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The evolution of the CJEU's case law on stem cell patents: Context, outcome and implications of Case C-364/13 *International Stem Cell Corporation*.

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Abstract***: On December, 18th 2014 the CJEU rendered its' much-anticipated decision in C-364/13 *International Stem Cell Corporation v Comptroller General of Patents (ISCC)*. Qualifying its' earlier ruling in *Brüstle v. Greenpeace (Brüstle)* with regard to non-fertilised human ova stimulated by parthenogenesis, the Court held that in order to constitute a 'human embryo' - and thus to be unpatentable under the EU Biotechnology Directive - the stimulated ovum must have the "*inherent capacity to develop into a human being*". This would allow patent claims on pluripotent parthenotes which had not been genetically modified to achieve totipotent capabilities. Hence the judgment establishes a crucial limitation of the broad interpretation of "human embryos" in *Brüstle*, where the CJEU held that parthenotes are covered by the term "human embryo" since they are "*capable of commencing the process of development of a human being*". The *ISCC* decision is to be welcomed since it provides an ethically justifiable leeway for patenting and offers reasonable support to the commercial viability of European cell therapy research. Yet, *ISCC*'s impact still depends on national implementations and the decision only applies to certain hESC cells. Thus, further clarifications would be helpful concerning other non-totipotent hESCs.

Introduction

On December, 18th 2014 the CJEU rendered a much-anticipated decision concerning the patentability of Human Embryonic Stem Cells (hESC) and the interpretation of *Article 6(2)(c) of Directive 98/44/EC on the Legal Protection of Biotechnological Inventions* (Biotech Directive). In Case C-364/13 *International Stem Cell Corporation v Comptroller General of Patents (ISCC)* the CJEU revisited the issue of patentability of hESC and qualified its earlier ruling in Case C-34/10 *Oliver Brüstle v. Greenpeace eV (Brüstle)* as far as it concerns non-fertilised human ova stimulated by parthenogenesis¹.

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*** This paper has been submitted on 6 March 2015. Any changes that happened after this date could not be considered.

¹ The term "parthenogenesis" is derived from the Greek words parthenos or "virgin" and genesis or "creation". Most simply it can be defined as reproduction without fertilization. It occurs when a female gamete develops a new individual without being fertilized by a male gamete. Parthenogenesis solely involves the production and stimulation of a female egg. For further information and illustrations, see: Regina Bailey, *Parthenogenesis Reproduction Without Fertilization*, available at: <http://biology.about.com/od/geneticsglossary/g/parthenogenesis.htm> (accessed 10 March 2015). Regarding recent scientific developments see also: Daughtry, Brittany, and Shoukhrat Mitalipov. *Concise*

In ISCC, the Court now held that in order to constitute a ‘human embryo’ - and thus to be considered non-patentable under the Biotech Directive - the stimulated ovum must have the “inherent capacity to develop into a human being”. This may allow patent claims on pluripotent parthenotes² which have *not* been genetically modified to achieve totipotent capabilities and thus cannot be considered to contain the inherent capacity to develop into a human being. Hence, we argue that the judgment establishes an important limitation of the broader interpretation of “human embryos” previously established in the *Brüstle* case, where the CJEU had held that parthenotes are covered by the term “human embryo” since they are “capable of commencing the process of development of a human being”. At the same time, however, we recognize that the judgment will – despite its general legal significance – probably only directly affect a rather small number of patent applications. Moreover, we contend that much uncertainty still remains on the patentability of pluripotent stem cell technology, which will require further legal and judicial clarifications.

To this end, section 1 will set out with a brief overview of the legal framework and state of the debate prior to the CJEU’s decision in ISCC. In sections 2 and 3 we will outline the facts and the procedural history of this important case. Section 4 summarizes the outcome and the relevant legal essence of the CJEU’s decision. Section 5 will analyse the legal implications that can be derived from this decision and identify unsolved questions. This will allow us to finally formulate some concluding remarks in section 6.

1. Brief background of Case C-364/13: The Biotech Directive and the Brüstle case

The EU Directive 98/44 on the legal protection of biotechnological inventions aims to balance the protection of dignity and integrity of the human being³ with the need to preserve the social function of patents as a vector for the competitiveness of European biotech industry.⁴ Hence, Article 6 (2) (c) of the Biotech Directive explicitly prohibits patenting the uses of embryos for industrial or commercial purposes where such use would be contrary to *ordre public* or morality. However, since the drafters of the Biotech Directive could not foresee the full implications and opportunities of modern stem cell science, the broad wording of the provision raises many questions with regard to the patentability of human embryonic stem cell (hESC) technology. Totipotent⁵ embryonic stem-cells can be understood as a stage in the formation and development of

Review: Parthenote Stem Cells for Regenerative Medicine: Genetic, Epigenetic, and Developmental Features, Stem Cells Translational Medicine 3.3 (2014): 290–298.

² A parthenote is a cell resulting from parthenogenesis. This may involve a 1. An embryo generated through parthenogenesis, occurring in certain plants and invertebrate animals, or, 2. An unfertilized, usually mammalian egg cell that has been artificially activated with chemicals so that it divides.

³ Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions OJ 1998 L213 (Biotech Directive), recital 16.

⁴ Biotech Directive (n 1), recitals 1-3 & 17.

⁵ Totipotent stem cells are the most versatile of the stem cell types. When a sperm cell and an egg cell unite, they form a one-celled fertilized egg. This cell is totipotent, meaning it has the potential to give rise to any and all human cells, such as brain, liver, blood or heart cells. It can even give rise to an entire functional organism. The first few cell divisions in embryonic development produce more totipotent cells. After four days of embryonic cell division, the cells begin to specialize into pluripotent stem cells.

the human body and thus they fall unequivocally both under the patentability prohibitions set forth in article 5 (1) of the Biotech Directive (a subject-matter exclusion rule) and under Article 6 (2) (c) of the Biotech Directive.⁶ The questions of patentability raised by pluripotent⁷ stem cell technology are, however, more complex. For many years it remained rather unclear how this prohibition relates to pluripotent human embryonic stem cell technology and the methods by which such stem cells are created.

Some of these questions were answered in October 2011, when the CJEU rendered its judgment in *Brüstle v. Greenpeace*⁸ and broadly interpreted the patent's exclusion of human embryos for use in commercial or industrial purposes. Adopting a *full history approach* the Court held *inter alia* that, Article 6 (2) (c) of the Biotech Directive excluded from patentability an invention where the technical teaching of the patent application requires the prior destruction of human embryos or their use as base material, *whenever* such destruction takes place and *even* if the claims' description does not refer to the use of human embryos. Moreover, the Court widely defined the notion of human embryo as:

“[A]ny human ovum after fertilization, any non-fertilized human ovum into which the cell nucleus from a mature human cell has been transplanted and any nonfertilized human ovum whose division and further development have been stimulated by parthenogenesis.”

The Court thus explicitly included non-fertilized ova after somatic cell nuclear transfer (SCNT)⁹ and – most importantly for this case - parthenotes, which are created by the artificial activation of an oocyte by a variety of chemical and electrical techniques so there are capable of further cell-division in absence of sperm-fertilization.

In the wake of *Brüstle* scientists in the field of hESC research became very much concerned about the wider impact of this controversial decision as it prohibits hESC patents that use publicly available stem cell lines that could be obtained in the United States or Asia, and thus would not imply *de novo* destruction of embryos. These worries were partially confirmed, when the EPO directly incorporated the *Brüstle* principles into its' Examination Guidelines¹⁰ and began to reject patent claims¹¹ that would

⁶ Biotech Directive (n 1), Article 5 (1).

⁷ These cells are like totipotent stem cells in that they can give rise to all tissue types. Unlike totipotent stem cells, however, they cannot give rise to an entire organism. On the fourth day of development, the embryo forms into two layers, an outer layer which will become the placenta, and an inner mass which will form the tissues of the developing human body. These inner cells, though they can form nearly any human tissue, cannot do so without the outer layer; so are not totipotent, but pluripotent. As these pluripotent stem cells continue to divide, they begin to specialize further.

⁸ Case C-34/10, *Oliver Brüstle v. Greenpeace eV*, EU:C:2011:669.

⁹ “Somatic cell nuclear transfer (SCNT) is a technique for cloning. The nucleus is removed from a healthy egg. This egg becomes the host for a nucleus that is transplanted from another cell, such as a skin cell. The resulting embryo can be used to generate embryonic stem cells with a genetic match to the nucleus donor (therapeutic cloning), or can be implanted into a surrogate mother to create a cloned individual, such as Dolly the sheep (reproductive cloning).” This definition is available at:

<https://www.hhmi.org/biointeractive/somatic-cell-nuclear-transfer-animation> (accessed 5 March 2015)-

¹⁰ Cf. Guidelines for Examination in the European Patent Office (November 2014 edition), Part G, Chapter II-17 to 18 on R 28 (c), available at: <http://www.epo.org/law-practice/legal-texts/guidelines.html> (accessed 5 March 2015).

arguably have been accepted under the EPO's previous more pragmatic approach resulting from the Enlarged Board of Appeal decision in *WARF*.¹²

However, when the German Federal Court of Justice (Bundesgerichtshof – BGH)¹³ applied the CJEU's preliminary ruling in *Brüstle* and delivered its' much awaited final decision in the *Brüstle* case on 27 November 2012¹⁴, it became apparent that, surprisingly, the BGH did not apply the prior CJEU considerations in a narrow and strict manner. Interpreting the CJEU's explanations in a rather patent-friendly way, the BGH decided to only partially revoke Oliver Brüstle's patent. It determined that the patenting of the process is only excluded according to § 2 Section 1 No. 3 of the Patents Act, if the process includes the prior destruction of embryos or their use as source material. Patenting is possible, however, where the relevant stem cells were extracted without necessitating the destruction of embryos. Also, the use of cell lines extracted from embryos that are no longer able to develop does – according to the BGH – not result in the exclusion of patentability. The negotiated patent claim was, in this respect, limited, and the appeal was only partially rejected. Amending this decision with a disclaimer the BGH appeared also to be willing to consider later (post-filing) technological developments that allowed the extraction of stem cells (e.g. through optimized “blastomere separation”) without necessarily destroying the embryo in the process. While the final BGH decision indicated that a reasonable and relatively broad patent protection on human stem cell-related technology is still possible in Germany, it also raised crucial questions about a potential “misinterpretation” of the CJEU's preliminary ruling and a potential conflict with the present approach taken at the European Patent Office (EPO).

Meanwhile, UK courts were also struggling with the precise scope and implications of the CJEU's findings in *Brüstle*. One of the most controversial issues concerned the applicability of the CJEU's *Brüstle* decision with regard to human parthenotes. This uncertainty resulted in a referral from the High Court of Justice of England and Wales, Chancery Division (Patents Court), which finally offered the CJEU an opportunity to reconsider the interpretation of the concept of ‘human embryos’ in article 6(2)(c) of the Biotech Directive¹⁵ with regard to human parthenotes. The specific question under referral in *Case C-364/13, International Stem Cell Corporation*¹⁶ asks for a clarification of whether the CJEU ruling in *Brüstle*¹⁷ applies without distinction to unfertilised human ova stimulated by parthenogenesis, which contains only pluripotent cells and are not capable of developing beyond the blastocyst stage. The CJEU decision was anticipated with a mix of hope and fear by the interested circles. Would the highest EU court confirm or distinguish *Brüstle*?

¹¹ See e.g. EPO, Boards of Appeal in T2221/10 *Technion/Culturing cells* [04.02.2014] unpublished. Cf. the detailed analysis by Mahalatchimy, A. et al., The Impact of European embryonic stem cell patent decisions on research strategies, *Nature Biotechnology*, Volume 33, Number 1 (January 2015), pp. 41-43.

¹² EPO, Enlarged Board of Appeal in G-2/06 *WARF/ Use of embryos* [25.11.2008] OJ EPO 2009, 306

¹³ The BGH is Germany's highest court of civil and criminal jurisdiction.

¹⁴ BGH Decision of 27 November 2012, case no.: X ZR 58/07.

¹⁵ Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions OJ 1998 L213, p.13 (Biotech Directive).

¹⁶ Case C-364/13, *International Stem Cell Corporation v Comptroller General of Patents*, EU:C:2014:2451.

¹⁷ Case C-34/10 (n 6).

2. Facts of the case

This case can be traced back to the decision by the UK Intellectual Property Office (UKIPO) to refuse two UK patent applications. Both were initially filed on 23 October 2006 in the name of LifeLine Cell Technology, and later assigned to International Stem Cell Corporation (ISCC), a California-based publicly traded biotechnology company.¹⁸ The two patent applications relate to the research results of a parthenogenesis based stem cell technology. The concerned patent applications included claims to (1) methods of producing pluripotent human stem cell lines from parthenogenetically-activated oocytes and stem cells produced according to the claimed methods Claims 1 to 29 (as proposed to be amended) concern methods of producing pluripotent human stem cell lines from parthenogenetically-activated oocytes, claims 30 and 31 refer to stem cell lines produced according to the method claimed, and claim 32 is an omnibus claim concerned with a stem cell line;¹⁹ and (2) methods of producing synthetic cornea or corneal tissue, all involving the isolation of pluripotent stem cells from parthenogenetically-activated oocytes, followed by product-by-process claims relating to synthetic cornea or corneal tissue produced by these methods and an omnibus claim.²⁰

During the course of patent prosecution at the UKIPO objections to patentability emerged, as the hearing officer considered that the inventions disclosed in the patent application were excluded from patentability due to constituting uses of human embryos under paragraph 3(d) of Schedule A” of the Patents Act 1977, a rule that implements Article 6(2)(c) of the Biotech Directive.²¹ Confronted with such objections, ISCC argued that the *Brüstle* decision should not apply, because the claimed inventions relate to parthenogenetically-activated oocytes and these are incapable of initiating the process of development of a human being due to the phenomenon of genomic imprinting. Confronted with research that suggested based on empirical evidence in animal models that such hurdles could be successfully overcome by genetic engineering, ISCC amended the claims introducing the word ‘pluripotent’ before ‘human stem cell line’ and referring to a lack of paternal imprinting, thus excluding any such method of genetic manipulation.²²

The arguments failed to persuade the patent office. The patents were refused under the reasoning that the inventions disclosed in the patent applications concerned uses of human embryos pursuant to CJEU jurisprudence in *Brüstle*.²³ ISCC appealed to the High Court of Justice of England and Wales, Chancery Division (the Patents Court), which in addition to its first instance jurisdiction, also hears several types of appeals including appeals from decisions of the UK Intellectual Property Office.

¹⁸ Cf. <http://www.internationalstemcell.com/Company> [accessed, 25 February 2015].

¹⁹ Application GB0621068.6 entitled ‘Parthenogenetic activation of oocytes for the production of human embryonic stem cells’.

²⁰ Application GB0621069.4 entitled ‘Synthetic cornea from retinal stem cells’.

²¹ Biotech Directive (n 1).

²² Opinion of Advocate General Cruz Villalón, delivered on 17 July 2014, Case C-364/13, *International Stem Cell v Comptroller General of Patents*, para 15.

²³ Comptroller General of Patents Decision n. BL O/316/12.

3. *The referral*

The Patents Court struggled with applying the CJEU jurisprudence set out in *Brüstle* to the facts of the case and decided to stay the proceedings in order to ask the CJEU for a preliminary ruling under Article 267 TFEU. During the procedures scientific evidence emerged that distinguished parthenotes from fertilised ova, differentiating the factual findings from those presented in *Brüstle*. The Patents Court relied on technical evidence contained in the expert reports and exhibits referred to in the appealed decision, as well as evidence presented in the German BGH *Brüstle* case,²⁴ and also the findings of fact made by the hearing officer, being that these were accepted by all parties and not challenged under the appeal proceedings.²⁵ It was accepted that parthenogenesis refers to a process of activation of an oocyte, in the absence of sperm, conducted through a variety of chemical and electrical techniques. The resultant oocyte or parthenote is capable of division and further development into a blastocyst-like structure. However, without further genetic manipulations these human parthenotes are unable to develop to term due to lacking paternal DNA, necessary for the development of extra-embryonic tissue. Unlike fertilised ova and its early stage descendent cells, parthenogenesis-activated oocyte cells are – without further manipulations - merely pluripotent and never totipotent.²⁶ Evidence examined pointed out that, so far, human parthenotes have only been able to develop to the blastocyst stage (around 5 days). However, despite concluding that the process ‘*will not lead to the development of a human being*’²⁷ the hearing officer had found that the ‘*stimulated human oocyte divided in a manner analogous to that of a fertilised human embryo, to produce a parthenogenetically -derived structure analogous to that blastocyst stage of normal embryonic development*’.²⁸ The central legal debate here is whether such biological analogy between a parthenogenetically derived structure and the blastocyst stage of normal embryonic development justified legal analogy, i.e. similar legal treatment, having in consideration that in *Brüstle* parthenotes were expressly declared to be non-patentable human embryos.²⁹ The Comptroller argued that *Brüstle* could be interpreted as concerned more with the commencement of the process of fertilisation rather than its outcome, pointing out that the CJEU states that ‘*any human ovum must, as soon as fertilised, be regarded as a ‘human embryo*’³⁰ thus concluding that the decision could be interpreted either broadly focusing merely in the fertilisation act or rather requiring such process to be capable of leading to a viable human being.³¹

ISCC submitted that it was crucial to establish what the CJEU meant by the expression ‘*capable of commencing the process of development of a human being*’ since such was the developed test to determine what might constitute a human embryo.³² Thus, this would require determining if such expression should be interpreted narrowly

²⁴ Bundesgerichtshof (German Federal Supreme Court) decision of 27 November 2012, Case X ZR 58/07.

²⁵ *International Stem Cell Corporation v Comptroller General of Patents* [2013] EWHC 807 (Ch) (17 April 2013), paras 10-22.

²⁶ *ibid*, para 18.

²⁷ *ibid*, para 21.

²⁸ *ibid*, para 22.

²⁹ Case C-34/10 (n 6), para 39.

³⁰ Case C-34/10 (n 6), para 35, cf. [2013] EWHC 807 (Ch) (17 April 2013), para 45.

³¹ [2013] EWHC 807 (Ch) (17 April 2013), para 50.

³² *ibid*, para 50.

including only organisms capable of commencing the process, or broadly, i.e. including also organisms capable of commencing such process, but incapable of leading to a fully human being.³³ ISCC argued that the CJEU decision should be interpreted according to the narrow understanding.

The Patents Court noted that the factual matrix in the case differed from the facts before the CJEU in *Brüstle*, suggesting that the CJEU may have relied on inaccurate or incomplete scientific submissions stating that human parthenotes were in fact capable of development into a human embryo.³⁴ The Patents Court concluded that parthenotes are not the same as fertilised ova and that treating them as analogues would defeat the purpose of the Biotech Directive, as stated in its recitals, of balancing the need to encourage research with the protection of fundamental principles of dignity and integrity of the person.³⁵

Against this background the following question was referred to the CJEU: ‘*Are unfertilised human ova whose division and further development have been stimulated by parthenogenesis, and which, in contrast to fertilised ova, contain only pluripotent cells and are incapable of developing into human beings included in the term "human embryos" in Article 6(2)(c) of Directive 98/44/EC on the Legal Protection of Biotechnological Inventions?*’³⁶

4. The Decision of the CJEU

The CJEU ruled that Article 6(2)(c) Biotech Directive must be interpreted in the sense that “*an unfertilised human ovum whose division and further development have been stimulated by parthenogenesis does not constitute a ‘human embryo’*” under the condition that “*it does not, in itself, have the inherent capacity of developing into a human being*”. The decision on whether such condition is fulfilled is left to national courts, but the CJEU establishes that the criterion for such evaluation is the “*current scientific knowledge*”.³⁷ Therefore, parthenotes should not be excluded from patentability provided that, in light of current scientific knowledge, these are considered not capable of developing into a ‘human being’ and therefore not considered ‘human embryos’ under the Biotech Directive. Particularly, in order to be classified as a human embryo, a non-fertilised human ovum must have the inherent capacity of developing into a human being.

In order to arrive at this decision the court confirmed *Brüstle* re-stating that ‘human embryo’, insofar as the interpretation of Biotech Directive is concerned, is an autonomous EU law concept to be interpreted uniformly and that such concept must be

³³ *ibid*, para 32.

³⁴ *ibid*, paras 51 to 54.

³⁵ *ibid*, para 58.

³⁶ *ibid*, para_59; Reference for a preliminary ruling from High Court of Justice (Chancery Division) (United Kingdom) made on 28 June 2013 – *International Stem Cell Corporation v Comptroller General of Patents* (Case C-364/13).

³⁷ Case C-364/13, EU:C:2014:2451 (n 14), para 39.

constructed in a wide sense.³⁸ Concerning the specific interpretation of the ruling in *Brüstle* the CJEU observes that the statement in paragraph 35 of *Brüstle*, which mentioned that any human ovum must, as soon as fertilised be regarded as an embryo since fertilisation implies the beginning of the process of development of a human being, must be interpreted according to the specification in the subsequent paragraph concerning non-fertilised ovum. Here the CJEU clarifies that *Brüstle*, in paragraph 36 states that non-fertilised ovum will only be considered human embryos, if found “capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can do”.³⁹ This critical and controversial expression was now interpreted following the opinion of the advocate general,⁴⁰ which had proposed applying a test of ‘inherent capacity’.⁴¹ The CJEU concluded that as far as non-fertilised ovum is concerned “the mere fact that an organism commences the process of development is not sufficient for it to be regarded as a ‘human embryo’”.⁴² As for the reason why parthenotes were considered human embryos in *Brüstle*, the CJEU acknowledged that in *Brüstle* it based its findings on submitted written observations that considered these to be capable of fully development. It is thus, symptomatic that this time the CJEU is more cautious leaving for national courts to decide, case-by-case, and in accordance with available scientific knowledge on whether an organism is inherently capable of developing into a human being.⁴³

5. Analysis

The CJEU has skilfully avoided touching the core of *Brüstle*’s approach declining to comment on observations of the referring court which might lead to a re-evaluation of the *Brüstle* doctrine. The decision was thus characterized as a “clarification” of *Brüstle*, and the issue was treated as a matter of factual determination, which was left to the national court to decide. Only indirectly, and falling short of actually recognising that there was a technical failure, or the court was misdirected or had misunderstood the science at issue, did the CJEU recognise that it had relied on incorrect scientific data concerning parthenotes in *Brüstle*.

Although the number of patent applications that directly claim human parthenotes may be limited, the broader legal implications of the CJEU’s decision to distinguish *Brüstle*⁴⁴ nevertheless offers a ray of hope for the patentability of European stem cell research. After closing the doors for the patentability of crucial areas human embryonic stem cell technology, it appears that *ISCC* has at least opened a small window infusing a breath of fresh air: inventions relating to unfertilised human eggs whose division and further development have been stimulated by *parthenogenesis* can once again be patented in Europe, i.e. as long as these parthenotes have not been genetically modified to achieve an ‘inherent capacity to develop into a human being’. Considering that

³⁸ *ibid*, paras 23-24.

³⁹ *ibid*, paras 23-26.

⁴⁰ Opinion of Advocate General, Case C-364/13 (n 21), para 73.

⁴¹ Case C-364/13, EU:C:2014:2451 (n14), paras 23-28.

⁴² *ibid*, para 23-29.

⁴³ *ibid*, para 36-38.

⁴⁴ Case C-34/10 (n 6).

promising alternative techniques, such as the re-programming of adult stem cells through induced pluripotent stem cell technology, are still immature and need to be optimized before they can be safely applied, and bearing in mind that this often still requires innovative applications of hESC related technology, this development can only be welcomed. However, caveat needs to be added.

First, it remains unclear how the European Patent Office will react and how national patent offices will interpret the present decision in practice.⁴⁵ In that context it is important to note that the EPO is not an EU institution. Hence the EPO is not formally bound by the Biotech Directive, nor is it obliged to accept the decisions of the CJEU.⁴⁶ However, the Administrative Council of the European Patent Office has in September 1999 introduced several of the relevant provisions of the Biotech Directive into the Implementing Regulations to the EPC (the “Rules”).⁴⁷ This includes Article 6 of the Biotech Directive, which is now to be found in Rules 26-29 EPC. As a matter of pragmatism and in the interest of harmonization it is therefore to be expected that the ISCC decision will be mirrored in the EPO guidelines for examination and implemented in the practice of the office, in similarity to the approach followed concerning *Brüstle*. Yet, considering the very strict post- *Brüstle* position recently taken by the EPO in T2221/10 *Technion/Culturing cells*⁴⁸ vis-à-vis the more permissible earlier approach followed by the EPO after its’ *WARF* decision (but before *Brüstle*), it remains to be seen how broadly or narrowly the EPO will interpret and incorporate this decision into its’ practice.

Second, at the level of national patent offices and courts divergences might also occur. After all, the Court “empowers” the national court to decide whether the parthenote has the ‘inherent capacity to develop into a human being’ without providing proper guidelines on this “inherency test” and without having established at what point an organism develops into a human being and is thus excluded from the concept of ‘human embryo’.⁴⁹ Moreover, and as pointed out by the Advocate General Opinion in *ISCC*,⁵⁰ member states might still decide to ban the patentability of human parthenotes in accordance with the more general exclusion in Article 6 (1) of the Biotech Directive on the basis of other grounds of public order and morality. Thus, national courts will have to both determine if the parthenote has the “inherent capacity to develop into a human being”, and if not, whether it is still prohibited from being patented on grounds of

⁴⁵ A more detailed comparative discussion of the implications of the case for innovation policy and practice is provided in Ana Nordberg & Timo Minssen, *A “ray of hope” for European stem cell patents or “out of the smog into the fog”?: The CJEU decision in C-364/13 and how it compares to recent US developments*, (accepted by IIC in September 2015).

⁴⁶ This has also been emphasized by the EPO’s Enlarged Board of Appeal in G2/06 *WARF/Use of embryos* [25.11.2008] OJ EPO 2009, 306.

⁴⁷ Administrative Council Decision, OJ EPO 7/1999, 437-440.

⁴⁸ See e.g. EPO, Boards of Appeal in T2221/10 *Technion/Culturing cells* [04.02.2014] unpublished. Cf. the detailed analysis by Mahalatchimy, A. et al., *The Impact of European embryonic stem cell patent decisions on research strategies*, *Nature Biotechnology*, Volume 33, Number 1 (January 2015), pp. 41-43.

⁴⁹ Cf. Anna Dannreuther, *The CJEU clarifies when stem cells can be patented in Europe*, available at: <http://eulawanalysis.blogspot.com/2014/12/the-cjeu-clarifies-when-stem-cells-can.html> (accessed 5 March 2015).

⁵⁰ Opinion of Advocate General, Case C-364/13 (n 21), para 43.

morality and/or public order.⁵¹ In light of the very different positions taken in the various EU member states on the definition of embryos and stem cell research as such, this persisting discretion entails a great risk for uncertainties and different approaches in each member state. While reflecting and acknowledging the differences between EU member states, this would be difficult to reconcile with the primary goal of referrals to the CJEU under Article 267 TFEU, i.e. to achieve an harmonious interpretation of the law.

Third, it is disappointing that no further clarification was given with regard to stem cells created through somatic cell nuclear transfer (SCNT). After all, the CJEU might also have misunderstood particular details of these techniques and it could be argued that the limitation set forth in *ISCC* concerning stem cells created through parthenogenesis could also apply to stem cells created by SCNT, which do not have the “inherent capacity” to develop into a human being. To assess if such an interpretation is legally valid would, however, necessitate another preliminary reference to the CJEU.

Further questions that remain unsolved, but which fall outside the scope of this short paper, concern e.g. the paradox with regard to European stem cell research regulations and the treatment of left-over embryos in *in vitro* fertilization treatments, as well as the division of competences between the CJEU and the European Court of Human Rights (ECHR), which has developed its very own case law on the definition of embryos.⁵²

6. Conclusions

Considering the significance of the *Brüstle* and *ISCC* rulings to such important medical areas as regenerative medicine and cellular therapy, the persisting legal uncertainty and the lack of generally applicable clear guidance is very unfortunate and does not serve the goal of a harmonious and effective European legal framework for innovation. The more permissive approach applied by the CJEU in *ISCC* may at this stage only apply to a very limited number of patents and patent applications. Nonetheless, the broader legal implications of the *ISCC* ruling appear at least to be a first step into the right direction. Ultimately this might lead to more nuanced approaches providing a reasonable leeway for patenting innovative products, methods and applications resulting from this promising technology. Hence, the *ISCC* decision might indeed have the “inherent capacity” of developing into a reasonable doctrine on stem cell patenting.

⁵¹ Ibid.

⁵² These questions and further practical implications will be addressed in our 2nd paper, see *supra* n.45.