at the blastocyst stage, however, the Court leaves it to national courts to determine whether they have this capacity and ‘therefore, are included within the concept of “human embryo” within the meaning and for the purposes of the application of Article 6(2)(c) of the Directive’.⁴⁸

b) My understanding of *Brüstle*

69. How is one to understand the term ‘capable of commencing the process of development of a human being’? At first sight it could seem ambiguous, emphasising either the parallelism of the first developmental steps, i.e. whether an organism engages in a process of cell division and differentiation similar to that of a fertilised ovum, or emphasising the fact that the organism has the inherent capacity of developing into a human being.

70. However, a closer look at the judgment shows that the Court meant to inquire whether an unfertilised ovum has the inherent capacity of developing into a human being.

71. In my view, in *Brüstle* the Court has established a functional equivalence between fertilised ova, non-fertilised ova subjected to somatic-cell nuclear transfer and parthenotes. Even though parthenotes, as it is now apparent, are the only organisms among these three that cannot develop into human beings, the Court treats parthenotes and non-fertilised ova subjected to somatic-cell nuclear transfer within the same paragraph without mentioning any distinction between them and stating instead that both organisms ‘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’.⁴⁹ Had the Court been aware of the fundamental difference between parthenotes and non-fertilised ova subjected to somatic-cell nuclear transfer and nevertheless wanted to establish a functional equivalence between the two, it would certainly have discussed this difference.

44 — Judgment in *Brüstle*, EU:C:2011:669, paragraphs 32 to 34.

45 — Judgment in *Brüstle*, EU:C:2011:669, paragraph 35, emphasis is mine.

46 — See judgment in *Brüstle*, EU:C:2011:669, paragraph 36.

47 — Ibid.

48 — Judgment in *Brüstle*, EU:C:2011:669, paragraph 37.

49 — Judgment in *Brüstle*, EU:C:2011:669, paragraph 36.

72. It is hence reasonable to assume that the observations submitted at the time in *Brüstle* caused the Court to have the impression that all three organisms possess the inherent capacity to develop into a human being. The Commission supported this point of view in its submission in the present case, giving examples of statements in submissions made in *Brüstle* that could have created this impression. The assumption is also confirmed by the opinion of Advocate General Bot, which argues that parthenotes are embryos ‘in so far as, *according to the written observations submitted to the Court*, totipotent cells’ could be obtained from them, i.e. cells that can develop into a human being.⁵⁰

73. According to my reading of the Court’s argument, the decisive criterion that should be taken into account for determining whether an unfertilised ovum is a human embryo hence is whether that unfertilised ovum has the inherent capacity of developing into a human being, i.e. whether it really constitutes the functional equivalent of a fertilised ovum.

74. Given the facts stated unequivocally by the referring court and the parties to the current proceeding it now appears that a parthenote does not, per se, have the required inherent capacity of developing into a human being and hence as such does not constitute a ‘human embryo’.⁵¹

75. Accordingly and with the one *caveat* that I shall come to subsequently the question referred by the High Court has to be answered in the negative, meaning that unfertilised human ova whose division and further development have been stimulated by parthenogenesis as described by the referring court are not included in the term ‘human embryos’ in Article 6(2)(c) of the Directive.

76. The caveat in question concerns the eventuality described above⁵² that a parthenote is manipulated genetically in such a way that it can develop to term and thus into a human being. As such manipulations have already been tried successfully on non-human mammalian parthenotes (namely mice), it cannot be excluded categorically that they are also possible, in the future, with respect to human parthenotes, even though these manipulations would often be illegal.⁵³

77. Nevertheless, the mere possibility of a posterior genetic manipulation altering the fundamental characteristics of a parthenote does not change the parthenote’s character *before* the manipulation. As I have stated before, a parthenote as such does not, according to current scientific knowledge, have the ability to develop into a human being. Where the parthenote is manipulated in such a way that it actually obtains the respective capacity, it can no longer be considered a parthenote and it cannot be, consequently, patented.

78. Accordingly, the question of the High Court cannot be answered with a simple negative. On the contrary, prudence imposes to make clear that parthenotes can only be excluded from the term embryos to the extent that they have not been genetically manipulated to become capable of developing into a human being.

79. In light of these arguments I propose that the answer to the question submitted by the referring court should be that unfertilised human ova whose division and further development have been stimulated by parthenogenesis are not included in the term ‘human embryos’ in Article 6(2)(c) of the Directive as long as they are not capable of developing into a human being and have not been genetically manipulated to acquire such a capacity.

50 — Opinion by Advocate General Bot in Case C-34/10 *Brüstle*, EU:C:2011:138, point 91. Emphasis added.

51 — See the discussion in Austriaco, N., ‘Complete Moles and Parthenotes Are Not Organisms’, in: Suarez, A., and Huarte, J., (eds), *Is this Cell a Human Being?*, Springer, Heidelberg, 2011, p. 45.

52 — See paragraph 32 of this opinion.

53 — France has pointed out in the hearing that such manipulations are illegal in France. See also, in this respect, Article 13 of the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, signed in Oviedo, 4 April 1997, banning certain interventions seeking to modify the human genome. The Convention of the Council of Europe has been ratified by 29 States, among which several Member States of the European Union, but not the Union itself.

V – Conclusion

80. In the light of the foregoing, I suggest that the Court should answer the question referred by the High Court of Justice, Chancery Division (Patents Court) as follows:

Unfertilised human ova whose division and further development have been stimulated by parthenogenesis are not included in the term ‘human embryos’ in 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 as long as they are not capable of developing into a human being and have not been genetically manipulated to acquire such a capacity.