Stem Cell Lines and Destruction of Human Embryos: the EPO Shares the Perspective of the Court of Justice

Case T 2221/10, *Culturing stem cells/TECHNION*, decision of the Technical Board of Appeal of the European Patent Office, 4 February 2014.

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The Technical Board of Appeal of the European Patent Office, in case T 2221/10[1], held that Article 53(a) and Rule 28(c) of the European Patent Convention do not merely exclude the patentability of biotechnological inventions that make use of human embryonic stem cells obtained by de novo destruction of human embryos, but also apply to inventions which employ publicly available cell lines which were initially derived by a process resulting in the destruction of human embryos. The decision relies on the judgment of the Enlarged Board of Appeal in the WARF case, falling in line with the perspective endorsed by the Court of Justice of the European Union in Oliver Brüstle v Greenpeace.

I. Facts

In October 2003, Technion Research and Development Foundation Ltd. filed the European patent application No. 03751238.1, concerning methods of maintaining human embryonic stem (HES) cells in an undifferentiated state, through co-culturing with a human foreskin feeder cell line (independent claim 1), or on a synthetic matrix supplemented with a human foreskin cell conditioned medium (independent claim 2). The invention also claimed a cell culture comprising HES cells and human foreskin cells (independent claim 5).

The examining division focused on the source of the HES cell lines necessary to put the invention into practice, in order to determine the patentability of the invention under Article 53(a) and Rule 28(c) of the European Patent Convention (EPC). These provisions prohibit the granting of patents for inventions whose commercial exploitation would be contrary to *ordre public* or morality (Article 53(a)), including biotechnological inventions concerning uses of human embryos for industrial or commercial purposes (Rule 28(c)). The panel also took into consideration the well-known *WARF* decision[2], where the Enlarged Board of Appeal of the European Patent Office (EPO) held that Rule 28(c) EPC forbids the patenting of claims directed to products that, at the date of filing, could only be prepared through methods involving the destruction of the human embryos[3]. The decision clarified that the prohibition applies even if such methods are not part of the claims.

The applicant submitted that established HES cell lines were already publicly available at the date of filing of the patent application, to the effect that the claimed invention could be practiced without requiring *de novo* destruction of human embryos. The examining division, however, found that evidence regarding the public availability of established HES cell lines at the date of filing was insufficient. In light of this finding, it concluded that the only way to put the claimed invention into practice consisted in sourcing the HES cells through methods that implied the *de*

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2 Case G 2/06, *Use of embryos/WARF*, decision of the Enlarged Board of Appeal, 25 November 2008, OJ EPO 2009, 306. See Sven Bostyn, "Patenting human embryonic stem cells in peril: the decision of the Enlarged Board of Appeal in G 2/06", *BioScience Law Review* (2009), pp. 13 *et sqq.*, and Ewan Nettleton, "EPO's Enlarged Board rules on patenting stem cell inventions', 4(5) *Journal of Intellectual Property Law & Practice* (2009), pp. 306 *et sqq*.

3 See also the decision of the EPO in *Greenpeace Deutschland e.V. v The University of Edinburgh*, 24 July 2012, where the Opposition Division held that Rule 23d(c) EPC - now Rule 28(c) – 'has to be interpreted broadly to encompass not only the industrial or commercial use of human embryos but also the human ES cells retrieved therefrom by the destruction of human embryos'. For an overview of the decision, see Matthew Rimmer, *Intellectual Property and Biotechnology: Biological Inventions* (Edward Elgar Publishing 2007), at pp. 266 *et sqq*.

novo destruction of human embryos. Therefore, it refused the patent application under Article 53(a) and Rule 28(c) EPC.

Technion appealed, disputing the conclusion reached by the examining division. The applicant argued that the decisive question concerned the public availability of any suitable HES cell line at the date of filing. In this perspective, it submitted further evidence regarding the availability of such cell lines and the possibility for a third party to obtain access to them, maintaining that HES cells that did not require destruction of human embryos had been publicly available since November 1998.

II. Judgment

1. The technical teaching of the application as a whole: taking into account the necessary preceding steps under Rule 28(c)

The Technical Board of Appeal first observed that the claims contained in the patent application did not explicitly specify a method for obtaining HES cells through the use, and destruction, of human embryos. However, it highlighted that the applicability of Rule 28(c) EPC is not conditional upon the explicit wording of the claims, but takes into account the teaching of the application as a whole, as clearly outlined in the *WARF* decision. According to the reasoning of the Enlarged Board of Appeal in *WARF*, this interpretation is supported by the use of the term 'invention' in Rule 28(c), as well as by the consideration that restricting its applicability 'to what an applicant chooses explicitly to put in his claim would have the undesirable consequence of making avoidance of the patenting prohibition merely a matter of clever and skillful drafting of such claim[4]'.

The patent application disclosed three methods for obtaining HES cells. The first embodiment described their isolation from human blastocysts, obtained from human in vivo preimplantation embryos or from in vitro fertilized embryos. The Board noted that such method, which implies the destruction of the human embryos, had already been found unpatentable in the *WARF* case.

The second method consisted in the use of commercially available HES cell lines. At first instance, the examining division had found the evidence submitted by the applicant insufficient to establish the availability of these cell lines at the filing date. Although Technion disputed this finding, submitting new evidence, the Board of Appeal concluded that 'there remain serious doubts with regard to the public availability of HES cell lines at the claimed priority date[5]'. In particular, the panel argued that the documents submitted by the applicant did not specify the cell lines made available to the public, nor the exact date of their public availability.

The Board suggested, however, that determining whether the mentioned HES cell lines were indeed publicly available at the filing date was not the decisive question. Observing that all the established cell lines mentioned by the applicant were initially derived from the inner cell mass of blastocyst stage human embryos, through methods that resulted in the destruction of human embryos[6], the panel found that a more crucial question lied in the background:

> [The fundamental issue] is whether or not the accomplishment of the invention by relying on the use of an established HES cell line, thus without de novo production of HES cells by destroying a human embryo, would nevertheless be in conflict with the requirements of Article 53(a) EPC if said HES cell line has been originally produced by a method involving the destruction of an human embryo[7].

To find the answer to this fundamental question, the Board turned again to the *WARF* decision. In that case, the Enlarged Board of Appeal had not addressed the use of commercially available HES cell lines, but clearly highlighted the necessity of taking the entire technical teaching of the invention into account, when evaluating the applicability of the exclusion from patentability. Further, it had dismissed an argument disputing the lawfulness of taking into account all the steps preceding an invention when assessing the applicability of Rule 28(c), stating that 'where the teaching to obtain the embryonic stem cells claimed is confined to the use (involving their

4 WARF, supra note 2, para. 22.

5 *TECHNION, supra* note 1, para. 15.

6 The Board noted that, for some of the cell lines allegedly available from the United States National Institute of Health, there was no evidence that they were obtained by methods not involving the destruction of a human embryo (ibid., para. 22).

7 Ibid., para. 16.

destruction) of human embryos, [such argument] is not relevant[8]'.

Interpreting the teaching of *WARF*, the Technical Board of Appeal held that, in order to evaluate whether an invention concerns uses of human embryos for industrial or commercial purposes under Rule 28(c), it is necessary to take into considerations all the steps that constitute a necessary precondition to put the invention into practice. The Board expressly refused to add any temporal or causal limitation to the extent of the preceding steps that need to be evaluated, advocating an approach that takes into account all the steps without which the invention could not be carried out. 'In this respect', it noted, 'the Enlarged Board of Appeal has neither made a distinction between steps which have been carried out by the inventor or by any other person, nor between steps which took place in direct preparation of the experiments leading to an invention and steps having taken place at a point in time further remote from these experiments[9]'.

Applying this interpretation to the case in hand, the Board found that, although the use of the commercially available HES cell lines mentioned by the applicant did not involve the *de novo* destruction of human embryos, such destruction occurred during a preceding step which is a necessary precondition for putting the claimed invention into practice. In this perspective, the panel observed that the decisive question for the applicability of the patentability restrictions is whether the step involving the destruction of human embryos is a necessary link in the chain of events leading to performing the invention. It also noted that the point in time at which the destruction occurs, the identity of the party that performs it, and the circumstance that the destruction be explicitly disclosed in the application or not, are equally irrelevant. Therefore, the Board concluded that even the second embodiment is excluded from patentability under Article 53(a) and Rule 28(c) EPC.

2. The judgment of the Court of Justice of the European Union in Brűstle: non-binding, yet persuasive

The Technical Board of Appeal engaged in an in-depth review of its findings in light of the judgment rendered by the Court of Justice in case C-34/10, *Oliver Brüstle v Greenpeace*[10].

In *Brüstle*, the Court of Justice examined, *inter alia*, whether a biotechnological invention concerning isolated and purified neural precursor cells, including processes for their production from HES cells, was to be considered unpatentable pursuant to Article 6(2)(c) of Directive 98/44[11], even if the use of human embryos was not disclosed in the claims, but constituted a necessary precondition for practicing the invention. The Court ruled that the mentioned provision, which is mirrored by Rule 28(c) EPC, '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[12]'. In particular, the judges noted that, in order to evaluate the applicability of Article 6(2)(c) of Directive 98/44, it is necessary to take into consideration all the necessary steps that lead to the implementation of the invention. Therefore, if the destruction of human embryos is a necessary precondition for carrying out the claimed invention, the sanction of unpatentability applies even if such destruction 'occur[s] at a stage long before the implementation of the invention, as in the case of the production of embryonic stem cells from a lineage of stem cells the mere production of which implied the destruction of human embryos[13]'. The Court of Justice, employing the same reasoning of the Enlarged Board of Appeal in *WARF*, suggested that a different conclusion would have allowed a patent applicant to avoid being caught in the patentability restriction through skillful drafting of its claims.

The Board highlighted that the EPO, as an international organization with its separate legal order, is

8 *WARF*, *supra* note 2, para. 23.

9 *TECHNION*, *supra* note 1, para. 26.

10 [2011] ECR I-09821. See, *inter alia*, Enrico Bonadio, "Stem Cells Industry and Beyond: What is the Aftermath of Brüstle?", 1 *EJRR* (2012), pp. 93 *et sqq*., and Martina Ines Schuster, "The Court of Justice of the European Union's Ruling on the Patentability of Human Embryonic Stem-Cell-Related Inventions (Case C-34/10)", 43 *International Review of Intellectual Property and Competition Law* (2012), pp. 626 *et sqq*.

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

12 BRUSTLE, supra note 10, para. 51.

13 Ibid., para 49.

not a member of the European Union and cannot be bound by the rulings of the Court of Justice. Consequently, as held in the *WARF* case[14], the Boards of Appeal of the EPO cannot refer questions to that court, nor bind themselves to follow its rulings. The panel recognized, however, that, although not legally binding on the EPO, the judgments of the Court of Justice 'should be considered as being persuasive[15]', in light of the need for uniformity in the context of a progressively harmonized European patent law[16]. In decision G 5/83[17], the Enlarged Board of Appeal argued that the adoption of harmonized legislation should be accompanied by a parallel process of harmonized interpretation, recognizing that 'it is incumbent upon the European Patent Office, and particularly its Boards of Appeal, to take into consideration the decisions and expressions of opinion of courts and industrial property offices in the Contracting States[18]'. Similarly, in decision G 2/02[19], it expressly contemplated the possibility of taking into consideration the decisions of the Court of Justice, despite reaffirming their non-binding character.

With regard to the specific provision at issue, the Board recited Rule 26(1) EPC, which states that Directive 98/44 shall be used as a supplementary means of interpretation for the EPC rules concerning biotechnological inventions.

The panel concluded that its decision is in line with the *Brüstle* ruling, as the CJEU's focus on the steps necessary for the implementation of the invention, in the application of Article 6(2)(c) of Directive 98/44, closely resembles the Enlarged Board of Appeal's emphasis on the technical teaching of the application as a whole, as well as the Board's evaluation of all the preceding steps that constitute a necessary precondition for putting the invention into practice, in the application of Rule 28(c) EPC.

3. Stem cells derived from human embryonic germ cells

The Board also discussed the third method for obtaining HES cells disclosed in the patent application, which consisted in their derivation from human embryonic germ cells. However, from the outset, it noted that the claims of the application explicitly referred to the use of HES cells and not to the use of embryonic germ cells. The panel recited previous case law[20], observing that, if the claims contain ambiguous terms, the description can be used to shed light on the correct meaning, unless the term has a clear technical meaning: in this case, the description 'cannot be used to interpret such a term in a different way[21]'. The interpretation of terms that are not consistently and coherently employed in the claims and in the description is conducted from the point of view of a person skilled in the art, without the help of the description.

Applying these principles, the Board found that the term HES cells 'has a clear technical meaning in the art which is distinct from the meaning of the term [embryonic germ] cells'. Despite similarities in the developmental potency of both cells, the former are derived from a preimplantation embryo, while the latter are extracted from a postimplantation embryo. Therefore, the panel held that the third embodiment is not a suitable method for obtaining the HES cells needed to practice the claimed invention.

III. Comment

The decision of the Technical Board of Appeal shows that the EPO shares the same perspective endorsed by the Court of Justice in *Brüstle*. This alignment is certainly not surprising, given the converging interpretative path taken by the Court of Justice and the Enlarged Board of Appeal. Both authorities explicitly focused on an evaluation of all the steps, whether disclosed in the claims or not, that are a necessary precondition for practicing (*implementing*, according to the Court of Justice, or *performing*, according to the Enlarged Board of Appeal) the invention. The *WARF* decision clearly set out the consideration that lies at the core of this interpretation:

14 *WARF*, *supra* note 2, paragraphs 2-11.

15 *TECHNION*, *supra* note 1, para. 39.

16 As recognized by the EPO in a Notice of 1 July 1999, concerning the amendment of the Implementing Regulations to the European Patent Convention, OJ EPO 1999, p. 573.

17 Case G 5/83, *Second medical indication*, decision of the Enlarged Board of Appeal of the EPO, 5 December 1984.

18 Ibid., para. 6.

19 Case G 2/02, *Priorities from India/ASTRAZENECA*, decision of the Enlarged Board of Appeal of the EPO, 26 April 2004.

20 Case T 197/10, *Wasch- oder Reinigungsmittel mit wasserlöslichem Buildersystem/HENKEL AG & Co.*, decision of the Technical Board of Appeal of the EPO, 28 October 2011.

21 *TECHNION*, *supra* note 1, para. 33.

> In this context, it is important to point out that it is not the fact of the patenting itself that is considered to be against ordre public or morality, but it is the performing of the invention, which includes a step (the use involving its destruction of a human embryo) that has to be considered to contravene those concepts[22].

In other words, the applicability of the provisions of Article 53(a) and Rule 28(c) EPC does not depend upon *what* the patent applicant choses to include in the claims, but takes into account *how* the invention, as a whole, is performed. As mentioned above, a different conclusion would essentially void the patentability restrictions set by these provisions, rendering them conditional upon (un)skillful drafting, despite the persistence of the same morality questions that prompted the enactment of the restrictions[23]. In this perspective, Recital 16 to Directive 98/44 makes it clear that 'patent law must be applied so as to respect the fundamental principles safeguarding the dignity and integrity of the person', implicitly advocating an evaluation of the morality issues raised by the invention as a whole, rather than by its individual claims.

The current Guidelines for Examination at the European Patent Office have already codified the principles endorsed by the Enlarged Board of Appeal in *WARF*, as well as those enucleated by the Court of Justice in *Brüstle*. Paragraph 5.3 of Part G, Chapter II, explicitly recognizes that the restriction set out by Rule 28(c) EPC applies when any preceding step, which is a necessary precondition to practicing the invention, requires the destruction of human embryos, regardless of its disclosure in the application and of the point in time in which the destruction takes place. The same provision clarifies that, when examining subject-matter relating to human embryonic stem cells under Article 53(a) and Rule 28(c), it is necessary to take into account (i) the entire teaching of the application, and (ii) the relevant disclosure in the description, to evaluate, in light of the state of the art at the date of filing, whether the stem cell cultures are obtained exclusively by the use, involving the destruction, of human embryos. The Board's ruling, therefore, falls perfectly in line with the Guidelines.

The acknowledged applicability of Rule 28(c) to inventions using publicly available HES cell lines obtained through methods that involve the destruction of human embryos has modified the approach of the EPO to biotechnological inventions concerning stem cells. In particular, it has shifted the focus from an assessment of the date at which *any* suitable HES cell line was first made available (conventionally identified as 9 May 2003[24]), to an evaluation of the date at which a suitable HES cell line *whose production did not imply the destruction of human embryos* was first made available (tentatively identifiable as late 2006[25]).

The decision of the Board of Appeal clarifies that, as far as the patentability of biotechnological stem cell related inventions is concerned, Article 53(a) and Rule 28(c) EPC do not merely apply when the patent applicant discloses a method to obtain HES cells which implies the destruction of human embryos. Rather, these provisions charge the applicant with the task of ensuring that none of the steps necessary to put the invention into practice results in the destruction of human embryos. This duty comprises both the methods disclosed in the patent application and those employed at a preceding stage, such as the processes performed by a third party to obtain the publicly available HES cell lines used by the invention. The effects of the Board's ruling, however, will not significantly affect future or current applications for biotechnological inventions, since recent advancements in scientific research have made it possible to obtain HES cells through alternative methods that do not incur in the patentability restrictions. However, the decision provides a clear indication of the approach that the EPO is likely to adopt in respect to all the patentability restrictions enlisted in Rule 28, and highlights the reciprocal sensitivity exhibited by the EPO and the European Union towards the opportunity of employing a harmonized approach to the provisions at issue.

22 *WARF*, *supra* note 2, para. 29.

23 For an overview of the morality questions surrounding stem cell research, see Kenneth C. Cheney, "Patentability of Stem Cell Research under TRIPS: Can Morality-Based Exclusions be Better Defined by Emerging Customary International Law?", 29 *Loyola of L.A. International and Comparative Law Review* (2007), pp. 503 *et sqq*. Relevant case law and legislation on the matter is examined by Amina Agovic, "Stem cell patents on a knife edge", 3(11) *Journal of Intellectual Property Law & Practice* (2008), pp. 718 *et sqq*.

24 S. Wright, "Minutes of EPO/epi Meeting on 15 November 2010", 3 *epi Information* (2011), p. 91.

25 See Klimanskaya I., Chung Y., Becker S., Lu S.J., Lanza R., "Human embryonic stem cell lines derived from single blastomeres", 444 *Nature* (2006), pp. 481 *et sqq.*, first published online on 23 August 2006.