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PATENTS ACT 1977

APPLICANT International Stem Cell Corporation

ISSUE Whether Patent Applications GB0621068.6 and GB0621069.4 comply with Schedule A2

HEARING OFFICER Dr L Cullen

DECISION

Introduction

1 This decision concerns two related GB patent applications GB0621068.6 entitled "*Parthenogenic activation of oocytes for the production of human embryonic stem cells*" and GB0621069.4 entitled "*Synthetic cornea from retinal stem cells*", both filed on 23 October 2006, initially in the name of LifeLine Cell Technology. GB0621068.6 has a declared priority date of 21 October 2005, while GB0621069.4 has a declared priority date of 24 July 2006. GB0621068.6 was published as GB 2431411 A, while GB0621069.4 was published as GB 2440333 A. Both applications were assigned to International Stem Cell Corporation in 2008.

2 The first examination report on GB0621068.6 was issued on 29 October 2009, and there followed several rounds of correspondence between the examiner and the applicant's representative. Objections relating to novelty, inventive step, clarity, support and patentability under paragraphs 3(a) and (3b) of Schedule A2 to the Patents Act 1977 (referred to hereafter as the Act) were overcome in the course of prosecution, but no agreement could be reached concerning patentability under paragraph 3(d) of Schedule A2 to the Act.

3 The first examination report on GB0621069.4 was issued on 3 August 2010. Again, there were then several rounds of correspondence between the examiner and the applicant's representative, and objections relating to novelty, inventive step, methods of treatment [section 4A(1) of the Act], clarity and support were overcome. However, as with GB0621068.6, no agreement could be reached concerning patentability under paragraph 3(d) of Schedule A2 to the Act. This application gave rise to a divisional application, GB1111329.7, filed on 1 July 2011 and published as GB 2480931 A; however, this divisional application was withdrawn by the applicant on 6 February 2012.

4 The unresolved questions concerning the patentability of GB0621068.6 and GB0621069.4 under paragraph 3(d) of Schedule A2 to the Act came before me to be decided at an oral hearing on 27 March 2012. The applicant was represented by Mr George Godar of DLA Piper UK LLP, a solicitor advocate; and Dr Lisa Haile of DLA Piper US LLP, who provided additional technical information regarding the invention. They were assisted by Mr Nick Bassil and Dr Jane Hollywood of Kilburn & Strode LLP, patent attorneys. Also present were the examiner, Dr Graham Feeney, and my assistant for the hearing, Mr Richard Sewards.

Compliance Period

5 The normal unextended period under Section 20 of the Act for putting application GB0621068.6 in order ended on 29 October 2010. This period was extended by the applicant as of right to 29 December 2010. The compliance period was then extended a further 10 times under the Comptroller's discretion, and the extended compliance period will now end (subject to any further discretionary extensions) on 28 August 2012. The reason for these discretionary extensions to the compliance period were to await the decision of the Court of Justice of the European Union (CJEU) in case C-34/10, *Oliver Brüstle v Greenpeace* (hereafter referred to as C-34/10 *Brüstle*), and, following its handing down on 18 October 2011, to allow for the judgment to be considered, its implications analysed, and finally to allow time for the issue of this decision. This judgment is directly relevant to the issue at question, i.e., is the invention excluded from patentability under Article 6(2)(c) of Directive 98/44/EC on the legal protection of biotechnological inventions[1] (hereafter referred to as the Directive) which refers to uses of human embryos for industrial or commercial purposes. This has been implemented into UK law in paragraph 3(d) of Schedule A2 to the Act (see paragraphs 18-21 below).

6 The normal unextended period under Section 20 of the Act for putting application GB0621069.4 in order ended on 3 August 2011. This period was extended by the applicant as of right to 3 October 2011. The compliance period was then extended a further 5 times under the Comptroller's discretion, and the extended compliance period will now end (subject to any further discretionary extensions) on 6 October 2012. The reasons for these discretionary extensions to the compliance period were the same as those for GB0621068.6.

The Invention

7 The applications in suit concern methods to produce human stem cells, and corneal tissues derived from such stem cells, using parthenogenesis to activate

[1] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions, see OJEC, L 213, 30.7.98, pages 13-21. This is commonly referred to as the Biotech Directive.

a human oocyte; i.e., stimulation of a human oocyte, without fertilisation by a sperm cell, to produce a parthenogenetically-activated oocyte. The stimulated human oocyte[2] divides in a manner analogous to that of a fertilised human embryo, to produce a parthenogenetically-derived structure analogous to the blastocyst stage of normal embryonic development, from which stem cells can be obtained.

8 At this point I need to explain the terminology I have used in this decision. The present applications, and at least some of the journal papers published on parthenogenesis (to which I will refer later), freely use the same terminology (i.e. "embryo", "blastocyst" and "embryonic stem cell") to describe the entities derived from a parthenogenetically-activated oocyte as is also generally used to describe the analogous entities derived from a fertilised ovum. However, as I will explain, one of the key elements of the applicants' case is that the results of parthenogenetic activation are **not** identical to fertilised human embryos. To avoid any confusion, I have not used these terms in relation to parthenogenetically-derived entities; instead, I have referred to "parthenogenetically-activated oocytes", "parthenogenetic blastocyst-like structures" and "parthenogenetic stem cells". In addition, the generic term "parthenote" is used to refer to any entity (whether single-celled or multicellular) resulting from the parthenogenetic activation of an oocyte or its subsequent division and development.

9 GB0621068.6 concerns the production of human stem cells from parthenotes, whilst GB0621069.4 concerns human synthetic corneas and corneal tissues derived from parthenotes.

The Claims

10 The claims under consideration at the hearing were those filed on 12 October 2011 in respect of both applications.

11 There are five independent claims for GB0621068.6. Claim 1 defines a method of producing a human stem cell line and reads:

A method of producing a human stem cell line comprising:

a) parthenogenetically activating a human oocyte, wherein activating comprises: i) contacting the oocyte with an ionophore in a gas mixture environment comprising 5% CO_2 and 20% O_2 and ii) contacting the oocyte with a serine-threonine kinase inhibitor in a gas mixture environment comprising an O_2 concentration of 2% O_2 to 5% O_2;

[2] The applications in suit refer throughout to "*oocytes*", whereas the CJEU decision in C-34/10 *Brüstle* uses the words "*ovum*" or "*ova*". Strictly, an *oocyte* is a developmental stage which leads to a mature *ovum* (or egg); however, the word "*oocyte*" is also used more broadly to encompass the female germ cell at all its stages – I construe the present applications in this broader sense, given that activation of both haploid and diploid oocytes is clearly envisaged. The two words, *oocyte* and *ovum,* are therefore used interchangeably in this decision depending on the context.

b) cultivating the activated oocyte of step (a) in a gas mixture environment comprising an O_2 concentration of 2% O_2 to 5% O_2 until blastocyst formation;

c) transferring the blastocyst to a layer of feeder cells, and culturing the transferred blastocyst in a gas mixture environment comprising 5% CO_2 and 20% O_2;

d) mechanically isolating an inner cell mass (ICM) from trophectoderm of the blastocyst of step (c); and

e) culturing the cells of the ICM of step (d) on a layer of feeder cells, wherein culturing step (e) is carried out in a gas mixture environment comprising 5% CO_2 and 20% O_2.

12 Claim 12 defines a further method of producing a human stem cell line, from either a cryopreserved (i.e., frozen) oocyte or a cryopreserved parthenote. This claim reads:

A method of producing a human stem cell line from a cryopreserved oocyte or parthenotes comprising:

a) microinjecting into the cytoplasm of the oocyte or parthenotes a cryopreservation agent;

b) freezing the oocyte or parthenotes to a cryogenic temperature to cause the oocyte or parthenotes to enter a dormant state;

c) storing the oocyte or parthenotes in the dormant state

d) thawing the oocyte or parthenotes

e) parthenogenetically activating a oocyte from step (d) comprising i) contacting the oocyte with an ionophore in a gas mixture environment comprising 5% CO_2 and 20% O_2 and ii) contacting the oocyte with a serine-threonine kinase inhibitor in a gas mixture environment comprising an O_2 concentration of 2% O_2 to 5% O_2;

f) cultivating the parthenote of step (d) or oocyte of step (e) in a gas mixture environment comprising an O_2 concentration of 2% O_2 to 5% O_2 until blastocyst formation;

g) isolating an inner cell mass (ICM) from trophectoderm of the blastocyst; and

h) culturing the cells of the ICM of step (g) on a layer of feeder cells or extracellular matrix (ECM) substrate,

wherein culturing step (g) is carried out in a gas mixture environment comprising 5% CO_2 and 20% O_2.

13 Claim 30 is a product-by-process claim to a human stem cell line produced according to the method of the previous claims. Claims 29 and 32 are omnibus claims to a method of producing human stem cells, and a stem cell line, respectively.

14 There are 4 independent claims for GB0621069.4. Claim 1 defines a method of producing a synthetic cornea or corneal tissue and (with the correction of two obvious typographical errors) reads:

A method of producing a synthetic cornea or corneal tissue comprising:

a) parthenogenetically activating a human oocyte obtained from a donor, wherein activating comprises: i) contacting the oocyte with an ionophore at high O_2 tension and ii) contacting the oocyte with a serine-threonine kinase inhibitor at low O_2 tension;

b) cultivating the activated oocyte of step (a) at low O_2 tension until blastocyst formation;

c) transferring the blastocyst to a layer of feeder cells, and culturing the transferred blastocyst under high O_2 tension;

d) mechanically isolating an inner cell mass (ICM) from trophectoderm of the blastocyst of step (c);

e) culturing the cells of the ICM of step (d) on a layer of human feeder cells under high O_2 tension, wherein retinal stem cells are identified in culture by human embryonic stem cell markers (hES) and neuron specific markers and allowing synthetic cornea or corneal tissue to develop.

15 Claim 11 is a product-by-process claim to a synthetic cornea or corneal tissue produced according to the method of the previous claims. Claims 10 and 14 are omnibus claims to a method of producing synthetic cornea or corneal tissue, and a synthetic cornea or corneal tissue, respectively.

16 Furthermore, as discussed below (see paragraphs 42-44), I invited the applicants to submit further evidence and/or argument in light of two scientific papers which were presented at the hearing and which had not been raised with the applicants prior to the hearing. In written submissions dated on 13 April 2012, the applicants provided further arguments together with a set of amended claims for both applications, for my consideration. The details of these amendments are discussed below in paragraphs 43-44.

The Issue to be Decided

17 The issue to be decided is whether the claimed methods of producing stem cell lines (GB0621068.6), or synthetic corneas or corneal tissue (GB0621069.4), and/or the stem cell lines or synthetic corneas or corneal tissue thus produced,

constitute uses of human embryos for industrial or commercial purposes, and thus are unpatentable under paragraph 3(d) of Schedule A2 to the Act.

The Law

18 Section 76A(1) of the Act states:

"76A.-(1) Any provision of, or made under, this Act is to have effect in relation to a patent or an application for a patent which concerns a biotechnological invention, subject to the provisions of Schedule A2."

19 Schedule A2 was introduced into the Act in 2000 to implement articles 1-11 of Directive 98/44/EC on the legal protection of biotechnological inventions (the Directive). Paragraph 3(d) of Schedule A2, which implements Article 6(2)(c) of the Directive, excludes from patentability certain human embryo related inventions as follows:

"3. The following are not patentable inventions –

…..

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

20 The relevant parts of corresponding Article 6 of the Directive are as follows:

"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;"

21 Neither the Act nor the Directive provides a definition of what constitutes an "embryo". For this reason, the examiner turned to the definition provided by the UK Human Fertilisation and Embryology Act 1990, as amended by the Human Fertilisation and Embryology Act 2008 (the "HFE Act"). Section 1 of the HFE Act, as amended, defines an embryo as follows:

"(1) In this Act (except in section 4A or in the term "human admixed embryo")–

(a) embryo means a live human embryo and does not include a human admixed embryo (as defined by section 4A(6)), and

(b) references to an embryo include an egg that is in the process of fertilisation or is undergoing any other process capable of resulting in an embryo."

Analysis & Argument

22 The examiner's objection, as set out in his letter of 8 March 2012, is that the claimed methods of producing stem cell lines (GB0621068.6), or synthetic corneas or corneal tissue (GB0621069.4), and/or the stem cell lines or synthetic corneas or corneal tissue thus produced, constitute uses of human embryos for industrial or commercial purposes, and are thus excluded from patentability under Paragraph 3(d) of Schedule A2 of the Act. In making this objection, the examiner's argument was essentially that the parthenogenetically-activated oocytes produced in step (a) of claim 1 of both applications, and/or the parthenogenetic blastocyst-like structures derived from them in the subsequent steps, fall within the definition of a "human embryo" for the purpose of Schedule A2 of the Act. The examiner gave two reasons for this argument; firstly, the decision of the CJEU in case C-34/10 *Brüstle* and, secondly, the definition of the term "embryo" provided by the HFE Act.

23 Schedule A2 implements articles 1-11 of the Directive. As this is a European Union Directive, its interpretation falls within the remit of the CJEU. In case C-34/10 *Brüstle,* the CJEU addressed three questions concerning inventions relating to human embryos and embryonic stem cells which had been raised by the German Bundesgerichtshof[3]. In particular, the referral included the following question:

"1. What is meant by the term "human embryos" in Article 6(2)(c) of [the Directive]?

(a) Does it include all stages of the development of human life, beginning with the fertilisation of the ovum, or must further requirements, such as the attainment of a certain stage of development, be satisfied?

(b) Are the following organisms also included:

...

- *unfertilised human ova whose division and further development have been stimulated by parthenogenesis?*

…

24 In answering part (a) of this question, the CJEU stated, at paras 34 and 35 that:

[3] The German Federal Patent Court

"*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."

25 On the specific question of whether parthenogenetically-activated human ova or oocytes are included within the term "human embryos", the CJEU held (at paragraph 38 of the judgment, emphasis added):

"...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' within the meaning of Article 6(2)(c) of the Directive;"*

26 On the face of it, this clear and unambiguous statement from the CJEU would appear to leave me with no choice other than to refuse the present patent applications, as they both claim methods in which an unfertilised oocyte is activated by parthenogenesis and caused to develop into a parthenogenetic blastocyst-like structure and this parthenogenetic blastocyst-like structure is then used to produce stem cells and/or corneal tissue.

27 If the parthenogenetically-activated oocyte and the parthenogenetic blastocyst-like structure constitute human embryos as held by the CJEU, then, for both applications, claim 1 relates to the unpatentable commercial or industrial use of a human embryo. Moreover, this conclusion appears to be supported in UK national law by the definition of an 'embryo' provided in the HFE Act, which includes "*an egg that is in the process of fertilisation* ***or is undergoing any other process capable of resulting in an embryo****."* At the hearing, Mr Godar presented a complex but coherent argument, concerning both the science and the law, as to why this should not be the case, which I need to set out below in some detail.

The Inventive Concept

28 Mr Godar began by setting out the inventive concept of the applications in suit. He stated that the applications concern methods of obtaining of pluripotent stem cells by parthenogenetically-activating human oocytes, cultivating the activated oocyte in an appropriate manner until the formation of a parthenogenetic blastocyst-like structure, extracting the inner cell mass from the parthenogenetic blastocyst-like structure and culturing those cells. This method, and the cells produced by such a method, provides the inventive concept of GB0621068.6. The inventive concept of GB0621069.4 includes these steps and the further step of identifying, amongst the pluripotent stem

cells, those which are retinal stem cells, and allowing synthetic cornea or corneal tissue to develop from them.

The Legal Context

29 Mr Godar argued that, where a directive has been transposed into UK law by amending an existing statute, or creating a new statute, the correct approach to statutory interpretation is to consider the wording of the directive itself, as held by the UK Court of Appeal in *Roche Products Ltd & Anor v Kent Pharmaceuticals Ltd* [2006] EWCA Civ 1775, *Laboratoires Goemar SA v La Mer Technology Inc* [2005] EWCA Civ 978 and *Football Dataco Ltd & Ors v Sportradar GmbH & Anor* [2011] EWCA Civ 330. I accept this point but I consider that nothing turns on it in this case because the wording of the Act and the Directive are essentially the same.

30 More significantly, Mr Godar argued that as the Directive has been interpreted by the CJEU, then that interpretation is binding on the Office, regardless of other provisions of UK national law such as the HFE Act. Indeed, the CJEU explicitly rejected the idea that member states should be free to interpret the term "human embryo" in Article 6(2)(c) of the Directive by reference to national laws:

> *"Although the text of the Directive does not define human embryo, nor does it contain any reference to national laws as regards the meaning to be applied to those terms. It therefore follows that it must be regarded, for the purposes of application of the Directive,* ***as designating an autonomous concept of European Union law which must be interpreted in a uniform manner throughout the territory of the Union****." (emphasis added)*

31 Mr Godar therefore argued that the definition of "human embryo" provided by the HFE Act is now irrelevant for the purpose of determining patentability under Article 6(2)(c) of the Directive (and therefore Paragraph 3(d) of Schedule A2 of the Act). I agree with the applicant's submission on this point – the CJEU has provided a definition of "human embryo" for the purpose of Article 6(2)(c) which is binding on me. The definition provided in Section 1 of the HFE Act is provided for an entirely different purpose, i.e., the regulation of embryo research and fertility treatment in the UK, and so, now, can be no longer serve as a source of guidance in interpreting the Act (i.e., the Patents Act 1977). This has been superseded by the decision in C-34/10 *Brüstle* which applies directly to the interpretation of the term 'human embryo' in paragraph 3(d) of Schedule A2 of the Act.

32 Of course, this still leaves the applicants with the problem that the CJEU in C-34/10 *Brüstle* clearly stated that parthenogenetically-activated human oocytes are considered to be human embryos for the purpose of the Directive. In dealing with this aspect, Mr Godar's argument focused on the over-arching definition of "human embryo" provided by the CJEU in this decision and the reasoning behind it. The CJEU considered the object and aims of the Directive, as set out in the preamble and the recitals, and held that the purpose of Article 6(2) was to exclude any possibility of patentability where respect for human

dignity could thereby be affected. The CJEU held (at paragraph 35) that a human ovum must be regarded as a "human embryo" from the moment of fertilisation "*since that fertilisation is such as to commence the process of development of a human being*". Mr Godar emphasised that the applicants do not contest this definition or the over-arching principle behind it.

33 The CJEU went on in paragraph 36 to consider **non-fertilised** human ova which are stimulated to division and further development by either nuclear transfer or, as in the present applications, by parthenogenetic stimulation. The CJEU held:

> "*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.*"

34 However, Mr Godar argued that a parthenogenetically-activated human oocyte is **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*", and so this part of the CJEU's decision was based on a flawed factual basis and should not be binding on me.

The Science

35 Before addressing the legal question of whether this aspect of the decision is binding on me, I first need to consider the scientific question of whether, and to what extent, an oocyte which is caused to divide by parthenogenetic stimulation according to the teaching of the present applications is capable of further development.

36 To support their argument that a parthenogenetically-activated human oocyte is **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*", the applicants presented expert declarations from Dr Paul De Sousa, a Senior Research Fellow at the Scottish Centre for Regenerative Medicine, University of Edinburgh and Chief Scientific Officer at Roslin Cells Ltd., and Professor John Anstell, Emeritus Professor of Molecular and Clinical Medicine, University of Edinburgh and Visiting Professor of Stem Cell Sciences at University Campus Suffolk, together with a number of published papers:

(1) *Revazova et al*., Cloning and Stem Cells [2007] Vol 9 pp 432-449;
(2) *Kastenberg et al.*, Transplantation Reviews [2008] Vol 22 pp 215-222;
(3) *Brevini & Gandolfi*, Cell Proliferation [2008] Vol 41 pp 20-30; and
(4) *Kim et al*., Cell Stem Cell [2007] Vol 1 pp 1-7.

37 Mr Godar's argument, supported by this evidence, was that a parthenogenetically-activated oocyte, which contains only maternal DNA (whether haploid or diploid) cannot ever develop to term, i.e. to provide a viable human being, and neither the activated oocyte, nor any of the cells produced by its division, are totipotent – they are only pluripotent and cannot give rise to

placental tissue. In contrast, in the first few cycles of cell division (before blastocyst formation), the cells of a human embryo derived from a fertilised ovum are totipotent.

38 It was explained that in the unfertilised oocyte, certain genes are repressed by a mechanism known as genomic imprinting, and for development to term the paternal copy (which is not repressed) of these genes must be provided by fertilisation. Similarly, there are genes which are repressed in the sperm cell and are only capable of being expressed from the maternal DNA. When an oocyte is caused to divide by parthenogenetic stimulation, the absence of the paternal copy of the maternally-repressed genes prevents normal development of the parthenogenetic "embryo" to term – in particular, there is no development of the placental tissue. Dr De Souza's declaration highlighted the following statement from the paper by *Brevini and Gandolfini* (see page 21, emphasis added):

> "*Mammalian parthenotes can develop to different stages after oocyte activation, but* ***never to term***."

I also note the conclusion from this paper (see page 22) that states:

> "*Irrespective of how activation has been performed and what ploidy has been generated, parthenotes are unable to develop to term."*

This characteristic is discussed in more detail and a number of examples are provided from studies in mice, sheep, rabbit and pig, which indicate that mammalian parthenotes will not develop and, indeed, arrest at a specific stage. The reason for this failure to develop to term is considered to be genomic imprinting.

39 The paper by *Revazova et al*., describes the isolation of 'human embryonic stem cells' from 'parthenogenetic embryos' (see, for example, page 437, section entitled '*Derivation of parthenogenetic hESC lines*') – indeed, the same wording has been used in the descriptions of the present applications. I note that four of the authors of this paper are listed as inventors for the two patent applications at issue in this case. However, Dr De Souza's declaration states that the *Revazova et al.* paper does not provide support for the conclusion that parthenogenetic stimulation could give rise to an embryo **according to the definition provided by the CJEU** – i.e., something that 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*".

40 It is an essential part of the applicants' case that the parthenogenetically-activated oocytes produced by the methods of the claimed inventions have an inherent biological limitation that prevents these activated oocytes from being "*capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do so*". However, the paper by *Kim et al.* (referred to in Professor Ansell's declaration) cited a paper by *Wu et al.*[4], which demonstrates live-born mice of parthenogenetic origin. The

[4] Reproduction [2006] Vol 131, pp 481-88

examiner also identified a paper by *Chen et al.*[5], which also disclosed live-born mice of parthenogenetic origin produced by a different method. As these two papers had not been presented to the applicants prior to the hearing, I invited the applicants to submit further arguments or evidence in writing after the hearing on whether, in the light of this evidence from mouse models, it is possible that the inherent biological limitation preventing development of the parthenote to term, as asserted by Mr Godar and his colleagues (and discussed above), could be overcome in human cells. In other words, is it possible that activated human oocytes which are "*capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do s*o" **could** be produced, by methods falling within the scope of the claims of these applications?

41 In the written submissions filed on 13 April 2012 following the hearing, the applicants' representatives argued that these two papers did not relate to parthenogenesis alone; in fact, they disclosed a combination of parthenogenesis with extensive genetic manipulation, including the addition of exogenous genetic materials, to "rescue" the maternally-inactivated genes. Specifically, *Wu et al*.[4], disclosed a method in which an oocyte from a mouse which was genetically-modified (to delete an imprinted gene and express a foreign copy of a different imprinted gene) was fused with a further oocyte. *Chen et al.*[5], disclosed a method in which cultured diploid (i.e., 2 copies of each chromosome) parthenogenetic stem cells are introduced into a fertilised tetraploid embryo (i.e., 4 copies of each chromosome) created by cell fusion – the tetraploid cells developed into placental tissues while the other tissues of the mouse were derived from the parthenogenetic stem cells. The applicants' submissions pointed out that both these papers supported their contention that a parthenogenetically-activated human oocyte cannot develop to term without further intervention or manipulation to overcome the maternal imprinting and absence of paternal imprinting.

42 In addition to their written submissions, the applicant also filed a set of amended claims. The objective of these amended claims is to exclude any method in which such manipulations referred to above are used to overcome imprinting. For GB0621068.6, claim 1 was amended to the following (insertions underlined):

A method of producing a <u>pluripotent</u> human stem cell line comprising:

a) parthenogenetically activating a <u>pluripotent, unfertilised</u> human oocyte, wherein activating comprises: i) contacting the oocyte with an ionophore in a gas mixture environment comprising 5% CO_2 and 20% O_2 and ii) contacting the oocyte with a serine-threonine kinase inhibitor in a gas mixture environment comprising an O_2 concentration of 2% O_2 to 5% O_2 <u>and wherein the oocyte is haploid or diploid and the oocyte genome lacks paternal imprinting</u>;

b) cultivating the <u>haploid or diploid</u> activated oocyte <u>lacking paternal imprinting</u> of step (a) in a gas mixture environment comprising an O_2

[5] Stem Cells [2009] Vol 27, pp 2136-2145

concentration of 2% O_2 to 5% O_2 until blastocyst formation, wherein cells of the blastocyst are haploid or diploid and lack paternal imprinting;

c) *transferring the blastocyst to a layer of feeder cells, and culturing the transferred blastocyst in a gas mixture environment comprising 5% CO_2 and 20% O_2;*

d) *mechanically isolating an inner cell mass (ICM) containing pluripotent cells of the blastocyst of step (c); and*

e) *culturing the pluripotent cells of the ICM of step (d) on a layer of feeder cells, wherein culturing step (e) is carried out in a gas mixture environment comprising 5% CO_2 and 20% O_2.*

Analogous amendments were made to claim 12 of GB0621068.6 and claim 1 of GB0621069.4.

43 The insertion of the word "pluripotent" in the first line of step (a) in claim 1 of GB0621068.6 does not appear to have a basis in the applications as filed (and is, in any case, contradictory, as an unfertilised oocyte would not normally be considered to be "pluripotent") – aside from this the draft amendments do not add matter and are allowable. However, I do appreciate that the purpose of this amendment would appear to be to make clear and unambiguous that the invention does **not** relate to an entity that is totipotent and so does not have the potential to develop into a human being. I will consider this issue further below

44 In light of the evidence provided by the applicants, I am satisfied that the parthenotes, and the cells and tissues produced from them, by the methods of the claimed inventions, are not capable of development into a human being, and the amended claims provided with the written submissions on 13 April 2012 exclude known methods of manipulation of the oocyte or the parthenote in ways which might allow further development.

Application of CJEU Decision C-34/10 Brüstle.

45 This then brings me to the argument presented by Mr Godar in relation to the decision of the CJEU in C-34/10 *Brüstle*, and how it applies to the scientific facts as discussed above.

46 As I have indicated above, I am satisfied that on the evidence presented, and discussed in the previous paragraphs, in relation to the science, the parthenotes produced by the methods of the invention are incapable of continued normal development i.e. they cannot develop into a viable human being. Given this finding, I then turn to consider the question whether, in view of the decision of the CJEU in case C-34/10 *Brüstle,* the claimed methods, cells and tissues are patentable, or are excluded from patentability.

47 Mr Godar argued that there was a body of case law, including both decisions from the Court of Justice and from UK law, which established that the role of the CJEU (previously known as the European Court of Justice or ECJ), as set

out in Article 267 of the Treaty for the Functioning of the European Union, is solely to interpret the Treaty, and legislation arising from it, such as Directive 98/44/EC. It is not a fact-finding court. This principle was set out in the Advocate-General's opinion in C-51/75 *EMI Records Ltd v CBS United Kingdom Ltd* [1976]:

> *"It is the law that the jurisdiction of this Court ... is limited to ruling on questions of Community law. The Court cannot apply that law to the facts of a particular case. This means that the Court cannot determine issues of fact that are relevant not to the ascertainment of that law, but to its application."*

48 The Court itself stated the same principle in cases C-36/79 *Denkavit Futtermittel GmbH v Finanzant Warendorf* [1979] and C-253/83 *Sektkellerei CA Kupserberg & CA CIE KG aB v Hauptzollamt Mainz* [1985]. In UK law, the House of Lords considered the role of the Court of Justice in *R v Secretary of State for Transport ex parte Factortame* [2000] 1 AC 524:

> *"But I would not be inclined to attach much importance to these expressions of opinion [by the Court of Justice], because in paragraph 58 of the judgment the Court made it clear that it was for the national courts to assess the seriousness of the breach. The national courts have the sole jurisdiction to find the facts in the main proceedings. It is for them to decide how to characterise the breaches of Community law which are in issue."* [Lord Hope of Craighead]

49 The application of CJEU rulings in national law was considered in more depth by Aldous LJ in the Court of Appeal's decision in *Arsenal Football Club Plc v Reed*, [2003] EWCA Civ 969 (21 May 2003) *(see paragraphs 25 and 26)*:

> *"...on a reference under Article 234, the purpose of the ECJ is "to decide a question of law and that the ruling is binding on the national court as to the interpretation of the community provisions and acts in question."... Even so, the ECJ has jurisdiction to review the legal characterisation of facts found by the national court... Also the ECJ has in the past provided guidance in order to enable the national court to give judgment..... On occasions it has "steered" the national court for the purpose of unified application of the law. However, as the House of Lords made clear in R v Secretary of State for Transport ex parte Factortame (No. 5), the English Court is not bound by that steer and therefore, with hesitation, could conclude the case in a different way. It is the national court alone that must find the facts.*
>
> *It follows that the judge was entitled to disregard any conclusion reached, in so far as it was based upon a factual background inconsistent with his judgment. Thus, upon his perception of the ECJ's judgment, he was entitled to disregard the conclusion in the ruling and decide the case upon the legal principles stated in the judgment of the ECJ."*

He went on to say (at paragraph 31):

Of course the ruling of the ECJ is binding in so far as it is a ruling upon interpretation. However I reject the submission of Mr Thorley that the national court should confine its attention solely to the ruling. Strictly speaking the judgment is the explanation of the ruling, but as Advocate General Warner explained in Robert Bosch GmbH v Hamptzollant Hildestein [1978] ECR 855 "the operative part of the judgment of this Court should always be interpreted in the light of the reasoning that precedes it." That is particularly apt in the present case as the ruling uses the words "in the circumstances such as those in the present case". To ascertain what the ECJ believed the circumstances were, it is necessary to have recourse to the preceding paragraphs of the judgment.

It is clear therefore from this decision that a national court may disregard findings of fact by the CJEU which are inconsistent with the findings of fact by the referring court.

50 Mr Godar argued that, in case C-34/10 *Brüstle,* the CJEU had gone beyond the findings of fact from the referring court in reaching its conclusion that a parthenogenetically-activated oocyte 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*".

51 As this latter point is critical to the applicants' case, it is necessary to consider the findings of the referring court, the German Bundesgerichtshof[2], concerning parthenogenesis; an English translation of the relevant paragraph of the referral is provided:

"*The defendant has cited so-called parthenogenesis as a further means for obtaining human embryonic stem cells, i.e. the division and further development of an unfertilised egg cell without fertilisation and without transplantation of a foreign nucleus. Whether this approach is actually feasible and whether such a cell could develop into a complete individual, has not yet been absolutely clarified from a scientific perspective. Independent of this one point in favour of qualification as an embryo as defined in Art. 6 para. (2c) of the Directive could be the fact that such cells in any event in the first division stages go through the same development as a fertilised egg cell and therefore appear equally worthy of protection.*"

52 What I would conclude from this is that the referring court made a finding of fact, that – in the initial cell division stages – parthenogenetically-activated oocytes go through the same developmental pathway (i.e. the development of a blastocyst or comparable structure) as an ordinarily-fertilised oocyte. However, Mr Godar stated that the Bundesgerichtshof[2] left unanswered the question of whether parthenotes could develop further. I agree with this view but I also note that the finding by the CJEU is in line with what the referring court suggested – that the initial stages of development appear to be the same for a parthenogenetically-activated oocyte and for a fertilised ovum.

53 Mr Godar argued that the CJEU had relied on the written observations, drawing on the wording used by the CJEU in paragraph 36 (emphasis added):

"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."*

54 The patent attorneys acting for the applicant obtained a copy of the observations of the UK in this case[6] and, Mr Godar noted that these observations stated that "*The [parthenogenetic] process can result in a parthenogenetic human embryo, and therefore also falls within a broad definition*", and refer to the *Revazova et al*. paper (see (1) above) as evidence in support of this statement. However, as discussed above, the applicants argue that this paper does **not** provide support for the conclusion that parthenogenetic stimulation could give rise to an embryo that 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*".

55 This *Revazova et al*. paper may be an example of an instance where the use of distinctive terminology to describe entities derived by parthenogenetic activation (rather than, for example, "embryo" and "blastocyst") might have led to a greater appreciation from the lay reader of the similarities and the differences between these entities and those derived from a normally-fertilised ovum (see paragraph 8 above also).

56 According to the decision in case C-34/10 *Brüstle* (see header note of decision), written observations were filed by a number of other EU member states (in addition to the UK) as well as by the parties in the proceedings. Neither Mr Godar nor I have had sight of any of these other written observations and so I cannot say whether similar or different points were made in relation to parthenotes.

57 Having considered this issue in detail (see discussion above), I am persuaded by the arguments made by the applicant concerning the science of parthenogenesis. At the very most, the entities produced by parthenogenetic activation of oocytes take a few steps in the process of development into a human being. However, because of the unmet need for paternal imprinting in parthenotes produced in this way, this process stops and development into a viable human being is not possible without further intervention or manipulation. A parthenote can begin the journey of development into a human being but it cannot actually reach its destination. By contrast an embryo created by fertilisation of an ovum can do so.

58 The referring court in case C-34/10 *Brüstle*, as noted in paragraph 51 above, did state that it was not clear from the science, whether a stem cell derived from a parthenogenetically-activated human embryo could develop into a human being. However, the Bundesgerichtshof[2] **did** suggest that, as such cells did undergo similar cell division steps at the initial stages, this was a point in

[6] A copy of the UK observations was obtained via the Chartered Institute of Patent Attorneys (CIPA) who made a request under the Freedom of Information Act 2000.

favour of including embryos derived via parthenogenesis into the definition of embryo for the purposes of the Directive.

59 Mr Godar argued that the CJEU, in reaching its decision in case C-34/10 *Brüstle,* was wrong to draw on the written observations as a finding of fact; instead, he said the CJEU should have referred the issue back to the referring court, as it did on the question of whether a stem cell derived from a human embryo at the blastocyst stage itself constitutes a "human embryo" within the meaning of Article 6(2)(c) of the Directive. I do not agree with Mr Godar on this point. In my view, the CJEU is not making a finding of fact in the way he characterises it. The CJEU is entitled to draw on all the material it receives in written observations in so far as it considers that this is helpful in answering the question(s) it has before it regarding the interpretation of EU legislation. Indeed, written observations are the principal means by which those parties and EU member states involved in any CJEU case submit material that they consider relevant and helpful to the CJEU in reaching its decision. Thus, it is entirely appropriate for the CJEU to draw on these materials when reaching its decision.

60 Mr Godar raised a further argument; that the CJEU's decision concerning parthenotes was a "conditional" decision; i.e., that the conclusion of the Court is conditional on the finding of fact that it is based on. The conditional finding in Mr Godar's view was that if a parthenogenetically-activated oocyte can develop into an embryo, and hence a human being, then it must be included in the definition of embryo that the CJEU considers is necessary for the proper application of the Directive. However, Mr Godar considered that as a parthenogenetically-activated oocyte, as disclosed in the invention, is able to develop as far as the blastocyst-like structure but is unable to go on to develop into a viable human being, then it does not meet the condition established by the CJEU. He therefore contended that it does not fall within the definition of a human embryo and hence is not excluded from patentability.

61 Although I do not accept that the CJEU was wrong to rely on the written observations in the way that it did, I do accept that – in view of *Arsenal v Reed* and the preceding *Factortame* decision referred to above – the UK courts are entitled to disregard a finding of fact made by the CJEU which is not based on a finding of fact made by the referring court, if it considers that the finding of fact by the CJEU is clearly incorrect. I consider that the same principle applies to me as the Hearing Officer, but as the lowest level of tribunal, I must clearly exercise the greatest of caution in departing from any aspect of the CJEU's decision. In addition, in *Arsenal v Reed,* it was pointed out that *"the operative part of the judgment of this Court should always be interpreted in the light of the reasoning that precedes it"*. This means that I cannot consider the conclusion of the CJEU in paragraph 38 – that "...*any non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis constitute[s] a 'human embryo' within the meaning of Article 6(2)(c) of the Directive"* – in isolation from the reasoning behind this conclusion in paragraphs 32-36. In particular, that patent law must be applied so as to respect the fundamental principles safeguarding the dignity and integrity of the person; that the concept of 'human embryo' must be understood in a wide sense; and that

parthenogenetically-activated oocytes are "*capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do so*"

62 As discussed above, I have concluded that parthenotes produced by the methods of claim 1 of the draft amended claim sets (as filed on 13 April 2012) for both applications are **not** capable of developing into a human being. Although, they can begin the **p**rocess by creating a parthenogenetically-derived blastocyst-like structure from which stem cells can be derived, they lack the capability to complete the process of development into a human being. This is the key issue, in my view. The initial steps in the process of development from parthenogenetically-activated oocyte to blastocyst-like structure can be considered to be analogous to the initial steps in the process of development from a fertilised ovum. However, a fertilised ovum has the capability to continue to develop into a human being whereas a parthenogenetically-activated oocyte does not.

63 The analogy this brings to mind is that the development process from an oocyte to a human is like a journey on a train which is passing through a tunnel. The entrance into the tunnel is activation of the oocyte in some way (i.e., by parthenogenesis or fertilisation), the exit from the tunnel is the development of a viable human being. All the intermediate steps in the development from activated oocyte to human being occur within this tunnel.

64 As already discussed above, the CJEU considers that any entity "*capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do so*" falls within the exclusion under Article 6(2)(c) of the Directive, and is, as a consequence, not patentable subject matter under the Directive and hence the Act. In applying the judgement from C-34/10 *Brüstle* to the present case, I think that it could be argued that there are two ways to approach the test provided by the CJEU:

(1) The first is to consider that it is only necessary for the train, i.e., the cells in question, to begin the journey through the tunnel – irrespective of whether or not the cells in question have the ability to actually complete the journey and emerge from the tunnel

(2) The second is to consider that it is necessary that the cells in question must not just begin the journey but that they must also be able to complete this journey and so emerge successfully from the other end of the tunnel.

As noted already, a parthenogenetically-activated oocyte and the blastocyst-like structures derived from them in the manner disclosed in the present applications do not appear to be capable of developing into human beings. Using our train journey analogy, they can begin the journey through the tunnel but they cannot complete it and have to stop. Thus, the invention of the applications in suit would appear to pass the test in (1) but fail the test in (2).

65 I note that in Advocate General (AG) Bot's Opinion[7] on case C-34/10 *Brüstle,* he suggested that the court answer the questions raised by the referring court in relation to parthenotes and whether they fall within the definition of human embryo, in the following manner (emphasis added):

> *"Unfertilised ova ... whose division and further development have been stimulated by parthenogenesis are also included in the concept of a human embryo* ***in so far as the use of such techniques would result in totipotent cells being obtained****"*

Thus he considered that the key test for exclusion from patentability in this area was the capacity to produce a human being, i.e. totipotency. However, the CJEU did not refer to totipotency in its judgement. It expressed itself in terms of parthenogenetically-activated oocytes falling within the definition of human embryo in so far as they are "*capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do so".*

66 Using our train journey analogy, the AG's criteria was whether the parthenote was capable of a journey that involved entering the tunnel and also a successful exit from the tunnel; on the other hand, the CJEU's definition was focussed solely on the start of this journey and entering the tunnel.

67 Given that the CJEU was fully aware of the AG's Opinion prior to issuing their decision on case C-34/10 *Brüstle,* it appears that they did not consider the approach suggested by the AG was the appropriate one. Despite this, I think that it could reasonably be argued that in order to be capable of undergoing the complete process of development into a human being in the same manner as an embryo created from a fertilised ovum, a cell needs to be totipotent – indeed, that is the definition of totipotency, i.e. it is capable of giving rise to all the elements of a developing human being. By contrast, if a cell is not totipotent and so does not have all the necessary elements needed to produce a new human being then, whether or not it is, in the words of the judgement, "*capable of commencing the process…."*, its inability to complete this process would seem to be an important limitation and one that should also play a part in any assessment. However, having considered the judgment in detail, I cannot find any explicit or implicit support for the AG's approach, which also appears to be the approach preferred by the applicant.

68 In the present case, the use of parthenogenesis to activate the unfertilised oocyte, starts a process that although similar to that which a fertilised ovum undergoes, will not lead to the development of a human being. The parthenogenetically-activated oocyte is only pluripotent, and lacks some of the elements essential for development of a human being. This was an topic that was explored in some detail at both the hearing and in the subsequent written submissions on these two patent applications. The degree of difference and the degree of similarity between the two processes – that undergone by a fertilised ovum and that undergone by a parthenogenetically-activated oocyte –

[7] Opinion of Advocate-General Yves Bot, delivered 10 March 2011 (in French), for case C-34/10, *Oliver Brüstle v Greenpeace.*

is important to the understanding of the present case. It is possible that the CJEU in reaching its decision in relation to parthenotes, and whether they fall within the definition of human embryo for the purposes of the Directive, may have done so on the basis of materials that suggested a greater degree of similarity between both processes than may actually exist. Certainly, in the present case, I have had the opportunity to consider this technology – use of parthenogenesis to produce stem cells – in some detail and to gain an appreciation of the similarities and differences.

69 However, the judgement in case C-34/10 *Brüstle* establishes what the CJEU considers to be the correct legal interpretation of Article 6(2)(c) of the Directive and the reasoning behind that. I do not consider that the CJEU has made an incorrect finding of fact. As mentioned above, the CJEU, in my view, has focused on what it considers to be the most important aspect of the development process – its start – and provided an interpretation of what human embryo means for the purposes of the Directive from that. In doing so they have paid less attention to whether or not the development process can be completed. This is clear from the use of the word '*commencing'* in para 36 of the decision, i.e. "*capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do so*".

70 As mentioned above, the CJEU could have taken on board the suggestion made by the AG in his opinion on this case but it did not. It made no mention or comment that they agreed or disagreed with the AG opinion on this point regarding totipotency. I do not think that I can conclude anything other than the CJEU had the opinion available to it in preparing its decision and chose to deal with the referred question on this point in their own way – based on a consideration of the context and purpose of the Directive (see paragraphs 24-38, especially paragraphs 31-38, of the decision in case C-34/10 *Brüstle)*. This appears to be analogous to what the CJEU did in deciding how to answer the questions referred to it in case C-206/01 *Arsenal v Reed*. Aldous LJ made it clear in the above mentioned UK Court of Appeal decision (*Arsenal Football Club Plc v Reed* [2003] EWCA Civ 969), after this case returned to the UK courts, that the CJEU decision was not based on an incorrect finding of fact, and nor did the Court of Justice ignore or reject a finding of fact by the referring court (in this case, the UK Patents High Court – *Arsenal Football Club PLC v Reed* [2001] RPC 46). Rather, what the CJEU did do was look at the problem and the basis on which the reference was made, and provide an analysis and answer to the referring court based, not on the questions referred (whether the use complained of was trade mark use), but rather one based on the most relevant consideration in the view of the CJEU (the likelihood that the use complained of would damage the intellectual property right which the owner of the trade mark was entitled to).

71 I have a great deal of sympathy with the applicant's situation, in that a parthenogenetically-activated oocyte cannot complete the process of development into a human being although it undergoes very similar steps at the start of this process as a fertilised ovum would. However, I cannot ignore the fact that the CJEU considers that to fall within the definition of a human embryo for the purposes of the Directive, and hence Schedule A2 of the Act, the key

feature is that the entity in question must be "*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). Given the binding nature of CJEU decisions in relation to the interpretation of EU legislation, I am bound by this decision. While, I have identified what might be considered as a second way to look at this criterion (see paragraph 64 above), I cannot ignore paragraph 38 of the *Brüstle* decision which makes clear that "*any non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis constitute a 'human embryo' within the meaning of Article 6(2)(c) of the Directive"*

72 Thus, I find that I must conclude that the amended claims defining methods of producing stem cells, synthetic cornea or corneal tissues constitute commercial or industrial uses of a human embryo as defined in Article 6(2)(c) of the Directive and paragraph 3(d) of Schedule A2 to the Patents Act.

Patentability of the Stem Cells and Corneal Tissue Per Se

73 In view of the above finding, I must also consider whether the stem cells produced by the methods of GB0621068.6, and the synthetic cornea or corneal tissue produced by the methods of GB0621069.4, fall within the definition of excluded matter under Article 6(2)(c) of the Directive and paragraph 3(d) of Schedule A2 to Act. If they do, then the product-by-process and omnibus claims to such cells and tissues are also not patentable.

74 There are two possible grounds for such an objection; either because the claimed cells and tissues are themselves human embryos, or because the production of these cells and tissues necessarily entails the destruction of a human embryo. To address these questions, I need to consider the answers provided by the CJEU in case C-34/10 *Brüstle* in relation to the second and third questions referred by the Bundesgerichtshof.

75 On the question of whether a stem cell derived from a human embryo at the blastocyst stage itself constitutes a "human embryo" within the meaning of Article 6(2)(c) of the Directive, the CJEU reached no conclusion – instead it referred the question back to the Bundesgerichtshof for further consideration in the light of scientific developments. This means that, although I have concluded that the parthenogenetic blastocyst-like structure is a "human embryo" as defined in Article 6(2)(c) of the Directive, this does not necessarily imply that a stem cell derived from it, as claimed in GB0621068.6, is also a "human embryo" – this question was left open by the CJEU.

76 However, the CJEU also held, in answer to a final question from the Bundesgerichtshof:

> "*Article 6(2)(c) of the Directive excludes an invention from patentability where the technical teaching which is the subject-matter of the patent application requires the prior destruction of human embryos or their use as base material, whatever the stage at which that takes place and even if the description of the technical teaching claimed does not refer to the use of human embryos*"

77 This means that, even though the CJEU did not reach a conclusion on whether stem cells derived from human blastocysts are themselves embryos, because such stem cells are derived from embryos, these cells, and any methods of using them, or cells or tissues derived from them, are nevertheless unpatentable. This is because they require "*the prior destruction of human embryos or their use as base material*". It therefore follows that, as I have decided that the parthenogenetic blastocyst-like structure is a human embryo as defined in Article 6(2)(c) of the Directive, any stem cells, synthetic cornea or corneal tissue produced from it are also not patentable.

78 However, the argument was made that stem cells could be derived from the parthenogenetic blastocyst-like structure without destruction of the source material, using the techniques of pre-implantation genetic diagnosis known before the priority date of the present applications. In support of this, the applicants representatives' referred to a paper by *Kliminskaya et al.* (Nature [2006] Vol 444 pp 481-485), published after the priority dates of the present applications but referring to earlier work in the same field, which demonstrates that single cells derived by non-destructive isolation from a blastocyst could be used to create embryonic stem cells. This question potentially has implications beyond the present invention to embryonic stem cells in general. However, I must consider the teaching of the present applications in this regard. Both applications appear to solely disclose methods in which the inner cell mass is mechanically isolated from the blastocyst-like structure – this would appear to inevitably result in the destruction of the blastocyst-like structure. I therefore cannot conclude that the cells and tissues defined in the present applications could be produced without destruction of the source material, as there is no teaching in the application to this effect. I therefore must find that the product-by-process and omnibus claims to stem cells, synthetic cornea or corneal tissue are excluded from patentability under paragraph 3(d) of Schedule A2 to Act.

Conclusion

79 Taking account of all of the above, I find that the invention disclosed in patent application GB0621068.6 entitled "*Parthenogenic activation of oocytes for the production of human embryonic stem cells*" and that disclosed in patent application GB0621069.4 entitled "*Synthetic cornea from retinal stem cells*", both relate to unpatentable subject matter, under paragraph 3(d) of Schedule A2 to the Act because they disclose uses of human embryos for industrial or commercial purposes.

80 I must therefore conclude that the claimed methods of producing stem cell lines and the claimed stem cell lines in patent application GB0621068.6, and the claimed methods of producing synthetic corneas or corneal tissue and the claimed tissues in patent application GB0621069.4 constitute the commercial or industrial use of a human embryo as defined in paragraph 3(d) of Schedule A2 to Act. All of the claims in both applications are therefore considered to define matter excluded from patentability under paragraph 3(d) of Schedule A2 to Act.

As I can find no saving amendment that would avoid this exclusion, I must refuse both applications.

Appeal

81 Under the Practice Direction to Part 52 of the Civil Procedure Rules, any appeal must be lodged within 28 days.

Dr L CULLEN

Deputy Director, acting for the Comptroller