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ARTICLE

A "Ray of Hope" for European Stem Cell Patents or "Out of the Smog into the Fog"? An Analysis of Recent European Case Law and How it Compares to the US

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Abstract In Case C-364/13, *International Stem Cell Corporation* (*ISCO*) *v. Comptroller General of Patents* (18 December 2014), the Court of Justice of the European Union distinguished its earlier ruling in *Brüstle v. Greenpeace* (*Brüstle*) with regard to the patent eligibility of non-fertilised human ova stimulated by parthenogenesis. The Court found that in order to be considered 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 permits the patenting of innovative pluripotent parthenotes and their applications. Yet the *ISCO* decision also leaves considerable discretion to national courts. Hence, the full impact of the decision still depends on national implementations. Moreover, *ISCO* only applies to very specific human embryonic stem cells (hESCs) and lacks further clarification concerning other non-totipotent hESCs, such as stem cells created through somatic cell nuclear transfer. Considering the significance of *Brüstle* and *ISCO* for regenerative medicine and cellular therapy, the persistent legal uncertainty is unfortunate. Irrespective of these flaws, however, *ISCO* has opened patentability doors that were previously closed and thereby reinvigorated crucial debates. Thus, this might have the "inherent capacity" of developing into a reasonable doctrine on stem cell patenting. Paradoxically, the patentability of isolated hESCs is now less certain in the US, making a brief comparison inevitable.

This article discusses the law as it stood on 1 March 2015 new developments are briefly mentioned in a postscript. We use the term "hESC-related inventions" to refer to non-excluded methods and products, and the broader term "hESC technology" or "technology" to mean any methods or products deriving from scientific research irrespective of their patent eligibility.

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1 Introduction

Despite enormous advances in the prevention, diagnosis and treatment of human illnesses, severe diseases continue to deprive people of health, well-being and independence. Attempts to find cures for these maladies give rise to legal issues. One of the biggest debates involving biotechnology and the law is the regulation of stem cell research and the patentability of such technology.[1]

Research into human developmental biology has led to the discovery and isolation of human stem cells. These are precursor cells that can give rise to multiple tissue types and include human embryonic stem cells (hESCs), embryonic germ cells (EGCs) and adult stem cells (ASCs). Recently, improved techniques have been developed for the in vitro culture and re-programming of stem cells, providing novel opportunities for understanding human embryology and for developing new applications for induced pluripotent stem cell technologies.[2] Although it seems to be impossible to precisely foresee the results of this research, some exciting applications are already emerging.[3] In any event, it is evident that scientists will gain immense new knowledge of the biology of human development that presumably will hold extraordinary potential for therapies and cures.[4]

The fact that human stem cell research may involve the use of cloning techniques, such as somatic cell nuclear transfer (SCNT), raises legal, but also ethical and religious, questions which concern public policy making, the governance of science and society at large. Potential uses of human stem cells to generate human tissues and organs are also the subject of ongoing public debate. Furthermore, the possible sources, risks and potential of different types of human stem cells are fiercely debated.[5]

One of the most discussed issues is whether biotechnologists should be allowed to produce stem cells from human embryos for research and/or clinical use and/or commercialisation and, eventually, to patent the methods and products resulting from the skilful application of modern stem cell technologies. Despite promising advances in induced pluripotent stem cell (iPSC) technology,[6] which might make the use of human embryos unnecessary in the future, this new technology still faces many limitations and safety issues, such as the risk of tumorigenesis.[7] For these and other

[1] Chapman et al. (1999), p. iii.

[2] Tonge et al. (2014), p. 192.

[3] *Id.*

[4] Chapman et al. (1999), p. iii.

[5] A good overview of the various sources and types of stem cells is provided by Cox et al. (2012), p. 1.

[6] Cyranoski (2014), p. 162, describing how scientists have been reprogramming adult cells into embryonic ones for decades – but they are only now getting to grips with the mechanics.

[7] Friedlander and Hinton (2013), p. 670.

reasons hESC technology unfortunately still appears to be required until iPSC technology has become more advanced.[8] Until recently, however, the reality was that the embryo was necessarily sacrificed in the process.[9] The technological potential to help find new treatments for severe illness and the simultaneous need to manipulate and destroy human fertilised ova (or similar) produce a societal and ethical dilemma between the duty of care and the dignity of life.[10] Moreover, a wide diversity of views and regulatory approaches coexist within the EU.[11] From an individual point of view, for example, an empirical study shows that with regard to stem cell research, by a small margin European citizens prioritise their right to health (53 %) over protection of dignity (47 %).[12] However, various individuals and groups have expressed concerns, ranging from religious institutions[13] to anti-abortionist groups, animal rights campaigners, bio-ethicists, scientists, governmental officials, members of parliament, patient advocate groups or organisations like Greenpeace.[14]

Against this complex and multifaceted background, this paper will focus on issues related to the patentability of hESC-related technology with respect to the *ordre public* and morality provisions embedded in European patent legislation. Brief comparisons will be made with recent US patent eligibility developments in the wake of the US Supreme Court judgment in *Myriad*.[15] After describing the most recent case law developments regarding the patentability of human embryonic stem cells from the Court of Justice of the European Union (CJEU), the European Patent Office (EPO), Germany and the UK, special attention will be given to the CJEU judgment in C-364/13 *International Stem Cell Corporation* (*ISCO*) *v. Comptroller General of Patents*.[16]

To this end, Sect. 2 of this paper will start out by outlining the applicable legal framework in Europe, while Sect. 3 will describe the most seminal recent case-law developments preceding *ISCO*. Section 4 will then summarise the procedural history and outcome of the CJEU's *ISCO* decision. Open questions and other problematic issues will be discussed in Sect. 5. This will provide the basis for a consideration of practical implications in Sect. 6, and a brief comparison with some recent US developments in Sect. 7. Finally, we will conclude the paper with a few general remarks in Sect. 8.

[8] *Cf.* Narsinh et al. (2011).

[9] *See e.g.* Chung et al. (2008), p. 113.

[10] European Group on Ethics in Science and New Technologies, "Opinion n°16 – 07/05/2002 – Ethical aspects of patenting inventions involving human stem cells", http://ec.europa.eu/archives/bepa/european-group-ethics/docs/avis16_en.pdf (accessed 16 November 2015).

[11] Elstner et al. (2009), p. 102.

[12] Gaskell et al. (2012), p. 393; Gaskell et al. (2010), pp. 55–59; *cf.* Gaskell et al. (2006), pp. 29–42.

[13] See *i.a.* the position of the Roman Catholic Church: "Congregation for the doctrine of the faith, Instruction Dignitas Personae on certain bioethical questions", Vatican, 8 December 2008. Available at http://www.vatican.va/roman_curia/congregations/cfaith/documents/rc_con_cfaith_doc_20081208_dignitas-personae_en.html. Accessed 16 Nov 2015.

[14] Dennis and Check (2005), p. 1076; for an overview *see* Siegel (2013) with further references.

[15] *Association for Molecular Pathology, et al. v. Myriad Genetics, Inc*. U.S., 133 S. Ct. 2107, 186 L. Ed.2d 124 (2013).

[16] Case C-364/13, *International Stem Cell Corporation v. Comptroller General of Patents,* EU:C:2014:2451. For the headnotes to this decision see 46 IIC 358 (2015), doi:10.1007/s40319-015-0328-x.

2 The European Legal Framework

The European controversy concerning the patentability of hESC-related inventions is primarily concerned with Art. 53(a) EPC,[17] which explicitly excludes certain inventions "the commercial exploitation of which would be contrary to 'ordre public' or morality" from patentability,[18] the EU Directive on the Legal Protection of Biotechnological Inventions (Biotech Directive)[19] and corresponding national stipulations.[20]

In September 1999, the Administrative Council of the EPO introduced several provisions of the Biotech Directive into the Implementing Regulations of the EPC (EPC Rules).[21] Although the Biotech Directive was merely addressed at the EU Member States and had no direct authority over the EPO, these rules are now binding on the various divisions of the EPO and the Boards of Appeal. The incorporation of the Biotech Directive into the EPC Rules included provisions relevant to the discussion concerning the patentability of hESCs. Article 5 Biotech Directive (Rule 29 EPC) specifies the circumstances under which elements isolated from the human body can constitute a patentable invention. The primary focus of this analysis, however, is on Art. 6(2) Biotech Directive (Rule 28(d) EPC), which resembles the morality clause in Art. 53(a) EPC and goes even further by defining more specifically which processes and uses of technology should be considered to be contrary to public policy or morality, and thereby non-patentable. The patentability exceptions defined in Art. 6(2) Biotech Directive (Rule 28 EPC) have a specific impact on the patentability of hESC technology and the methods that could be associated with it, since they *inter alia* comprise processes for cloning human beings, for modifying the germ line's genetic identity, and, in particular, in Art. 6(2)(c) (Rule 28(c)), uses of human embryos for industrial and commercial purposes.

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 and the lack of definitions in particular raise many questions with regard to the patentability of hESC technology and the definition of the human embryo. Totipotent hESCs[22] can be understood as a stage in the formation and development of the human body and product claims thus fall unequivocally under the patentability prohibition set forth in Art. 5(1) Biotech Directive. However, the

[17] Convention on the Grant of European Patents (European Patent Convention or EPC) of 5 October 1973, as revised by the Act revising Art. 63 EPC of 17 December 1991 and the Act revising the EPC of 29 November 2000. Note also that Art. 52(2) EPC positively defines categories which may not be regarded as patentable inventions as a matter of principle. In particular, Art. 52 (2)(a) excludes discoveries, scientific theories and mathematical methods.

[18] Art. 53(a) EPC (*supra* note 17).

[19] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions, OJ EU L 213.

[20] For an overview of the complex interface between these norms, *see* Hellstadius (2015), pp. 105–139.

[21] Administrative Council Decision, OJ EPO 7/1999, 437–440.

[22] 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 fertilised egg. This cell is totipotent, meaning that 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 4 days of embryonic cell division, the cells begin to specialise into pluripotent stem cells.

questions of patentability raised by pluripotent hESCs[23] and method claims concerning totipotent hESC uses remained rather unclear.

The situation appears even more complex when taking into account that the member states have introduced differing legislations with regard to the materials and techniques that are allowed in stem cell research, as well as various legal definitions of what constitutes an embryo. Thus, a wide variety of legal frameworks, resting on diverse ethical considerations, can be found within Europe.[24] Although it is well established that a morality clause cannot exclude an invention from patentability merely because that invention is prohibited by law or regulation, these laws and regulations still have to be considered, in order to define the technologies that are deemed to fall under the morality exclusion. In doing so, the national courts and patent offices would focus on the national legal rules on stem cell research, the EU mandated rules and the international treaties signed by the domestic state. The EPO and the CJEU, however, would have to define a European standard and take this as the basis for their decisions.[25] In that context it does not seem surprising that the provisions in national patent law and in the EPC which correspond to Arts. 5 and 6 Biotech Directive are equally subject to various interpretations and much debate, which ultimately has to be resolved by case law.

3 Preceding Case Law

The first *high profile* European case that directly addressed essential questions related to the interpretation of Art. 53(a) EPC (Rule 28(c)) referred to the EPO Enlarged Board of Appeal (EBA) under Art. 112(a) EPC was the *WARF* case. The patent application referred to primate (including human) embryonic stem cells, which are estimated by the scientific research community to hold potential promise for the treatment of many serious diseases and disabilities.[26] In November 2008, the EBA considered the above-described European legal framework and the relevant EPC provisions on the non-patentability of inventions using human embryos for

[23] 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. Even though they can form almost any human tissue, these inner cells cannot do so without the outer layer, so they are not totipotent, but pluripotent. As these pluripotent stem cells continue to divide, they specialise further.

[24] As of 2010, twenty-five European countries had adopted legislation explicitly prohibiting human reproductive cloning. Seven EU countries specifically allowed hESC research and the derivation of new hESC lines from supernumerary embryos from in vitro fertilisation (Belgium, Sweden, UK, Spain, Finland, Czech Republic and Portugal). These countries also allowed SCNT, except Finland and the Czech Republic, which did not have legislation on the subject. Three countries have adopted legislation to allow the creation of embryos for research purposes under strict conditions (Belgium, Sweden and the UK). Seventeen EU member states allowed the procurement of SCs from supernumerary embryos, while five countries had not adopted legislation regarding hESC research (Bulgaria, Croatia, Cyprus, Luxembourg and Romania). Højgaard and Makarow (2010), p. 10.

[25] Art. 53(a) EPC (*supra* note 17).

[26] Interestingly, three similar US patents owned by WARF had also been challenged in the US without the possibility of basing the attack on a morality provision. *See* Sect. 7.

industrial or commercial purposes in Europe to reject the patent application.[27] However, the Board left open the possibility of patenting products and methods using hESCs available in biobanks because these were derived from cell lines. In the aftermath of the *WARF* decision, the EPO used this loophole to develop a more liberal approach towards patent claims directed to hESCs which were available from certain pre-existing stem cell lines, that is, claims on technical inventions that did not *directly* require the destruction of an embryo.[28]

This was, of course, good news for patent applicants and patentees. However, things were developing rather differently at the national and EU levels, where questions similar to those addressed by *WARF* were to be considered by the German Federal Patent Court, the German Federal Supreme Court[29] and, ultimately, the CJEU in the *Brüstle* proceedings. This case concerned a patent granted by the German Patent Office.[30] The patent basically claimed neuronal precursor cells, a method of their production and their therapeutic use for neuronal disorders. It was subsequently challenged by Greenpeace due to the fact that the claims comprised hESCs. Greenpeace filed for nullity of Brüstle's patent, asserting that it was against public morality (*sittenwidrig*) under Sec. 2 of the German Patent Act, which is the German equivalent of Art. 6(2)(c) Biotech Directive. On 5 December 2006, the Federal Patent Court declared major parts of the claims to be invalid insofar as they related to human embryonic stem cells.[31] While the judgment of the Court had no legal effect on the pending EPO decision and had to be discussed in the light of very specific legal stipulations, such as Germany's Embryo Protection Act[32] and the Stem Cell Act,[33] the *Brüstle* case nevertheless left room for speculation concerning the potential implications it might have for the interpretation of the fundamental questions raised by the then still ongoing *WARF* proceedings at the EPO. Such considerations became even more interesting after the Federal Patent Court decision was appealed to the Federal Supreme Court. The Supreme Court recognised that any decision in the case would require further clarification by the CJEU. It therefore stayed the proceedings and referred a number of questions to the CJEU under the preliminary ruling procedure in Art. 267 TFEU.[34]

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

[28] A good description of this more liberal EPO approach is provided by Paton and Denoon 2011; *see also* Hellstadius (2015), pp. 290–306.

[29] The Federal Supreme Court (*Bundesgerichtshof*) is Germany's highest court of civil and criminal jurisdiction.

[30] German patent DE19756864.

[31] Available at: http://juris.bundespatentgericht.de/cgi-bin/rechtsprechung/document.py?Gericht=bpatg&Art=en&Datum=2006-12-5&nr=1909&pos=7&anz=12&Blank=1.pdf [in German] (accessed 16 November 2015).

[32] *Cf.* the German 1991 Embryo Protection Act (*Embryonenschutzgesetz*), adopted on 13 December 1990 (BGBl. I S. 2746), as amended on 21 November 2011 by Art. 1 of the Act (BGBl. I S. 2228), available at: http://www.gesetze-im-internet.de/eschg/BJNR027460990.html (accessed 16 November 2015).

[33] *Cf.* the German 2002 Stem Cell Act (*Stammzellgesetz*), adopted on 28 June 2002 (BGBl. I S. 2277), as amended on 7 August 2013 by Art. 2, Sec. 29 and Art. 4, Sec. 16 of the Act (BGBl. I S. 3154), available at: http://www.gesetze-im-internet.de/bundesrecht/stzg/gesamt.pdf (accessed 16 November 2015).

[34] *See* Case C-34/10 *Oliver Brüstle v. Greenpeace e.V.*, EU:C:2011:669.

In October 2011, the CJEU rendered its judgment in *Brüstle*,[35] broadly interpreting the patent exclusion of human embryos for commercial or industrial purposes, and adopting a "full history" approach.[36] The Court held *inter alia* that Art. 6(2)(c) 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.[37] Moreover, the CJEU 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 non-fertilized human ovum whose division and further development have been stimulated by parthenogenesis."[38]

The Court thus explicitly included non-fertilised ova after somatic cell nuclear transfer (SCNT)[39] 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 that they are capable of further cell division in the absence of sperm fertilisation.

In the wake of the CJEU's *Brüstle* judgment, scientists in the field of hESC research became concerned about the wider impact of this controversial decision and the full-history approach, as it prohibits hESC patents that use publicly available stem cell lines, which thus would not imply de-novo destruction of embryos.[40] The judgment was also fiercely debated and criticised in the academic literature, *inter alia* for artificially creating a fictional consensus in Europe on the definition of human embryos, and on the morality of stem cell research and regulation, and also for not complying with international standards and treaties, such as the TRIPS Agreement.[41]

However, when the German Federal Supreme Court ultimately applied the CJEU's preliminary ruling in *Brüstle* and delivered a final decision,[42] it became apparent that, surprisingly, the Court did not apply the prior CJEU considerations in a narrow and strict manner. Interpreting the CJEU's explanations in a rather patent-

[35] *Ibid.*

[36] *Id.* at paras. 49 and 52. Regarding the term "full history" approach, *cf.* Enrico Bonadio (2012b), p. 26.

[37] Case C-34/10 (*supra* note 34), at para. 52.

[38] *Id.* at para. 38.

[39] "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)." Available at: https://www.hhmi.org/biointeractive/somatic-cell-nuclear-transfer-animation (accessed 16 November 2015).

[40] Grund and Farmer (2012), pp. 39, 44; Bance (2012), pp. 33–38; Mahalatchimy et al. (2015), pp. 41–43.

[41] *Id. See also*: Straus (2010), p. 911; Abbot (2011), p. 1; *cf.* Plomer (2012), pp. 110 et seq.; Zimmer and Quest (2012), p. 271; Bonadio (2012c), pp. 93, 97. For a different view *see* Schneider (2011), pp. 475, 510 (pointing, however, towards democratic deficits); Callaway (2011), p. 441.

[42] German Federal Supreme Court Decision of 27 November 2012, Case X ZR 58/07.

friendly way, the Federal Supreme Court decided to only partially revoke Oliver Brüstle's patent. It determined that the patenting of the process is only excluded, according to Sec. 2(1) No. 3 Patent 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 are extracted without necessitating the destruction of embryos. Also, the use of cell lines extracted from embryos that are no longer able to develop does not – according to the Federal Supreme Court – result in exclusion from patentability. The negotiated patent claim was, in this respect, limited, and the appeal was only partially rejected. Amending this decision with a disclaimer, the Court also appeared to be willing to consider later (post-filing) technological developments that allowed the extraction of stem cells (e.g. through optimised blastomere separation) without necessarily destroying the embryo in the process. While the final Supreme Court decision indicated that a reasonable and relatively broad patent protection of 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 EPO.

In that context it should be noted that the EPO took a rather different path, which partially confirmed the aforementioned concerns of patentees and scientists. Shortly after the CJEU's judgment – although not formally bound by it – the EPO decided to directly incorporate the CJEU's *Brüstle* principles and the full-history approach into its guidelines for examination.[43] Accordingly, the EPO began to reject patent claims that would arguably have been accepted under the EPO's previous more pragmatic approach resulting from the EBA decision in *WARF*.[44] On 4 February 2014, this new restrictive approach was rigorously applied in the *Technion* decision, in which the TBA departed from the EBA's prior decision in the *WARF* case, deciding instead to align itself with the CJEU's decision in *Brüstle*.[45] Following a strict interpretation of Art. 53(a) EPC (Rule 28(c)) and the new EPO Guidelines, the TBA decided to exclude from patentability "inventions which make use of HES cells obtained by de-novo destruction of human embryos or of publicly available HES cell lines which were initially derived by a process resulting in the destruction of the human embryo".[46] Thereby, the TBA clearly brought the patentability of hESCs at the EPO more into line with the CJEU's decision in *Brüstle*. However, it appears less clear how far such a strict interpretation comports with the more permissible approach applied by the German Federal Supreme Court in its 2012 decision in *Brüstle*. Meanwhile, the UK courts were also struggling with the precise scope and implications of the CJEU's findings in *Brüstle,* resulting in a new referral

[43] *Cf.* Guidelines for Examination in the European Patent Office (EPO Guidelines), November 2014 edition, Part G, Chapters II-17 to 18 on Rule 28(c).

[44] G 2/06 *Use of embryos/WARF* (*supra* note 27).

[45] *See e.g.* EPO, Boards of Appeal in T 2221/10 *Culturing stem cells/TECHNION* [04.02.2014] unpublished. *Cf.* the more detailed analysis of the case by Mahalatchimy et al. (2015), pp. 41–43.

[46] *Id.*

to the CJEU seeking clarification of whether the CJEU ruling in *Brüstle* applies without distinction to unfertilised human ova stimulated by parthenogenesis. This is an interesting question, since such ova may develop into pluripotent cells that – in the absence of further genetic manipulation – are not capable of developing beyond the blastocyst stage. National courts were obviously confused about the full implications of the CJEU's *Brüstle* judgment in the light of these scientific facts. This provided the basis for the second stem cell judgment of the CJEU in C-364/13, *International Stem Cell Corporation*, which will be described in more detail in the next section.

4 The CJEU in C-364/13 International Stem Cell Corporation

In the following, we will outline the facts and procedural history, and summarise the main arguments and outcome of this case.[47]

4.1 Facts of the Case

The UK Intellectual Property Office (UKIPO) rejected two national patent applications assigned to International Stem Cell Corporation (ISCO), relating to research of a stem cell technology called parthenogenesis.[48] Objections were raised by the UKIPO on the grounds that the inventions were excluded from patentability due to their constituting uses of human embryos under para. 3(d) of Schedule A of the Patents Act 1977 – the rule that implements Art. 6(2)(c) Biotech Directive.[49] The applicant argued that the CJEU *Brüstle* decision should not apply, because the claimed inventions related to parthenogenetically activated oocytes, which are incapable of initiating the process of development of a human being, due to the phenomenon of genomic imprinting. ISCO was then confronted with research suggesting that such obstacles could be overcome by genetic engineering. As a result, an amendment to the claims was submitted, introducing the word "pluripotent" before "human stem cell line" and referring to a lack of paternal imprinting, thereby excluding any such method of genetic manipulation.[50] The patent applicant arguments were not found completely persuasive, and thus ISCO appealed to the High Court of Justice of England and Wales, Chancery Division (the Patents Court).[51]

[47] *See generally* case report: Minssen and Nordberg (2015a); *cf.* Stazi (2015) doi:10.1007/s40319-015-0389-x.

[48] Application GB0621068.6 "Parthenogenetic activation of oocytes for the production of human embryonic stem cells". of 23 January 2006, and Application GB0621069.4 "Synthetic cornea from retinal stem cells" of 23 October 2006.

[49] Biotech Directive (*supra* note 19).

[50] Applications GB0621068.6 and GB0621069.4 (*supra* note 48). For a summary of the patent prosecution history at the UKIPO *see* Comptroller General of Patents Decision No. BL O/316/12 of 16 August 2012, paras. 22–43.

[51] Decision No. BL O/316/12 (*id.*), paras. 63, 71–72 and 79–80.

4.2 The Referral

During the proceedings, scientific evidence emerged distinguishing parthenotes from fertilised ova and 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, evidence presented in the German Supreme Court *Brüstle* case,[52] and also the findings of the UKIPO. It was accepted by all parties 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 manipulation, parthenotes are unable to develop to term, due to lacking paternal DNA, which is necessary for the development of extra-embryonic tissue. Unlike fertilised ova and their early-stage descendent cells, parthenogenesis-activated oocyte cells are merely pluripotent and never totipotent. The evidence examined pointed out that, so far, human parthenotes have only been able to develop to the blastocyst stage (around 5 days).[53]

The legal debate revolved around whether biological analogy between a parthenogenetically derived structure and the blastocyst stage of normal embryonic development justified legal analogy, having in consideration that parthenotes had been expressly declared to be non-patentable human embryos.[54] The Comptroller argued that the test set in *Brüstle* could be interpreted as being concerned more with the commencement of the process of fertilisation than its outcome, but conceded that *Brüstle* could also be interpreted as requiring such a process to be capable of leading to a viable human being.[55] ISCO submitted that a narrow understanding of *Brüstle* should prevail.[56]

The Patents Court pointed out that the factual matrix in the case differed from the facts in *Brüstle*, suggesting that the CJEU may have relied on inaccurate or incomplete scientific submissions.[57] Therefore 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?".[58]

[52] German Federal Supreme Court Case X ZR 58/07 (*supra* note 42).

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

[54] Case C-34/10 (*supra* note 34), para. 39.

[55] [2013] EWHC 807 (*supra note* 53), para. 50.

[56] *Id*., para. 32.

[57] *Id*., paras. 51–54.

[58] *Id*., para. 59; Reference for a preliminary ruling from the 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).

4.3 Opinion of Advocate-General Cruz Villalón

The Advocate-General (AG) reasoned that while the wording in *Brüstle,* interpreted literally, includes parthenotes in the definition of "human embryos", the operative part of the judgment should be interpreted in the light of the grounds for such a decision.[59] The criterion used by the CJEU to include an organism in the definition of a human embryo was whether such an organism has the capability of commencing the process of development of a human being, and is thus functionally equivalent to an embryo.[60] The expression "capable of commencing the process of development of a human being" should therefore be understood as an organism possessing the inherent capability of developing into a human being.[61] Furthermore, the mere possibility of further genetic manipulation of parthenotes does not change their character before such manipulation.[62] The AG suggested the following answer to the referred question: "Unfertilised human ova whose division and further development have been stimulated by parthenogenesis are not included in the term 'human embryos' … as long as they are not capable of developing into a human being and have not been genetically manipulated to acquire such a capacity."[63]

4.4 The Decision of the CJEU

The CJEU ruled that Art. 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 proviso that "it does not, in itself, have the inherent capacity of developing into a human being". The decision of whether such a condition was fulfilled was left to the national courts. However, the CJEU established a criterion for such evaluation: "current scientific knowledge".[64] Pursuant to this reasoning, parthenotes should not be excluded from patentability provided that, in the light of current scientific knowledge, these are not considered to be capable of developing into a human being and are therefore not considered to be human embryos under the Biotech Directive. In its reasoning, the CJEU began by confirming the court's decision in *Brüstle*, and re-stating that *human embryo*, insofar as the interpretation of the Biotech Directive is concerned, is an autonomous EU law concept to be interpreted uniformly, and that such a concept must be construed in a wide sense.[65] Concerning the specific interpretation of *Brüstle* it was observed that the statement that any human ovum must, as soon as it is fertilised, be regarded as an embryo, since fertilisation implies the beginning of the process of the development

[59] Opinion of Advocate-General Cruz Villalón, delivered on 17 July 2014, Case C-364/13, *International Stem Cell v. Comptroller General of Patents*, paras. 62–63.

[60] *Id*., para. 67.

[61] *Id*., para. 71.

[62] *Id*., para. 77.

[63] *Id*., para. 80.

[64] Case C-364/13 (*supra* note 16), para. 39.

[65] *Id*., paras. 23–24.

of a human being,[66] must be interpreted according to the specification in the subsequent paragraph concerning non-fertilised ova. Clarifying that, it was also stated that non-fertilised ova would only be considered to be 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".[67] This critical and controversial expression was interpreted following the opinion of the AG,[68] which had proposed applying a test of "inherent capacity".[69] The CJEU concluded that as far as non-fertilised ova are concerned "the mere fact that an organism commences the process of development is not sufficient for it to be regarded as a 'human embryo'"[70] As for the reason why in *Brüstle* parthenotes were considered human embryos, the CJEU acknowledged that it had based its findings on submitted written observations which considered these to be capable of full development. It was left to the national courts to decide, in accordance with available scientific knowledge, whether an organism is inherently capable of developing into a human being.[71]

5 Discussion: Out of the Smog into the Fog?

The CJEU's decision to allow the patentability of certain parthenotes and parthenote-related technology, as we will argue below, may open up new venues for the patentability of hESC research and might thus be welcomed by potential patent applicants, irrespective of the practical relevance of patent applications directed to parthenotes in current patent practice. However, when read in conjunction with *Brüstle* a number of questions remain open for debate.

5.1 Elusive Definitions of "Human Being" and "Human Embryo"

A first controversial issue is the need to rely on a patent law-mandated definition of what constitutes a human being and a human embryo. Previously, in *Brüstle*, the term "human embryo" was defined as any human ovum as soon as it was fertilised (and its equivalents). The human embryo was automatically considered a stage of human development. In *ISCO*, this definition has now been complemented with the added criteria that it should, "in itself, have the inherent capacity of developing into a human being".[72] Consequently, this creates a reasoning that is still unclear and likely to support different interpretations.

The legal argument employed to exclude hESCs from patentability is vested in the legal text of the Biotech Directive in two legal mechanisms, corresponding to different

[66] Case C-34/10 (*supra* note 34), para. 35.

[67] *Id*., para. 36; Case C-364/13 (*supra* note 16), paras. 23–26.

[68] Opinion AG Case C-364/13 (*supra* note 59), para. 73.

[69] Case C-364/13 (*supra* note 16), paras. 23–28.

[70] *Id*., paras. 23–29.

[71] *Id*., paras. 36–38.

[72] Case C-364/13 (*supra* note 16), Operative part of the judgment (a contrario).

rationales: (1) subject-matter exclusion of the human body at any stage of development due to its occurring naturally and lacking technical character[73]; and (2) exception from patentability for ethical reasons precluding the patentability of uses of human embryos.[74] Although subject-matter exclusions and exceptions follow different rationales and should not be confused, these are interconnected. Stages of human development are products of nature and not patentable due to lack of technicality. Furthermore, private entitlements over the human body are considered ethically inadmissible, as they conflict with basic human rights such as dignity and autonomy. The recitals of the Biotech Directive indicate that this piece of legislation was grounded mostly in ethical considerations and intended to prevent the patentability of a human being, at any stage of development, regardless of whether it may be considered a product of nature (discovery) and thus as such non-patentable subject-matter, or a patentable technical creation (invention) that is denied patentability for being the object of an exception to patentability. Article 5(1) Biotech Directive is generally understood as a subject-matter exclusion norm. However, the motivation for its statutory inclusion in the Biotech Directive as a specific example of non-patentable subject-matter is ethical, as the recitals and historic elements clearly indicate (i.e. recital 16).Therefore, arguably, the subject-matter exclusion can also be said to be indirectly linked to ethical considerations. Such connection may help understand why, under US patent law, the issue has been discussed as a matter of patent eligibility (see Sect. 7).

Totipotent stem cells, per se, cannot be patented due to their being considered a stage of human development and thus not an invention.[75] Furthermore, uses of totipotent stem cells are also barred from patentability due to considerations of respect for human dignity (protection of life)[76] and autonomy (exploitation, commodification and objectifications of the human body).[77] In *Brüstle* the AG considered totipotent cells to be the first stage of the human body[78] and thus an embryo, regardless of the means by which it was obtained.[79] The CJEU followed a different approach, declaring that whether stem cells themselves are to be considered a human embryo depends on whether these are "capable of commencing the process of development of a human being", a task left to national courts to ascertain,[80] and that any human ova after fertilisation (or its equivalents) are considered themselves to constitute a human embryo.[81]

[73] Biotech Directive (*supra* note 19), Art. 5(1) and Recital 16.

[74] *Id*., Art. 6(2)(c) and Recital 38.

[75] *Id*., Art. 5(1).

[76] *Id*., Art. 6(2)(c) and Recital 38. Some authors link the issue of commercialisation directly to human dignity. *See* Sterckx and Cockbain (2010), p. 100.

[77] Viens (2009), p. 111, analysed the possible sources of wrongness of commercialising hESC, concluding that "at best, the definition of morality is one of cultural normative relativism", and that in Europe there are no formal definitions or criteria to access wrongful commercialisation (based either on exploitation, commodification or objectifications of the human body), or to justify a prohibition on patenting stem cells. *Cf.* Sterckx and Cockbain (2010), pp. 100–103.

[78] Opinion of Advocate-General Bot, delivered on 10 March 2011, Case C-34/10, *Oliver Brüstle v. Greenpeace e.V.*, EU:C:2011:669, para. 85.

[79] *Id*., para. 91.

[80] Case C-34/10 (*supra* note 34), para. 37.

[81] *Id*., para. 53.

The patentability status of *pluripotent cells* has been even more unclear. In this case, too, both the subject-matter exclusion and the morality-based exception have to be factored into the analysis. Regarding the subject-matter exclusion, it is relevant to determine what constitutes "the human body, at the various stages of its formation and development".[82] In respect of the morality-based exception, it is furthermore relevant to determine whether an invention includes the use of a human embryo for industrial or commercial purposes.[83] Pursuant to the ruling in *Brüstle*, inventions involving pluripotent stem cells may be excluded from patentability if their retrieval or the technical teaching of the invention requires the use of an embryo for commercial or industrial purposes. If embryos are destroyed in order to establish stem cell lines, arguably at a previous moment, this would imply the use of embryos, even when the method for obtaining the stem cell lines is not part of the invention as claimed, nor mentioned in the claims.[84]

Clearly, the construction of the Biotech Directive was anchored in the protection of human dignity and the integrity of the person.[85] However, the CJEU has refrained from referring to both law and jurisprudence concerning the scope of application of such principles. By considering *human embryo* for patent law purposes as an autonomous concept of EU law, the CJEU did more than what it arguably intended – to establish its jurisdiction. It also created a situation of legislative conflict between competing legal and regulatory definitions or understandings of the human embryo and its legal and moral status, largely because matters of health law and criminal and civil rules concerning the beginning and end of life are not subject to harmonisation at EU level.[86]

On a first reading, the *ISCO* ruling introduces some clarification and reduces the scope of the doctrine set in *Brüstle*. However, both these expressions – "inherent capacity of developing" and "human being" – are legally ambiguous. The *ISCO* requirement of inherent capacity could either be interpreted broadly – in the sense of *without need for any further technical steps or technical intervention* – or narrowly, as meaning *without further need for a qualified intervention, such a genetic manipulation*.

In the *first case*, the mere necessity of implantation in a human womb would imply the need for further technical intervention and the logical conclusion that such an organism is a non-viable entity and thus not an embryo. As far as we know, under the current state of scientific research it is not possible for a fertilised ovum to survive and continue to develop without further human intervention past the blastocyst phase. The embryo will, at least, need to be implanted in a human uterus at some stage. Even if further techniques allowed for in vitro full-term development,

[82] Biotech Directive (*supra* note 19), Art. 5(1).

[83] *Id*., Art. 6(2)(c).

[84] Case C-34/10 (*supra* note 34), para. 53. The CJEU answered the third question as follows: "Article 6(2)(c) of Directive 98/44 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."

[85] Biotech Directive (*supra* note 19), Recitals 16, 38–46.

[86] *See generally* Faeh 2015.

such would necessarily consist of further technical intervention in a broad sense, placing the organism outside the scope of the patent exception.

In the *second case*, an organism would still be considered an embryo, provided that its cells were totipotent. The need to employ assisted reproduction techniques for full-term development would not disqualify the organism from being considered a human embryo. It is possible to establish a parallel with the issue of determining when a process is essentially biological, for the purposes of determining the scope of Art. 53(b) EPC. While the CJEU has not interpreted Art. 4(1)(b) Biotech Directive, the EBA has considered that the mere need for human intervention is not sufficient criterion for a process not to be considered as "essentially biological".[87] It has also determined that an additional technical step that introduces or modifies a trait in the genome qualifies the process as non-essentially biological.[88] Thus, analogic reasoning would suggest that the EPO would take the second approach – not all types of human interventions would suffice to prove that an organism does not, in itself, have the inherent capacity of developing into a human being. On the other hand, firstly the EBA has previously departed from a uniform application of the three exceptions in Art. 53 EPC, on the grounds that each exception corresponds to different policy concerns.[89] Secondly, it is not a given either that the CJEU would follow similar reasoning, since the EU court could have chosen to construct the answer to the referral by resorting to the type of stem cell criterion – that is, whether the cells are or are not totipotent – as implied by the referred question. The option to depart from such solution and instead resort to the concept of human being could logically be read as intentional. Finally, given all of the above, it is difficult to predict which of these solutions (if any) will be adopted by the EPO, national patent offices and courts. It is not completely unrealistic to expect either hybrid solutions or a scenario of case-by-case approaches concerning different stem cell sources and techniques.

Relying on a patent law-specific notion of human being, even if indirectly, constitutes a weak point of the CJEU construction of Art. 6(1)(c) Biotech Directive, opening it to accusations of creating a non-falsifiable circular argument.[90] On the one hand, the CJEU jurisprudence appears to imply that a fertilised ovum is to be considered a mere stage of human development.[91] However, as will be mentioned below, by grounding the exception on human dignity, the CJEU implicitly denies any differentiation (for patent law purposes) extending the concept of human being to fertilised ova. Simultaneously, a fertilised ovum will only be an embryo provided

[87] *See* T 320/87 *Hybrid plants/LUBRIZOL* [10.11.1988] OJ EPO (1990), 71.

[88] *See* Consolidated decision of the Enlarged Board of Appeal G 2/07 *Broccoli/PLANT BIOSCIENCE* OJ EPO (2012), 130 and G 1/08 *Tomatoes/STATE OF ISRAEL* OJ EPO (2012), 130, 206, answer to questions 2 and 3.

[89] Consolidated decision of the Enlarged Board of Appeal of 25 March 2015, G 2/12 *Tomatoes/STATE OF ISRAEL* (*Tomatoes II)* and G 2/13 *Broccoli/PLANT BIOSCIENCE (Broccoli II)*; *See* Minssen and Nordberg (Minssen and Nordberg 2015a, 2015b). *Cf.* Sterckx and Cockbain (2012), pp. 309–319.

[90] A statement is called falsifiable if it is possible to conceive an observation or an argument which refutes it. A non-falsifiable argument is non-scientific in nature because it reverts to itself. *See* Popper (2005), p. 17.

[91] Case C-34/10 (*supra* note 34), answer to question 1.

that it has *the inherent capacity of developing into a human being*. The CJEU, perhaps wisely, deferred the opportunity to issue further guidance, leaving the subject for national authorities and thus indirectly declining competence to adjudicate in such a matter. It remains to be seen how national courts and the EPO will ultimately apply the present ruling.

5.2 Parthenotes as Non-Viable Organisms

ISCO introduced a qualifying criterion that arguably resembles a test of *viability of life*, raising further legal and ethical considerations. By using the criterion of inherent capacity of developing into a human being, the ruling leads to the logical conclusion that any embryo – or organism – that is somehow impaired, inviable, or unable to survive beyond a certain stage of development, is not a human being, nor a stage of human development for patenting purposes. Although it makes sense to distinguish parthenotes from the concept of embryo adopted in *Brüstle*, the adopted criterion in *ISCO* raises the question of whether certain disabilities or impairments, whether accidental or engineered, may disqualify an organism from such qualification. The main issue is the inclusion of the qualitative "human being", arguably purposely, as part of the test to determine whether an organism can be considered to be an embryo.

In *Brüstle* the CJEU opted for assuming jurisdiction over the uniform interpretation of the concept of human embryo as far as the Biotech Directive is concerned. This already debatable option was accompanied by a decision to define embryo in its broadest possible sense.[92] However, the concept of human being is not defined in either the Biotech Directive or in international law. In fact, the European Court of Human Rights (ECtHR) has reiterated that determining the concept of human being for the purposes of evaluating the scope of protection conferred under the right to life – Art. 2 Council of Europe Convention for the protection of Human Rights and Fundamental freedoms (ECHR) – lies within the margin of appreciation which each state enjoys.[93] The EU has not acceded to the ECHR and is unlikely to do so in the immediate future.[94] Thus, unlike all of its member states, the EU cannot be considered to fall under the scrutiny of the ECtHR. However, the CJEU is not prevented from finding the arguments of the ECtHR persuasive. On the contrary, this may be advisable and sustainable due to both substantive and formal considerations. On the one hand, there is merit in the ECHR reasoning. On the other, it would be reasonable for the CJEU to take such jurisprudence into consideration in the light of a future accession of the EU to the convention and considering that all EU member states are bound by such decisions.

[92] *See* Sommer (2013), pp. 220–222, arguing that because a patent is not a truly harmonised and Unitarian right, as it will remain even after the new European patent with unitary effect is in force, the CJEU intervention is at best premature.

[93] *Vo v. France* [CG], No. 53924/00 para. 82; *Evan v. UK*, No. 6339/05 para. 46; *A.B.&C. v. Ireland* [2010] ECHR 2032.

[94] The Treaty of Lisbon created the legal basis for such EU accession to the ECHR, *i.e.* Art. 6 TEU. However, the CJEU has declared that accession is not possible unless further conditions are met; *cf.* Opinion 2/13 of the Court (Full Court), 18 December 2014, at para. 153.

While intending to protect the value of life and human dignity, *ISCO* may indirectly result in the opposite, entering into conflict with the ethical and legal status of the embryo, foetus and unborn person in Europe. The unborn human organism lacks biological autonomy, being up to a certain stage of development incapable of surviving by itself, and being intrinsically and reciprocally connected with a woman. For this reason, in most European jurisdictions, under specific circumstances, which vary, the law allows the voluntary interruption of the gestational process and is especially permissive in cases of severe malformations. However, an impaired life can never be considered a *non-life*, or non-human, as opposed to a healthy one, pursuant to the principles of dignity,[95] equality[96] and non-discrimination.[97] In this sense, it is particularly relevant to consider the prohibition of eugenics practices, a ban that is consecrated as a fundamental principle of EU law.[98] Article 11 Oviedo Convention also prohibits discrimination based on genetic heritage,[99] given that it is also possible to argue that the provision precludes discrimination based on genetic identity even in the case of induced genetic modifications such as would be the case for organisms purposely created with some form of genetic impairment by technological means.[100]

If *Brüstle* was accused of inducing a lack of formal and substantive coherence in Europe between a more permissible regulatory framework and research funding and the strict interpretation of the patentability exception,[101] the present *ISCO* decision, while having positive aspects, has not improved matters in this specific regard. The adopted legal construction does not result in a more coherent legal solution, leads to uncertainty and maintains the potential to foster further litigation.

[95] Art. 2 Treaty on European Union, OJ EU C 326/13–390, 26.10.2012; Art. 1 (human dignity) Charter of Fundamental Rights of the European Union of 7 December 2000, as adapted at Strasbourg, on 12 December 2007; Art. 2 (right to life) Council of Europe Convention for the Protection of Human Rights and Fundamental Freedoms, as amended by Protocols No. 11 and No. 14, Rome, 4.XI.1950 (ECHR); Art. 1 Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.IV.1997 (Oviedo Convention).

[96] Art. 9 Treaty on European Union; Art. 20 (equality before the law) Charter of Fundamental Rights of the EU; Art. 3 (prohibition of eugenic practices) Charter of Fundamental Rights of the EU.

[97] Art. 14 (prohibition of discrimination) ECHR; Art. 1, Protocol No. 12 to the ECHR; and Art. 11 of the Oviedo Convention.

[98] Art. 3 Charter of Fundamental Rights of the EU (*supra* note 95).

[99] Note: this is an international instrument administered by the Council of Europe and not an EU treaty. The EU has not acceded to this convention, and some, but not all, of its members are signatory parties.

[100] Nordberg, A, "Patentability of human enhancement: from ethical dilemmas to legal (un)certainty" (forthcoming 2016), with further references.

[101] Brownsword (2014), p. 238; Plomer (2009), pp. 180–184; *See also* Isasi and Knoppers (2009), pp. 29–56. Bregman-Eschet et al. argue that empirical evidence suggests that such disconnection may have a ripple effect, decreasing all R&D in both embryonic and adult stem cell research. *See* Bregman-Eschet et al., "The Ripple Effect of Intellectual Property Policy: Empirical Evidence from Stem Cell Research and Development". Journal of Technology Law & Policy (forthcoming), p. 44. Available at: http://ssrn.com/abstract=2490823 (Accessed 16 November 2015). Murdoch (2010), p. 55, argues that "Inconsistent regimes within legal jurisdictions have the potential to put researchers in unusually precarious positions with respect to their research methodology and output".

5.3 Parthenotes and Human Ova Subjected to Somatic Cell Nuclear Transfer

Another major issue that remains unsettled is whether the differences between parthenotes and human ova that have been subjected to SCNT are sufficient to justify different legal treatment, or whether, on the contrary, the doctrine set in *Brüstle* concerning ova subjected to SCNT has now implicitly been revoked and/or needs to be re-visited.

In *Brüstle* the court ruled that any fertilised ovum is a human embryo, and that such classification must also apply to a non-fertilised human ovum subjected to SCNT and a human ovum stimulated by parthenogenesis. The argument used is one of functional equivalence: although those organisms have, strictly speaking, not "been the object of fertilisation", they are "capable of commencing the process of development of a human being", just like a fertilised ovum.[102] In *ISCO* it was stated that a parthenote is not a human embryo if "it does not, in itself, have the inherent capacity of developing into a human being". This opens the question of whether the test developed in *Brüstle* (fertilised ova and equivalents) and the test emerging from *ISCO* (inherent capability) should be considered as two cumulative conditions; or rather understood as two alternative criteria.

ISCO was presented as a clarification of *Brüstle*, thus it could be argued that *ISCO* has developed *Brüstle* by introducing a further cumulative condition, that is, that the finding of a "human embryo" would require: (1) its being a fertilised ovum or equivalent; and (2) its being inherently capable, by itself, of developing into a human being. In this case, it is a logical deduction to argue that any organism at the blastocyst phase (fertilised ovum or equivalent), that inherently or by itself is incapable of further development, is excluded from the concept of embryo. This understanding, which follows a line of reasoning similar to that of the German Federal Supreme Court, would have broader consequences, since it would imply generalising a more permissible approach in Europe. In the German *Brüstle* decision,[103] the use of cell lines extracted from embryos that are no longer capable of developing was considered to lie outside the scope of the patentability exception.[104]

Another possible reading is to understand these decisions as setting two alternative tests, the first determining whether the organism is a fertilised ovum (naturally occurring or resulting from in vitro fertilisation). These organisms are by default human embryos, since in *Brüstle* no bottom limit or moral differentiation has been established depending on the stage of development. The second test, concerning organisms that cannot be considered fertilised ova, would be one of establishing analogy through functional equivalence, that is, inherent capability of development into a human being. In this case, in practice it could be considered that these are two separate alternative tests to be applied to different organisms, resulting from different fertilisation techniques. Under this reading, the second criterion could no longer be applied to a fertilised ovum, even if it does not, "in itself, have the

[102] Case C-34/10 (*supra* note 34), paras. 35–36.

[103] German Federal Supreme Court Case X ZR 58/07 (*supra* note 42).

[104] *See* Sect. 3.

inherent capacity of developing into a human being". This means that the *ISCO* criteria would not be applicable to the so-called inviable embryos, limiting the scope of the decision to parthenotes and, eventually, human ova subjected to somatic cell nuclear transfer.

In both cases, the concrete legal and factual arguments that might justify differentiation or equal treatment remain undetermined. This might include debating whether functional equivalence is the optimal criterion for establishing similar ethical significance and legal analogy. Scientific evidence will have to be analysed by courts, however arguable it is that, in the light of the *ISCO* criteria, no major differences can be found between partenothes and human ova subjected to cell nuclear transfer.

It is unlikely that the CJEU intended to allow a broad reading that would disqualify from the exception any organism, including fertilised ova, that, by itself, at the time of use is incapable of further development, such as inviable embryos.[105] However, the opposite can also be reasonably argued, since the decision of the German Federal Supreme Court in *Brüstle* was known to the court. Ultimately, the fact that the EU court did not further elaborate on the matter leaves the question open.

5.4 Selection and Use of Legal Sources

The referred question offered an opportunity to re-think the contested jurisprudence set in *Brüstle*, but the CJEU skilfully avoided re-opening the debate by treating the issues raised as matters of factual determination. The key issue remains: there are biological, ethical and legal differences between a blastocyst, an embryo, a foetus and a person/human being. These differences are generally accepted, both at European and national level. Furthermore, the use of embryos in research, including their destruction, is considered to be morally justified and legally admissible under the regulatory frameworks of several European countries.[106]

The CJEU in *Brüstle*, facing the lack of European consensus on the matter, has been criticised for ignoring matters of both fact and law while ruling that any fertilised ovum is an embryo and an embryo is a person.[107] The decision could be, and has been, criticised for choosing to harmonise legislation interpreting the Biotech Directive in the most patent-restrictive manner that the text allowed, even after acknowledging that "the definition of human embryo is a very sensitive social issue in many Member States, marked by their multiple traditions and value systems".[108] Given the legislative history of the Directive,[109] a most plausive interpretation would have been to consider that the legislature did not further elaborate on the concept of embryo due to the lack of consensus on the matter between different EU member states and the omission

[105] *See* Sect. 5.1.

[106] Plomer (2012), pp. 126–127.

[107] *Id*., pp. 125–126.

[108] Case C-34/10 (*supra* note 34), para. 30.

[109] *See* Straus (1995), pp. 942–947 anticipating some of the issues now being debated.

was thus intentionally made in order to defer the issue to the national legal orders.[110]

The Biotech Directive must necessarily be interpreted according to the EU Treaty and framed within the context of other derivative legislation and relevant jurisprudence of the EU courts. It has been argued that the CJEU cannot extend the protection of human dignity beyond what is permitted under the Treaty on European Union and that such protection begins at birth.[111] The *Brüstle* decision is also at odds with the approach followed in EU legislation enacted after the Biotech Directive, namely the EU Directive on Human Tissue and Cells[112] and the Regulation on Advanced Therapies.[113] A default permissive approach was enacted for regulatory purposes, deferring to the member states the task of addressing in national law questions relating to moral and legal constraints on uses of human embryos and stem cells. This supports both a narrower interpretation of the Biotech Directive and the thesis of national jurisdiction concerning morality matters.[114]

The concepts of *ordre public* and morality that the Biotech Directive elaborates upon are open concepts.[115] As a matter of interpretative technique, because the resort to open concepts conflicts with legal certainty, and in the interest of systematic coherence, interpretation should necessarily include reference to both higher normative sources, such as the EU Treaties, and regulatory sources that may provide for specific contextual meaning.[116] The CJEU would be expected to be more sensitive to such matters, being a judicature whose competence is limited firstly in functional terms to ensuring harmonised interpretation of EU law,[117] and secondly, limited as a matter of formal competences by the EU Treaties and the

[110] In this sense, Faeh (2015) (*supra* note 86) with further references; *see also*: Sommer (2013), pp. 211–223; Warren-Jones (2008), p. 651; Van Overwalle (Van Overwalle 2005), p. 222; Straus (2013), p. 34.

[111] *See* Hitchcock and Sousa e Brito (Hitchcock and Sousa e Brito 2014), p. 397.

[112] Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells, OJ EU L 102/48, 7.4.2004.

[113] Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No. 726/2004 OJ EU L 324/121, 10.12.2007.

[114] *See* above Sect. 4.3. *See also* Hitchcock and Sousa e Brito 2014, pp. 394–395, arguing that the intervention of the CJEU was not necessary because the EU regulatory framework accepts and even encourages commercialisation and clinical use of hESC products.

[115] Bonadio (2012a, b, c), p. 439 (with further references); Gervais (2003), p. 36; Watal (2001), p. 42; Pires de Carvalho (2002), p. 171; Porter (2009), pp. 343–344.

[116] *Kingdom of the Netherlands v. European Parliament and Council of the European Union*, [2000] Judgment of the Court of 9 October 2001, ECLI:EU:C:2000:415. Here the CJEU argued that "it is common ground that this provision [Art. 6 of the Biotech Directive] allows the administrative authorities and courts of the Member States a wide scope for manœuvre in applying this exclusion".

[117] The CJEU does not have competence to apply law to specific factual situations. *See* Advocate-General's opinion in C-51/75 *EMI Records Ltd v. CBS United Kingdom Ltd.* [1976]; C-377/98 *Kingdom of the Netherlands v. European Parliament and Council of the European Union* [2001]; 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].

functions of the Union.[118] It has been argued that, had the CJEU adverted to the primary legal sources which are specifically mentioned in the Directive, and followed its own jurisprudence regarding the interpretation of fundamental rights, it would have reached a different conclusion.[119] It has also been mentioned that it is of paramount relevance that the construction of the morality exception is consistent with respect for EU principles, and the diversity of views and national autonomy of member states.[120] Proportionality is among the most important principles of the EU legal order, serving both the purpose of limiting the EU legal competences, thus creating a mechanism of reconciliation between fundamental values, and that of framing the interpretative task regarding application to specific material facts.[121] A broad construction of the exception overlooks the nature and functions of the patent right and seems inconsistent with the principle of proportionality.[122] Also mentioned in the literature is the question of the general scope of exceptions. It has been claimed that the CJEU had previously adopted a principle of narrow interpretation of exceptions to fundamental EU Treaty principles.[123] Against this, it should be mentioned that the *Brüstle* case can be read either as the broad interpretation of an exception to the right to intellectual property, or as the broad interpretation of the right to human dignity. Thus, in cases involving conflicting fundamental rights applying by default, a principle of narrow interpretation of exceptions would hardly be a useful interpretative technique.[124] Instead, emphasis should be given to legislative intent and secondary sources of law, which, as mentioned, would point in the direction of a narrow interpretation.[125]

The interface between IP and human rights is complex.[126] There are advantages,[127] but also known dangers of deciding patent law cases in the light

[118] In this sense: Plomer (2009), p. 177.

[119] Plomer (2012), p. 126.

[120] Engelbrekt (2009), pp. 236–246. The author analyses the CJEU's jurisprudence in cases related to *ordre public* and morality, concluding that the "analysis seems to point in the direction of greater sensitivity to national perceptions of ethics and morality, even in the field of the allegedly common Community principles of protection of fundamental rights".

[121] Pila (2013), p. 11.

[122] Christoffersen (2015), p. 36, argues that proportionality is more than essential in legal interpretation. It is inherent in the adjudication of human rights.

[123] *See* Consolidated Cases G 2/12 *Tomatoes II* and G 2/13 *Broccoli II* (*supra* note 89), Reasons, VI .2.

[124] Art. 6(1) Treaty on European Union states: "The Union recognises the rights, freedoms and principles set out in the Charter of Fundamental Rights of the European Union of 7 December 2000, as adapted at Strasbourg, on 12 December 2007, which shall have the same legal value as the Treaties"; Art. 1 Charter of Fundamental Rights of the European Union (EU Charter): "Human dignity is inviolable. It must be respected and protected"; and Art. 17(2) EU Charter (right to property): "Intellectual property shall be protected".

[125] The EPO developed a similar approach in G 2/06 *Use of embryos/WARF* (*supra* note 27), Reasons, 16 *et seq*.

[126] For a general framework analysis *see* Helfer and Austin 2011.

[127] For a variety of perspectives *see* Geiger 2015.

of a human rights reasoning.[128] This is a path that the EPO Boards of Appeal have carefully avoided.[129] One of the main difficulties is that using a human rights reasoning implies the need to evaluate all connected legal sources. In the current context this entails considering rules and jurisprudence concerning the definition and legal status of the human embryo and human tissues as far as the right to life and the dignity of the person are concerned. An overview of the EU and European legal framework concerning the limits of human life and the protection of the right to life vis-à-vis the right to health points in the direction of a lack of European consensus and strengthens the argument for national jurisdiction.

The argument that lack of harmonisation of the concept of embryo and the scope of protection conferred to embryos in relation to patentability would prejudice the realisation of the internal market[130] is not very persuasive. This is, first, because Art. 6(1) Biotech Directive leaves open the possibility for the member states to consider whether an invention is in breach of *ordre public* or morality even outside the specific examples provided in Art. 6(2) Biotech Directive; and, second, due to the nature of patent rights and the lack of a truly uniform EU patent right.[131] Patent rights remain national administrative concessions that presuppose an act of will – the patent application. Applicants are furthermore not obliged to apply for a patent right in all EU member states. There will always be situations where an invention is patented in some EU member states and in the public domain in others, given that freedom of movement issues are generally addressed under the doctrine of exhaustion.

5.5 The CJEU and Ethical Expertise

The Biotech Directive was enacted with the objective of introducing a balance between competing policy issues: (1) preserving human dignity, the right to life and human autonomy, in the sense of non-commercialisation of parts of the human body; and (2) maintaining an adequate level of incentives to ensure that the research and development of life-saving technologies remains attractive to private

[128] *See generally* Yu (2015), arguing that there are considerable conceptual and practical challenges to the development and use of a human rights framework for intellectual property.

[129] Minssen and Nordberg (2015a, b) (*supra* note 100), pp. 127–128. Only a handful of EPO decisions mention human rights conventions: D 11/91 *Disciplinary penalty* [14.09.1994] OJ EPO 1995, 721; G 3/98 *Six-month period/UNIVERSITY PATENTS* [12.7.2000] OJ EPO 2001, 62; J 15/04 *Possible reason for exclusion*/MITSUBISHI HEAVY INDUSTRIES, LTD. [30.05.2006] unpublished; G 1/05 *Exclusion and objection/**XXX*** [22.12.2006] 2007, 362; T 190/03 *Partiality/**XXX*** [18.3.2005] unpublished; T 1465/07 *Ion mobility and mass spectrometer/INDIANA UNIVERSITY RESEARCH AND TECHNOLOGY CORPORATION* [09.05.2008] unpublished; Consolidated Cases G 2/02 and G 3/02 *Priorities from India/ASTRAZENECA* [26.4.2004] OJ EPO 2004, 483; D 23/08 [03.06.2009] unpublished; T 2/09 *Public availability of an e-mail transmitted via the Internet/KONINKLIJKE PHILIPS ELECTRONICS N.V.* [12.03.2012] unpublished. And only one decision clearly links Art. 53(a) EPC to human rights conventions: *See* T 149/11 *Method and device for processing a slaughtered animal or part thereof in a slaughterhouse/MEYN FOOD PROCESSING TECHNOLOGY B.V.* [24.01.2013] unpublished.

[130] Case C-34/10 (*supra* note 34), paras. 27–28.

[131] Whether this argument will still hold true in the advent of the European patent with unitary effect and the Unified Patent Court is difficult to predict accurately. *See generally* Minssen and Lundqvist (2014).

investors.[132] However, consensus between the relative values to be attributed to each of these policy objectives was and is far from being achieved, both at political and cultural level. Evidence that the legislature understood the social and political sensitivity of the subject can be found in Art. 7 Biotech Directive, which determines that provisions of the Directive entailing an element of ethical evaluation of biotechnology inventions should be interpreted according to the decisions of the Commission's European Group on Ethics in Science and New Technologies (EGE).[133]

The EGE has examined ethical issues related to stem cell patenting, expressing the opinion that no ethical reason could be found for a complete ban on the patenting of inventions relating to stem cells or stem cell lines, since this would be contrary both to the public interest – the right to health – and to the EU's encouragement of research and scientific progress – as expressed in the recitals of the Biotech Directive. Furthermore, the EGE distinguishes between non-modified hESCs, which should not be patentable, and patentable modified hESCs. The EGE does not take a position on what is to be considered an embryo and, most importantly, does not consider embryo destruction to be a determinant ethical consideration.[134]

Even though the merits of the EGE's reasoning can be questioned, it is apparent that the legislature expressly attributed some legal interpretative value to these opinions. In contrast, the CJEU has ignored the EGE and avoided references to Art. 7 Biotech Directive. Arguably, the CJEU has implicitly made a restrictive interpretation of the mandate conferred on the EGE and the value of its opinions as a secondary source of law, and opted for its own evaluation, framed by the experience of the Court and the submissions of the parties.[135] Independently of how the role and mandate of the EGE are understood, this case demonstrates that it is important to debate the limits of jurisdictional adjudication concerning matters that transcend the borders of the law and enter the fields of both science and ethics, and whether the CJEU has crossed those boundaries. It has been suggested that the use of ethical expertise, or a pre-exam by an ethics council, could offer courts and patent offices the benefits of ethical expertise.[136] Comparatively, and despite the debate, no such

[132] Biotech Directive (*supra* note 19) recitals 1, 2, 16, 17 and 37–43.

[133] Biotech Directive (*supra* note 19) Art. 7 reads: "The Commission's European Group on Ethics in Science and New Technologies evaluates all ethical aspects of biotechnology". The EGE is a group of experts from different EU member states with expertise in different fields of knowledge.

[134] European Group on Ethics in Science and New Technologies, *Opinion n°16—07/05/2002—Ethical aspects of patenting inventions involving human stem cells*, para. 2.1. Available at: http://ec.europa.eu/archives/bepa/european-group-ethics/docs/avis16_en.pdf (accessed 16 November 2015). Often the EGE asks experts to deliver reports to inform its decisions. Opinion No. 16 was based on the following study: Van Overwalle (2002).

[135] The EGE was created as an advisory body to the European Commission in its previous composition. The mandate of the EGE is restricted to the task of advising the Commission on ethical questions relating to sciences and new technologies, either at the request of the Commission or on its own initiative. The opinions of the EGE are not legally binding. *Cf.* Commission Decision of 23 December 2009 on the renewal of the mandate of the European Group on Ethics in Science and New Technologies (2010/1/EU). Therefore the reference in Art. 7 of the Biotech Directive can be interpreted both as establishing the interpretative value of such opinions – a role akin to expert testimonials – or as merely establishing the legal basis for the functioning of this consulting body.

[136] Bonadio (2012a), p. 438.

institutional solution has been created within the framework of the EPO, nor within the new Unified Patent Court system. Formally, it is within the powers of the CJEU to decide whether a measure of inquiry is necessary, since the commissioning of expert reports is expressly allowed by the court statute.[137] This possibility could help inform future decisions, but is not immune to criticism and practical difficulties.

5.6 The CJEU and Scientific Expertise

In *ISCO* the CJEU recognised that in *Brüstle* it had relied on incorrect scientific data concerning parthenotes, but it did so only indirectly, and fell short of actually acknowledging that there had been a technical failure,[138] or that the CJEU was misdirected or had misunderstood the science at issue. Hence, both decisions revive an old debate concerning the limits of judicial adjudication in scientifically very complex matters. It could be argued that a broad discretion of the Court in deciding on legal and scientific facts is necessary to fulfil the Court's function in ensuring a harmonious interpretation of EU law. However, the function of general courts of last resort, such as the CJEU, is primarily to rule on matters of law. If the decision on whether parthenotes – or oocytes created by nuclear cell transfer – constitute embryos in accordance with the Biotech Directive is indeed merely a matter of factual determination (as admitted by the CJEU), the Court would have been wise to avoid adjudicating directly on such matters.[139] Alternatively, and in the absence of any information indicating the contrary,[140] the CJEU should at least have based such a decision not merely on the submissions of the parties, but also on commissioned independent expert reports on the state of scientific knowledge and technical possibilities.

On a positive note, *ISCO* nevertheless signifies an important step, since the CJEU appears to at least indirectly recognise the inherent dangers and difficulties of ruling in complex matters concerning sensitive scientific facts. This appears even more important now, since the CJEU will also have limited opportunity to ultimately judge on particular issues arising within the emerging Unitary Patent System.

There is another point to be made: questions are raised by the re-enforcement of "current scientific knowledge"[141] as a criterion to determine whether a parthenote, or another organism, is inherently capable of developing into a human being. Firstly, the issue of determining the relevant moment in time to consider when

[137] Arts. 63(1) and 64(2)(d) Rules of Procedure of the Court of Justice, OJ EU L 265/1-42, 29.9.2012.

[138] The CJEU decision in *Brüstle* was widely criticised by scientists for containing crucial errors concerning the underlying science relating to parthenogenesis. *See i.a.* Green (2011), p. 41.

[139] *See* Advocate-General's opinion in C-51/75 *EMI Records Ltd v. CBS United Kingdom Ltd* [1976], C-377/98 **XXX?** 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].

[140] This observation is based solely on the content of the final decisions, since other procedural documents were not accessible. It is also recognised that commissioning reports might present additional challenges such as choice of experts, increase in time length of the case, the possibility of an inconclusive report, etc.

[141] Case C-364/13 (*supra* note 16), para. 39.

defining "current" remains unresolved. In comparison, the EPO post-*WARF* practice has been to consider the date of filing.[142] However, in *ISCO* the CJEU has accepted arguments concerning the nature of parthenotes based on scientific papers published long after the applications' filing dates.[143] The CJEU naturally based its findings on the material facts as settled by the referring court. The use by courts of scientific evidence posterior to the filing date may be defendable from a procedural point of view, since the decision is limited to a matter of interpretation of legal concepts. However, considering the functions and nature of the patent rights, this approach creates unwarranted legal uncertainty: at any moment during the life of the patent right new scientific developments may render the claims in total or partially non-patentable.[144] Likewise, at the filing date, applicants (and similarly potential opponents) will still have difficulty in determining with certainty whether an invention is excluded or patentable, and deciding on the appropriate IP strategy. This was already apparent from the final decision of the German Federal Supreme Court in *Brüstle*, where the court appeared to be willing to consider post-filing technological developments that allowed the extraction of stem cells without necessarily destroying the embryo. Another related matter is the procedural issue of determining the value to be attributed to the scientific evidence presented, and the level of consensus in the scientific community required, for an expert opinion to be considered reliable by the courts. The CJEU relied on its previous decision in *Smits and Peerbooms*[145] and declared the standard to be "knowledge which is sufficiently tried and tested by international medical science".[146] The chosen standard is on the one hand unclear because in the context of the present norm it requires proof of a negative fact[147]; and on the other hand dependent on non-harmonised national procedural rules.

5.7 TRIPS Compliance

Until *Brüstle*, most important patentability decisions in Europe were issued either by the EPO or by national patent offices and courts. The EPO is an international organisation, and although all of its member states are simultaneously members of the WTO[148] and thereby signatory parties to TRIPS,[149] the EPO in itself is not

[142] EPO Guidelines (*supra* note 43), G-II, 5.3 "A claim directed to a product, which at the filing date of the application could be exclusively obtained by a method which necessarily involved the destruction of human embryos from which the said product is derived is excluded from patentability under Rule 28(c), even if said method is not part of the claim (see G 2/06). The point in time at which such destruction takes place is irrelevant."

[143] GB0621068.6 and GB0621069 (*supra* note 48).

[144] Similarly: Ribbons and Lynch (2015), p. 6.

[145] Case C-157/99, *Smits and Peerbooms*, EU:C:2001:404, para. 94.

[146] Case C-364/13 (*supra* note 16), para. 36.

[147] Ribbons and Lynch (2015), p. 6.

[148] WTO is an international organization established by the Marrakesh Agreement Establishing the World Trade Organization, signed in Marrakesh, Morocco on 15 April 1994.

[149] The TRIPS Agreement is Annex 1C to the Marrakesh Agreement, and under Art. II (2) an integral part of the Marrakesh Agreement, binding on all signatory parties.

formally obliged to comply with TRIPS. However, during the revision of the EPC, consistency with TRIPS and EU law was acknowledged as a necessity.[150] Article 27(2) TRIPS allows signatory parties to include in their domestic patent law "provisions necessary to protect *ordre public* or morality".[151] Article 53(a) EPC and corresponding national norms predate TRIPS and compliance with it has been mostly presumed. However, this norm was rarely invoked until the advent of biotechnology. Moreover, exclusions and exceptions were traditionally interpreted narrowly.[152] The expansionary evolution of EPO practice,[153] the posterior enactment of the Biotech Directive and its broad interpretation by the CJEU, have changed the legal landscape, creating a shifting paradigm for the morality exception. This jurisprudential morality standard has to be debated in the light of the international obligations consubstantiated by TRIPS.[154]

The CJEU decision in *Brüstle* created a historical approach equivalent to an original-sin doctrine that has established a perpetual link between a damaging action – the immoral act of embryo destruction – and a fruit-of-the-poisonous-tree or strict-liability standard. This understanding was subsequently included in the EPO Guidelines, expanding the original scope of the EPC provision, which had been generally held to be necessarily construed narrowly.[155] Strict adherence to the CJEU's broad construction of the exception could result in excluding the entire field of technology based on hESC research from patentability.[156]

[150] Explanatory remarks to the transitional arrangements adopted by the Administrative Council, Special Edition No. 1 OJ EPO EB, Art. 7 "The revised version of Article 53(a) EPC likewise simply brings it into line with Article 27(2) of the TRIPs Agreement and the relevant provisions of Directive 98/44/EC on the protection of biotechnological inventions; it leaves EPO practice unaffected."

[151] Art. 27(2) TRIPS (*supra* note 149).

[152] The postulate *singularia non sunt extendenda* has no clear legal basis in patent law; however it is frequently mentioned, and consistently applied, by the EPO Boards of Appeal. *See* Holzapfel and Werner (2009), p. 107.

The EPO has considered that a principle of narrow construction emerges from the case law of the Boards of Appeal. *See Case Law of the Boards of Appeal of the European Patent Office*, 7th ed. (EPO, September 2013) at I.B:1.2: Basic Principles. Available at: https://www.epo.org/law-practice/case-law-appeals/case-law.html (Accessed 16 November 2015). However, recent decisions of the EBA have reiterated that exceptions do not necessarily have to be interpreted narrowly, although in specific cases it may be appropriate to do so. *See*: G 1/04 *Diagnostic methods* OJ EPO 2006, 334, Reasons, 6; G 2/06 *Use of embryos/WARF* (*supra* note 27), Reasons, 16 *et seq.*; G 1/07 *Treatment by surgery/MEDI-PHYSICS* OJ EPO 2011, 134, Reasons, 3.1; Consolidated cases G 2/12 *Tomatoes II* and G 2/13 *Broccoli II* (*supra* note 123).

[153] A comparison between different EPO decisions shows how the morality exception at the EPO has been evolving in an expansionary manner. From the more cautious approach in T 19/90 *Onco-mouse/HARVARD* [03.10.1990] OJ EPO 1990, 476 and T 356/93 *Plant cells/PLANT GENETIC SYSTEMS* [21.02.1995] OJ EPO 1995, 545; to G 2/06 *Use of embryos/WARF* (*supra* note 27), and the complete assumption of the CJEU broad approach by the EPO in T 2221/10 *Culturing stem cells/TECHNION* (*supra* note 45). In this sense: O'Sullivan (2012), pp. 686–689.

[154] The subject of TRIPS compliance was analysed by the CJEU in *Kingdom of the Netherlands v. European Parliament and Council of the European Union*, [2000] Judgment of the Court of 9 October 2001, ECLI:EU:C:2000:415. This decision precedes the *Brüstle* case.

[155] T 356/93 *Plant cells/PLANT GENETIC SYSTEMS* (*supra* note 153); T866/01 *Euthanasia Compositions/MICHIGAN STATE UNIV.* [11.05.2005] unpublished; T 1374/04 *Stem cells/WARF* [07.04.2006] OJ EPO 2007, 313.

[156] Bonadio (2012a), pp. 440–441; Sommer (2013), pp. 220–223; Van Overwalle (2005), p. 222.

Compliance with the TRIPS Agreement has to be considered by reference to its Art. 27(2), which allows members to "exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is *necessary* to protect *ordre public* or morality" (emphasis added). As observed by several commentators, the ability of member states to introduce *ordre public* and morality exceptions is not absolute, but rather conditional on the necessity of the measure.[157] Joseph Straus mentions that this should entail that "firstly, and most importantly, exclusion from patentability of a specific invention is only allowed, if the commercial exploitation of that invention is prohibited in the territory of the respective Member".[158] The letter of the law states that the patentability exclusion cannot be based on mere legal prohibition of commercialisation. This is clearly because it will not always be necessary to deny patent incentive, and on the contrary compelling reasons may dictate that incentive be granted to further research in order to invent non-detrimental (or less detrimental) versions. It may also be the case that regulatory prohibition has been determined for reasons that cannot be subsumed under the concepts of *ordre public* and morality. Through the use of the word "necessary", Art. 27(2) TRIPS introduces a two-step test: (1) that the exclusion necessarily contributes in practice to the protection of *ordre public* and morality values; and (2) that no less restrictive measures are available.[159] In the light of the current EU regulatory framework, it is at best debatable whether the CJEU's jurisprudence fulfils these conditions. This is something that the national courts may have realised, which explains to a certain extent the German Supreme Court's *Brüstle* decision,[160] but also the difficulties of the UK court and the later referral in *ISCO*.[161]

The present decision in *ISCO* re-introduces a more nuanced approach and indirectly re-establishes some balance in the jurisdictional construction. However, Straus' compelling arguments remain unblemished and this decision has not altered their validity. In strict legal terms, member states could be brought before the dispute settlement body of the WTO for lack of compliance with Art. 27(2) TRIPS,[162] naturally depending on political and patent policy considerations, which are beyond the scope of this paper. This more balanced approach may signify that other arguments will be less likely to succeed, since it can no longer be argued that any technology based on hESC research is, per se, necessarily immoral and thus that a field of technology has been banned from patentability.

[157] Straus (2013), p. 21. *See also*: Pires de Carvalho (2010), pp. 298–299; Correa (2007), p. 291, who mentions that "it is debatable whether the exceptions under this Article can only be applied when there is an actual ban on commercialization", with further references.

[158] Straus (2013), p. 23.

[159] Similarly Straus (2013), pp. 22 *et seq.* with further references.

[160] German Federal Supreme Court Case X ZR 58/07 (*supra* note 42).

[161] [2013] EWHC 807 (*supra note* 53).

[162] Straus (2013), p. 38.

6 Practical Implications

Considering the legal reasoning and material findings of the referring court, it is expected that it will conclude that, under the current scientific knowledge, parthenotes cannot be considered inherently capable of developing into a human being. As a consequence, the patent will probably be granted as amended. However, given the issues examined above, a high level of uncertainty will persist.

6.1 Implications at the National Level

The CJEU in *ISCO* deferred to national courts the evaluation of whether parthenotes, and arguably other organisms resulting from genetic manipulation, "have the inherent capacity of developing into a human being" and thus whether these can be subsumed under the definition of human embryo under Art. 6(2)(c) Biotech Directive. No further guidance was offered as to what constitutes a "human being", nor what point in the biological development process, if any, determines such qualification. Simultaneously, an analysis of human rights law shows that there is no uniform European definition of human being, nor any consensus on its lower and upper limits.

ISCO also introduced the requirement that such evaluation should be made according to "current scientific knowledge". However, it is left undetermined what point in time should be considered when assessing the state of "current scientific knowledge". Therefore, applicants may tend to develop strategies guided by the consideration of whether the invention's patentability is likely to suffer or benefit with time.

The approach currently followed at the EPO, as stated in the EPO Guidelines, is to consider the state of the art at the filing date.[163] This might be extremely complex in cases where the possibility of obtaining the said base material by a certain method is anticipated in the literature, but there is still uncertainty as to whether such a method would produce the intended results, or in cases where there are still technical problems to be overcome. It was also left undetermined whether the standard in *ISCO* for determining the current scientific knowledge will translate into a novelty/state-of-the-art standard, or rather an inventive-step standard. It is noteworthy that the test set in *ISCO* is one of "current scientific knowledge" and not a test of "technical state of the art", as used in patent examination. This may point in the direction of national courts using a broader concept than the EPO or patent offices, meaning that the mere scientific possibility of obtaining hESCs by methods considered ethical would defeat the original-sin legal presumption set in *Brüstle*. In theory, linking patentability decisions to the "current scientific knowledge" would make it possible to introduce objectivity and reach a higher level of harmonisation and legal certainty in Europe. However, as explained above, this may not be the case.

Another potential practical concern is that national courts may be bound to different extents by the material facts and scientific evidence presented by the

[163] EPO Guidelines (*supra* note 43), G-II 5.3.

parties in the specific proceedings, depending on each jurisdiction's procedural rules and stance concerning the court's powers of discovery and the parties' legal obligations of disclosure during civil proceedings. This procedural aspect, often overlooked, should also be carefully considered by potential applicants for national patents.

The CJEU has not defined the term "human being", but the patentability test is based on the ability, or lack thereof, of autonomous development into a human being. The reasoning makes it difficult to apply with certainty the same logic to other technology developments. It can be argued that the test set in *ISCO* only applies to parthenotes, or on the other hand, that it should also apply to any organisms created by technical means, such as SCNT. It remains an open question whether and how national courts will apply this decision in relation to similar, but not identical, factual situations, and whether national courts will eventually decide that further referrals are necessary.

Taking into consideration the solution found in *Brüstle* by the referring court – the German Federal Supreme Court[164] – it is likely that jurisdictions with a patent-holder-friendly tradition will tend to apply the *ISCO* ruling in its most permissive reading. There is also a possibility that some national courts may extend the inherency test to other organisms, allowing the patentability of hESCs obtained from other sources. It is likely that any attempt to apply the current ruling to new factual circumstances will generate further referrals. Simultaneously, it appears equally possible that some jurisdictions may follow a stricter approach and even resort to the general *ordre public* and morality exception. As pointed out by the AG,[165] the decision to consider parthenotes as not included in the concept of human embryo does not preclude that, at national level, parthenotes and hESCs originating in parthenotes, or other pluripotent cells and their uses, may be considered, either in general or in specific cases, offensive to morality in accordance with the general exclusion in Art. 6(1) Biotech Directive on the basis of other grounds of public order and morality. Furthermore, despite the fact that some parthenote-derived stem cell lines and inventions based on these may be patentable, caution remains advisable concerning applications which do not mention the origin of the hESCs, since these will still cover every stem cell line and thus also the use of embryos, including their destruction, for commercial purposes.

6.2 At the EU Level

The *ISCO* decision may have a broader implication concerning the patentability of all stem cell research: it has now been established that pluripotent human embryonic stem cells can be obtained without necessarily destroying an embryo. Arguably, this could mean the beginning of the end of the *Brüstle* historical approach.

Faced with unsurpassable evidence that the *Brüstle* decision was inconsistent with scientific facts, the court adapted the legal fiction to reality. It is possible that future referrals will provide opportunities for further clarification of the doctrine set

[164] *See* above Sects. 3 and 5.6.

[165] Opinion AG Case C-364/13 (*supra* note 50), para. 43.

in *Brüstle* and eventually its full replacement. In the long run, provided that technological advances do not render the legal discussion obsolete, it is likely that the *Brüstle* historical approach may prove to be unsustainable. A generalisation of the *Brüstle* reasoning to the entire biotechnology field implies the conclusion that if an act or research step at the outset of the process that leads to an invention is found to be immoral, then the invention will not be patentable.[166] A practical example could be found in the case of data and biological materials obtained previously in serious breach of acceptable ethical norms, for instance using human beings as test subjects without their consent or knowledge. Naturally, the issue relates to a broader ethical dilemma: should information and biological materials obtained unethically be destroyed, or is their use for therapeutic and medical research purposes morally acceptable?[167] Inventions are based on scientific information created using data and biological materials. If these were obtained in serious breach of ethical standards, under the fruit-of-the-poisoned-tree reasoning in *Brüstle*, the resulting invention would not be patentable.[168] It would be irrelevant how much time had passed, or that the claims did not mention the origin and retrieval methods of the source materials, or arguably, that the inventor had no connection with, knowledge of or influence on the methodology used to obtain such data and source material.

It can be argued that *ISCO* marks the beginning of the end of the historical approach set in *Brüstle*. The idea that all forthcoming stem cell research is morally tainted by the stain of the original unethical conduct – the previous destruction of a blastocyst to establish stem cell lines – will be easier to circumvent/disclaim, since now at least one morally acceptable source of pluripotent stem cells is available. Indirectly, it is also now established that pluripotent hESCs should not, by themselves, be considered embryos, since they are not capable of originating all types of cells. The uncertainty concerning the legal status of pluripotent cells has thus now been resolved. This is a welcome step, and although it remains to be seen whether these stem cells are as safe and useful as stem cells obtained by other methods, this decision re-opens patent possibilities for stem cell-related inventions.

As soon as they are in force, the European patent with unitary effect[169] and the Unified Patent Court[170] will create an extra route of patent protection in Europe and another layer of jurisdictional adjudication. It is difficult to predict how the new Unified Patent Court will reason. However, it is not completely out of the question to expect that the current CJEU jurisprudence will be observed and applied, including in respect of the European patent with unitary effect.[171]

[166] In this sense: Bonadio (2012a), p. 442.

[167] The question is far from academic, since a large number of examples of important research conducted in breach of ethical standards (and current regulations) can be found both in medical history and in recent years.

[168] In this sense: Opinion AG Bot Case C-34/10 (*supra* note 78), paras. 106–108.

[169] Regulation (EU) No 1257/2012 of the European Parliament and of the Council of 17 December 2012 implementing enhanced cooperation in the area of the creation of unitary patent protection, OJ EU L 361/1, 31.12.2012, Document 32012R1257.

[170] Agreement on a Unified Patent Court, OJ EU C 175, 20.06.2013, Document C:2013:175:TOC.

[171] For a debate on the possible routes of legal reasoning and institutional relations with the CJEU *see* Petersen et al. (2015); generally *see* Pila and Wadlow (2014).

6.3 Implications at the EPO Level

It remains to be seen how the EPO will incorporate this decision. If previous actions are an indication, the Boards of Appeal will most likely adopt a similar reasoning and follow the CJEU jurisprudence. The EPO is not formally obliged to accept the decisions of the CJEU, since the EPO is not an EU institution. However, it is to be expected that the *ISCO* decision will also be reflected in the EPO Guidelines and implemented in the practice of the EPO. The current practice has been to take into consideration the entire teaching of the application and the relevant description, in order to establish whether, in the light of the state of the art at the filing date, the stem cells used "are obtained exclusively by the use, involving the destruction, of a human embryo or not".[172] As mentioned in the previous section, the EPO will also have to determine whether "in the light of current scientific knowledge", a parthenote or other organism, "in itself, ha[s] the inherent capacity of developing into a human being". The dependence on the state of "current scientific knowledge" to determine the scope of an exception to patentability is problematic.[173]

It can be said that, directly, the *ISCO* decision will only apply to the limited number of patent applications that concern parthenote-related inventions. However, in the silence of the application, the mere technical possibility of obtaining stem cell lines from parthenotes would seem to destroy the legal presumption as to the *non-ethical* origin of the stem cell lines. Caution is still advised, since the current wording of the EPO Guidelines appears to point to the contrary and, in the sense of a requirement, to at least disclaim the use of stem cell lines obtained involving embryo destruction. Already in *WARF*,[174] and even more so now with *Technion*,[175] it is the applicant that is required to either disclaim or submit references that establish that the source material used is not immoral. This conflicts with the intention of the drafters of the EPC and with the traditional EPO approach of narrow construction of exceptions to patentability.[176] Exceptions are not positive requirements, and in this sense can be said to have been intended to be invoked and argued against the applicant. Under the general rule concerning the burden of proof, it is the party that invokes the lack of ethical compliance that should be required to offer evidence of misconduct.[177] On the other hand, it has been the longstanding practice

[172] EPO Guidelines (*supra* note 43), G-II 5.3.

[173] *See* Consolidated Cases G 2/07 *Broccoli I* and G 1/08 *Tomatoes I* (*supra* note 88), reason, 6.4.1, where the EBA reasoned that (1) such approaches "conflates the considerations which are relevant for patentability with those relevant for novelty and inventive step"; and (2) are"detrimental to legal certainty, since the qualification of a process as being patentable subject-matter or, on the contrary, excluded from patentability could then change with every new state of the art that comes to be considered in the various procedural stages which an application and a patent granted on it may run through during the whole lifetime of the patent".

[174] G 2/06 *Use of embryos/WARF* (*supra* note 27).

[175] T 2221/10 *Culturing stem cells/TECHNION* (*supra* note 45).

[176] *See* T 356/93 *Plant cells/PLANT GENETIC SYSTEMS* (*supra* note 153), where the board examined the preparatory works and concluded that the legislative intent was to create a narrow exception applicable only where the commercial exploitation of the invention is abhorrent in the light of the European ethical standards, founded in the totality of European culture and civilisation.

[177] Concerning procedural issues *see* Warren-Jones (2007).

of the EPO to deny patentability when the claims may encompass excluded subject-matter. Therefore, it has been suggested that repositories of hESCs should contain and make available to researchers information concerning the techniques used for obtaining cell lines.[178] In the absence of such data, it is advisable that patent applicants should be proactive in securing such information.

ISCO establishes that stem cells derived from parthenotes may be outside the scope of the morality clause. While the doctrine in *Brüstle* has not been recanted, it does offer new possibilities for applicants. For patent applicants wishing to apply for patents under the PCT-EPC scheme, careful claim drafting is still advisable. In particular, the applicant might consider disclaiming the use of hESCs, or limit the claims to the use of cell lines obtained from parthenotes, or to the use of iPSC lines, and include references that sustain that this is possible in the light of the scientific state of the art. In the light of *ISCO*, it will also be advisable to disclaim any further genetic manipulation of parthenotes that might allow them to be considered totipotent, or inherently capable of developing into a human being. The use of disclaimers to avoid the prohibited subject-matter should be considered with great care, since merely including a general disclaimer, such as for example "wherein the method does not involve use of a human embryo for industrial or commercial purposes" is likely to affect the clarity of the claims (Art. 84 EPC) and be rejected for not meeting the requirements of Art. 123(2) EPC.[179]

7 A Brief Comparison with the US Situation

Historically US courts have examined patent eligibility questions under US patent statutes with reference to the "Patent Clause"[180] of the US Constitution. The object of the Patent Clause is to promote the progress of science and the useful arts by bestowing upon inventors a temporary reward in return for the benefit to the public provided by the invention.[181] While the Patent Clause speaks of securing exclusive rights for inventors without expressly mentioning patents, 35 U.S.C. § 101 of the US Patent Statute provides that "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."

Unlike European patent legislation, however, US patent statutes do not include an explicitly codified morality clause and have generally not defined which types of inventions or discoveries fall outside the scope of patentability.[182] The

[178] Mahalatchimy et al. (2015), p. 43.

[179] *See* T1441/13 *Embryonic stem cells/ASTERIAS*, disclaimer [9.9.2014] unpublished.

[180] U.S. Const. Art. 1, Sec. 8, cl. 8. "[T]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries".

[181] *See e.g. Eldred v. Ashcroft* 537 U.S. 186, 217 (2003).

[182] Until recently nuclear weapons were the only invention category completely excluded from patent eligibility (albeit not from a prize system). Yet this exclusion is not codified in the Patent Act, but in the Atomic Energy Act. 42 U.S.C. § 2181(a) (2000).

generally accepted explanation is that these are Constitutional limitations based upon the framers' intent in enacting the Patent Clause. It has thus traditionally been the province of the courts and the US Patent and Trademark Office (USPTO) to establish limits for subject-matter that may not be granted patent protection.[183] In the past, the USPTO has in rare circumstances refused to issue patents for inventions of incredible or specious utility, or for inventions whose utilisation is not adequately disclosed in the application. Additionally, the courts have interpreted the utility requirement to exclude inventions deemed to be "injurious to the well-being, good policy, or good morals of society".[184] Although several bills[185] had attempted to categorically exclude from patent protection certain biological material that had been isolated from its natural environment, such as genes, proteins and stem cells, the US Patent Reform Act of 2011[186] principally still leaves these fundamental questions to the courts and the USPTO.[187]

Despite rejecting patent applications for gambling machines[188] and human chimera[189] under the so-called "moral utility doctrine",[190] the USPTO has so far pursued a more liberal approach in the stem cell area than its European counterparts and has already granted several patents that directly claim hESCs, including culture methods, differentiated cells derived from hESCs and even hESCs per se.[191] This approach, in combination with President Obama's decision to lift the ban on governmental funding for stem cell research,[192] has led to a very research- and patent-friendly environment for stem cell technology in the US.

[183] *Cf. e.g. Diamond v. Chakrabarty,* 447 U.S. 303, 309 (1980) at p. 315. Some scholars question whether the rules governing unpatentable subject-matter can be based in the Constitution or the framers' intent*; see* Oliar (2009), pp. 457 and 460.

[184] *Cf. Lowell v. Lewis*, Fed. Cas. No. 8568 (C.C. Mass. 1817) (Story, J.), quoted in *Tol-O-Matic, Inc. v. Proma Product-und Marketing Gesellschaft M.b.H*, 945 F.2d 1546, 1552, 20 USPQ2d 1332, 1338 (Fed. Cir. 1991). *See also* Justice Story's opinion in *Bedford v. Hunt*, 3 F. Cas. 37, 37 (C.C.D. Mass. 1817).

[185] In 2007, for example, Michael Crichton teamed up with Lori B. Andrews, from the Chicago-Kent College of Law, and found support from Representatives Xavier Becerra and Dave Weldon, who unsuccessfully introduced a Bipartisan Bill (HR 977) in the 110th Congress to restrict future patenting of genes and proteins.

[186] *Leahy-Smith America Invents Act*, HR 1249.

[187] With the minor exception that HR 1249 (the America Invents Act) introduced an immediately effective ban on patents covering tax strategies and/or claims 'directed to or encompassing' human organisms. These will apply to all pending applications (Dr Frankenstein must now rely on trade secrets). Moreover, the USPTO had previously refused to grant patents on human chimera.

[188] *Brewer v. Lichtenstein*, 278 F. 512 (7th Cir. 1922) (patent invalid because only utility of machine patented is to appeal to gambling instinct of customers); *Nat'l Automatic Device Co. v. Lloyd*, 40 F. 89 (C.C. Ill. 1889), (patent invalid because horse race machine can only be used for gambling).

[189] U.S. Application Serial No. 08/993,564 (filed on 18 December 1997), and divisional application U.S. Application Serial No. 10/308,135 (filed on 3 December 2002).

[190] A detailed explanation of this doctrine is provided by Bagley (2003), pp. 469 seq.

[191] Porter et al. (2008), p. 653.

[192] Stolberg (2009), pp. 1–2.

However, in the aftermath of the much-debated US Supreme Court decisions in *Myriad*[193] and *Prometheus*,[194] the patentability of stem cells that have been isolated from their natural environments, and of biological processes and methods that are employed in stem cell technology, now *stands on shaky ground* in the US. While previous challenges were typically based on prior art and the US standards for novelty and non-obviousness,[195] *Myriad* and *Prometheus* have opened the gates for new challenges based on arguments related to patent eligibility. This has resulted in considerable legal uncertainty.[196]

The elusiveness of the current situation is also illustrated by the new USPTO guidelines.[197] With regard to stem cell-related technology, these new guidelines and the case examples indicate that their patent eligibility will rely on whether the claimed subject-matter is "significantly different" to the product as it is found in nature. It now remains to be seen how exactly the USPTO will interpret and apply these instructions. One central question will be: how much human involvement and manipulation is required to make such cells "significantly different" to the product as it is found in nature under the *Myriad* and *Prometheus* standards of patent eligibility? And: to what extent would such manipulations be acceptable with regard to other laws and regulations?

Be that as it may, it can be expected that these recent US developments will lead to an increased number of proceedings and challenges in US courts and at the USPTO against patent claims directed to technologies that utilise isolated hESCs. This is exemplified by recent challenges against the US equivalents[198] to the European *WARF* patent claims that were rejected by the EPO's EBA in November 2008. In the same year, that is, prior to the US Supreme Court decisions in *Myriad* and *Prometheus*, the USPTO did not follow the EPO's approach and in a heavily debated decision upheld important claims of the three WARF patents for in vitro cultivation of human embryo-derived cells.[199] However, after enduring controversy revolving around the prior art and an asserted lack of novelty and non-obviousness,

[193] *Assoc. for Molecular Pathology, et al. v. Myriad* (*supra* note 15). For a further discussion of the US Supreme Court decisions, *see* with further references: Minssen and Nilsson (Minssen and Nilsson 2011a, b, 2012a, b, 2013) and Minssen and Schwartz (2013, 2015).

[194] *Mayo Collaborative Services v. Prometheus Laboratories*, 566 U.S., 132 S. Ct. 1289, 182 L.Ed.2d 321 (2012).

[195] *See* for example Rimmer (2008), p. 261.

[196] Chan et al. (2014), p. 633, Noonan (2013), p. 89.

[197] *See* 2014 Interim Guidance on Patent Subject Matter Eligibility, Federal Register/Vol. 79, No. 241/Tuesday, December 16, 2014/Rules and Regulations, at pp. 74618 *et seq*., available at: http://www.gpo.gov/fdsys/pkg/FR-2014-12-16/pdf/2014-29414.pdf (accessed 16 November 2015).

[198] Thomson (1998) "Embryonic Stem Cells", United States Patent No. 5,843,780; Thomson (2001), "Primate Embryonic Stem Cells", United States Patent No. 6,200,806; and Thomson (2006), "Primate Embryonic Stem Cells", United States Patent No. 7,029,913.

[199] *See* the proceedings in The Foundation for Taxpayer and Consumer Rights and the Public Patent Foundation (2006), "Request for *Ex Parte* Re-examination" in respect of US Patent No. 5,843,780, available at: http://www.pubpat.org/assets/files/warfstemcell/780Request.pdf (accessed 16 November 2015). On 29 February 2008, a USPTO patent examiner upheld the validity of the '913 patent. On 11 March 2008, the USPTO upheld the validity of the modified claims of the remaining two WARF claims without any possibility of appeal; *see* Plas (2008).

these claims were subsequently limited by another USPTO decision from 2010.[200] Then, in 2013, Consumer Watchdog challenged the WARF patent in an appeal to the US Court of Appeals for the Federal Circuit,[201] asserting that the claimed cells are "products of nature" and that the patent should thus be invalidated under the new patentability standard established in *Myriad*.

In June 2014, the challenge was rejected since Consumer Watchdog did not itself work the claimed patents or plan to use hESC-derived technology, thereby lacking legal standing based on the principles established by the US Supreme Court in *Lujan*[202] and *MedImmune*.[203] It is, however, only a matter of time before parties with legal standing challenge such claims; the patentability of such cells therefore remains uncertain in the wake of *Myriad*.[204]

8 Concluding Remarks

In our view, *ISCO* constitutes a first step in the right direction, introducing a more nuanced approach to stem cell patenting. However, difficulties will persist. Considering the combined significance of the *Brüstle* and *ISCO* rulings to such important medical areas as regenerative medicine and cellular therapy, the persistent legal uncertainty and the lack of generally applicable clear guidance are very unfortunate and do not serve the goal of a harmonious and effective European legal framework for innovation.

Legal norms should be interpreted *inter alia* by reference to their purposes and their systematic insertion and by taking into consideration the other norms that are part of the broader legal system. Within an *incomplete* system, such as EU law, this interpretative precaution is even more important. Legislative and judicial determination of ethical and scientifically uncertain or controversial concepts should be approached carefully and only as far as strictly necessary. The present ruling raises matters of legal interpretation and further difficulties in subsuming the factual reality of scientific development under the normative construction. Relying on a patent law-specific notion of human being, albeit indirectly, constitutes a weak point of the CJEU's jurisprudence. In our view, such an understanding also creates the legal fiction of an EU consensus concerning the scope of protection of human dignity and the extent to which it applies to unborn humans. This contravenes the history of the provision, the ECHR jurisprudence, and the CJEU's own admission. It is also an interpretative solution contradicted by the EU regulatory framework. *ISCO* has done little to reduce the inconsistency between patent law and other fields

[200] *See* Decision by the Board of Patent Appeals and Interference in *Foundation for Tax Payer and Consumer Rights v. Wisconsin Alumni Research Foundation*, Appeal No. 2010-001854, (28 April 2010).

[201] *Consumer Watchdog v. Wisconsin Alumni Research Foundation*, No. 13-1377 (Fed. Cir. 4 June 2014).

[202] *Lujan*, 504 U.S. at p. 577.

[203] *MedImmune, Inc. v. Genentech*, Inc., 549 U.S. 118 (2007). For further discussion of this judgment and the US doctrine on legal standing in patent cases *cf.* Minssen and Schindler (2008); *see also* Minssen and Nilsson (Minssen and Nilsson 2011a, b).

[204] *See also* Matthews and Cuchiara (2014), p. 200.

of EU law and regulation. Stem cell-based therapies provide hope for millions of people suffering from *inter alia* severe self-immune degenerative diseases, for which currently no cure is available. Meanwhile, myriads of fertilised human ova are discarded in in vitro fertilisation treatments. For this reason, research involving embryo destruction is allowed under specific conditions in several national jurisdictions, considered ethically justified according to EU regulations and even supported by public research grants. However, the results of such therapeutic research are – somewhat paradoxically – declared immoral for patent law purposes.

The introduced criterion of inherent capacity has not improved legal certainty, since it may sustain different interpretations, which indirectly implies that further clarification is required concerning the intended meaning of such distinction. The approach also leaves room to consider the moral status of non-viable embryos. It can be argued that there is a moral differentiation between destroying an embryo and destroying a non-viable embryo or a parthenote. In this sense, the distinction created by *ISCO* is welcome. However, linking the concept of human embryo to its viability raises the spectre of eugenics, which is inconsistent with humanitarian law and national constitutions. The relationship between the interpretative approach set out in *Brüstle* and the added criterion introduced by *ISCO* is also open to interpretation as either cumulative or alternative conditions. Moreover, the present decision leaves unsolved the patentability status of ova subjected to SCNT and related methods and products. In this sense, it is reasonable to expect that this has not been the last word of the CJEU on stem cell patentability.

Despite the more flexible approach now introduced, compliance with TRIPS also remains debatable. Our comparison with the US approach, which does not entail a similar statutory exception from patentability, demonstrates that the issue is equally controversial on both sides of the Atlantic, albeit for different reasons. In the light of the emerging unitary patent system it furthermore became clear that we should perhaps not only worry about the *tunnel vision* of overly specialised unified patent courts, but also about the occasional involvement of general courts in highly complex and sensitive matters demanding multifaceted expertise and broader debate. It will be important to develop an appropriate infrastructure ensuring that such involvement is not only based on an in-depth understanding and respect for general legal principles, but also on correct fact-finding and scientific expertise.

Seen in an overall context, in its efforts to avoid divergent national interpretations the CJEU jurisprudence has to a certain extent lost track of the purposes and functions of patents and the limits of EU harmonisation. It introduced new layers of complexity and arguably opened further venues for divergent national patentability practices, thus defeating the purpose of the referrals.

Despite all of the problems identified above, *ISCO* still brings some clarification and re-instates some much-needed balance into CJEU jurisprudence concerning the interpretation of Art. 6(2)(c) Biotech Directive. Although it could be argued that the *ISCO* decision will have limited practical relevance since it will only apply directly to a minor number of patent applications, it nevertheless offers venues for general legal argumentation regarding patent exceptions, as well as specific arguments in favour of restricting the scope given to the *Brüstle* decision and corresponding EPO Guidelines.

Finally, the authors fully recognise the importance of promoting induced pluripotent stem cell technology, which 1 day might make the use of hESCs unnecessary. Yet, despite recent advances, this promising technology still faces many significant problems and hESC research is still required to improve it. In the absence of an established alternative to the use of hESCs, it is therefore positive that certain parthenotes are now deemed to be a morally acceptable source of hESCs. *ISCO* can thus be read as pointing the way forward to a narrower and more consistent interpretation of patentability exceptions and the Biotech Directive. Thus, it might indeed have the "inherent capacity" of developing into a reasonable doctrine on stem cell patenting.

9 Postscript

Some time has elapsed since the present article was submitted for publication; therefore an update is in order. As predicted, after the CJEU decision on ISCO, the High Court of Justice of England and Wales, Chancery Division ordered the decision of the comptroller excluding from patentability ISCO's patent applications to be set aside and the patent applications to be remitted to the Intellectual Property Office for further consideration.[205] Both patents were granted as amended in October 2015.[206]

More recently, the EPO has published the 2015 version of its Guidelines.[207] The CJEU jurisprudence was indirectly incorporated in EPO practice through the inclusion in the EPO Guidelines. In particular, a new paragraph was inserted clearly stating that although the CJEU judgments on the interpretation of the Biotech Directive are not binding on the EPO they may be considered as being persuasive. This understanding follows from the EPO decisions *Technion*[208] and *Asterias*[209] (see above Sect. 6.3).

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[205] Order of the High Court dated 22 January 2015 (CH/2012/0488), published 4 March 2015 (Patents Journal 6563).

[206] UK Patent GB2431411 "Parthenogenic activation of human oocytes for the production of human embryonic stem cells", and UK Patent GB2440333 "Synthetic cornea from retinal stem cells derived from human parthenotes", both granted 06 October 2015,and Published in the Patents and Designs Journal on 04 November 2015. Procedural docs available at: https://www.ipo.gov.uk/p-ipsum/Case/PublicationNumber/GB2431411 and https://www.ipo.gov.uk/p-ipsum/Case/ApplicationNumber/GB0621069.4 (accessed 16 November 2015).

[207] Guidelines for Examination in the European Patent Office (November 2015 edition), Part G, Chapters II-5.3-III on Rule 28(c).

[208] T 2221/10 *Culturing stem cells/TECHNION* (*supra* note 45).

[209] T 1441/13 *Embryonic stem cells/ASTERIAS*, disclaimer *(supra* note 179).

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