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Datasheet for the decision of 9 September 2014

Case Number: T 1441/13 - 3.3.08

Application Number: 02799217.1

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Title of invention:
ISLET CELLS FROM HUMAN EMBRYONIC STEM CELLS

Applicant:
Asterias Biotherapeutics, Inc.

Headword:
Embryonic stem cells, disclaimer /ASTERIAS

Relevant legal provisions:
EPC Art. 53(a), 123(2)
EPC R. 28(c), 26
RPBA Art. 12(4)

Keyword:
Admissibility of the Main Request and of Auxiliary Requests 1 to 4 (yes);
Main Request: requirements Article 53(a) EPC in combination with Rule 28(c) EPC (no);
Auxiliary Requests 1 and 2: disclaimers allowable (no) (see points 8 to 17);
Auxiliary Requests 3 and 4: remittal to the department of first instance (yes)

Decisions cited:
G 0001/03, G 0002/06, G 0002/10, T 0866/01, T 1836/10, T 2221/10

Catchword:

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Case Number: T 1441/13 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 9 September 2014

Appellant: (Applicant)	Asterias Biotherapeutics, Inc. 230 Constitution Drive Menlo Park, CA 94025 (US)
Representative:	Bassil, Nicholas Charles Kilburn & Strode LLP 20 Red Lion Street London WC1R 4PJ (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 1 February 2013 refusing European patent application No. 02799217.1 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	M. Wieser
Members:	P. Julià
	D. Rogers
	B. Stolz
	J. Geschwind

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse the European patent application no. 02 799 217.1, originally filed on 6 December 2002 as International patent application PCT/US02/39089 (published as WO 03/050249, hereinafter "*the application as filed*") and claiming the priority date of 7 December 2001 (US 60/338,885). The examining division considered the set of claims filed on 8 November 2010 not to fulfil the requirements of Article 53(a) EPC in combination with Rule 28(c) EPC.

II. With the statement setting out its Grounds of Appeal, the applicant (appellant) maintained, as its Main Request, the claims filed on 8 November 2010, and further filed Auxiliary Requests 1 to 4 and new documentary evidence.

III. The appellant requested accelerated processing of the appeal.

IV. The appellant was summoned to oral proceedings. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) annexed thereto, the appellant was informed of the board's preliminary opinion on the issues of the case.

In particular, the board gave its opinion on: i) the admissibility of Auxiliary Requests 1 to 4 and of the new documentary evidence filed with the Grounds of Appeal (Article 12(4) RPBA), ii) the requirements of Article 53(a) EPC and Rule 28(c) EPC with regard to the Main Request, iii) the allowability of the disclaimers present in Auxiliary Requests 1 and 2, and the requirements of Articles 53(a), 83 EPC and Rule

28(c) EPC with regard to Auxiliary Request 1. The board further indicated that, if Auxiliary Requests 3 or 4 were admitted into the appeal proceedings, a remittal of these requests to the department of first instance would be the most appropriate course of action in the circumstances of the present case.

V. On 7 February 2014, the board sent a copy of the decision T 2221/10 of 4 February 2014 to the appellant.

VI. In a letter dated 3 March 2014, the appellant maintained its Main Request and Auxiliary Requests 1 to 4 and informed the board of its intention not to file any further requests and not to attend the scheduled oral proceedings. Besides presenting further arguments supporting the admissibility of Auxiliary Requests 1 to 4 and of the documentary evidence filed with its statement of Grounds of Appeal, the appellant made no further substantive submissions.

VII. In a letter dated 13 March 2014, the board cancelled the oral proceedings scheduled for 3 April 2014.

VIII. Claims 1 and 5 of the **Main Request** read as follow:

"1. A method for obtaining polypeptide-secreting cells, comprising culturing pPS cells in activin A to differentiate the pPS cells to form gut endothelium, and culturing the gut endothelium in a mixture of islet cell differentiation factors comprising one or more of cyclopamine, betacellulin, exendin-4, glucagon-like peptide-1, hepatocyte growth factor, nicotinamide, IGF-1, n-butyrate, retinoic acid (all trans), growth hormone, placental lactogen, VEGF, IGF-II, IBMX, wortmannin, gastrin, cholecystokinin, NGF, EGF, KGF, PDGF, Reg or INGAP, thereby obtaining a cell population

in which at least 5% of the cells secrete at least one of the following proteins from an endogenous gene: insulin, glucagon, somatostatin, and pancreatic polypeptide."

"5. A method of producing islet cells from primate pluripotent stem cells comprising

1) differentiating pPS cells to gut endoderm by culturing the pPS cells in a medium comprising activin A or retinoic acid;

2) differentiating the gut endoderm to a pancreas precursor by culturing the gut endoderm in a medium comprising a TGFß antagonist, a member of FGF family and EGF; and

3) differentiating the pancreas precursor to a mature islet cell by culturing the pancreas precursor in a medium comprising nicotinamide."

wherein "pPS" stands for "primate pluripotent stem". Claims 2-4 and 6-11 were directed to preferred embodiments of claims 1 and 5, respectively.

IX. Claims 1 and 5 of **Auxiliary Request 1** were identical to claims 1 and 5 of the Main Request except for the following disclaimer at the end of both claims:

"... wherein said pPS cells are not obtained by means of a process in which human embryos are destroyed."

Dependent claims 2-4 and 6-11 of Auxiliary Request 1 were identical to the corresponding claims in the Main Request. Auxiliary Request 1 comprised three further independent claims, namely claims 12, 15 and 18,

directed, respectively, to a culture medium comprising activin A and a mixture of islet cell differentiation factors (claim 12), and to systems for producing islet progenitor cells comprising specific culture media (claims 15 and 18). Claims 13-14, 16-17 and 19-24 were directed to preferred embodiments of claims 12, 15 and 18, respectively.

X. Claims 1 and 5 of **Auxiliary Request 2** were identical to claims 1 and 5 of the Main Request except for the following disclaimer at the end of both claims:

"... wherein the method does not involve use of a human embryo for industrial or commercial purposes."

Dependent claims 2-4 and 6-11 of Auxiliary Request 2 were identical to the corresponding claims in the Main Request. Auxiliary Request 2 also comprised claims 12-24 identical to claims 12-24 of Auxiliary Request 1.

XI. Claims 1-13 of **Auxiliary Request 3** were identical to claims 12-24 of Auxiliary Request 1. Claims 1-10 of **Auxiliary Request 4** were identical to claims 15-24 of Auxiliary Request 1.

XII. The following documents are referred to in the present decision:

Judgment of the Court (Grand Chamber) of the European Union (CJEU) in case C-34/10 issued on 18 October 2011;

Urteil X ZR 58/07 des Bundesgerichtshof (BGH) verkündet am 27. November 2012;

English translation of the decision X ZR 58/07 of the Federal Court of Justice (Germany) pronounced on 27 November 2012;

Y. Verlinsky et al, Journal of American Medical Association (JAMA), 27 June 2001, Vol. 285, No. 24, pages 3130 to 3133;

Y. Chung et al., Nature, 12 January 2006, Vol. 439, pages 216 to 219;

I. Klimanskaya et al., Nature, 23 November 2006, Vol. 444, pages 481 to 485;

Y. Chung et al., Cell Stem Cell, February 2008, Vol. 2, pages 1 to 5;

J.A. Thomson et al., Science, 6 November 1998, Vol. 282, pages 1145 to 1147.

XIII. Appellant's submissions, insofar as they are relevant to the present decision, may be summarised as follows:

Admissibility of Auxiliary Requests 1 to 4

Although on 22 January 2013, the date of the scheduled oral proceedings before the department of first instance, the CJEU and the BGH had issued their decisions C-34/10 and X ZR 58/07, respectively, the reasons of the BGH were not made public until at least around 23 January 2013. Oral proceedings in the opposition proceedings concerning the European patent no. 1 040 185 (which contained subject-matter and disclaimers relevant to the present case) took place only on 15 March 2013 - an appeal was now pending with this matter as T 1808/13. Thus, at the date of the

scheduled oral proceedings before the examining division, the appellant was unaware of the reasoning of the BGH in case X ZR 58/07 and of the outcome in the opposition proceedings on European patent 1 040 185.

The filing of Auxiliary Requests 1 to 4 was a serious attempt to overcome the objections raised by the examining division under Article 53(a) EPC. The disclaimers, introduced into Auxiliary Requests 1 and 2, intended to overcome these objections and the new claims introduced into these requests corresponded to embodiments of the invention already set out in the Main Request, which did not raise any new issues. In Auxiliary Requests 3 and 4, the claims were restricted to these alternative embodiments of the invention.

Main Request
Article 53(a) EPC, Rule 28(c) EPC

Relevant legislation and case law

The decision under appeal referred to Article 53(a) EPC and Rule 28(c) EPC and cited the decisions G 2/06 (OJ EPO, 2009, page 306) and T 866/01 of 11 May 2005. In a discussion of patentability under Rule 28(c) EPC, reference had to be made to Rule 26 EPC concerning the interpretation of the Directive 98/44/EC, the source of the content of Rule 28(c) EPC. The decision C-34/10 of the CJEU was of relevance for this interpretation, as shown by the updated Guidelines for Examination in the EPO of June 2012. This update took into account the decision of the CJEU, in particular, the reasoning in paragraph 49 of this decision, namely that, if for implementation of an invention a human embryo was destroyed, the point in time at which such destruction took place was irrelevant.

However, as noted in point 20 of G 2/06 (*supra*), neither the EU nor the EPC legislators had defined the term "*embryo*". In paragraph 37 of decision C-34/10, the CJEU directed the referring court BGH to ascertain whether stem cells obtained from a human embryo at the blastocyst stage were included within the concept of "*human embryo*" within the meaning, and for the purpose of the application, of Article 6(2)(c) of the Directive 98/44/EC - corresponding to Rule 28(c) EPC.

In the headnote of decision X ZR 58/07, the BGH stated that a cell taken from a human blastocyst - without destroying the embryo - did not fall under the definition of "*human embryo*" for the purpose of Rule 28(c) EPC by virtue of Rule 26 EPC. If the EPO did not follow the reasoning of the BGH in case X ZR 58/07, then a divergence in the interpretation and application of the Directive 98/44/EC existed between the EPO and the EPC Contracting States which were Member States of the EU (and by extension of the States which were Member States of the European Economic Area as well) and which were subject to the provisions of the Directive 98/44/EC.

Claims of the Main Request

1) The derivation of human embryonic stem (hES) cells did not require embryo destruction

At the filing date of the application, methods were available to a skilled person for obtaining embryonic stem (ES) cells without the necessary destruction of human embryos, such as the alternative methods which used *in vitro* fertilised (IVF) human embryos and which were cited in the application as filed. IVF human

embryos could be created in licensed facilities according to the terms of the European Union Tissues and Cells Directives (EUTCD) and thus, their preparation was not contrary to *ordre public* or morality in Europe.

The technique of pre-implantation genetic diagnosis (PIGD) was practised on human IVF embryos and was of widespread use. It comprised a non-destructive step of micromanipulation of a human embryo to biopsy a single blastomere cell from day 3 cleaving embryos. PIGD was an established, non-destructive technique for obtaining single blastomere cells from human embryos (Y. Verlinsky et al., 2001, see pages 3130 and page 3131, left-hand column). Techniques and procedures for culturing cells *in vitro* and expanding one-cell human embryos to the blastocyst stage were also described on page 8 of the application as filed. Subsequent research confirmed that it was possible to derive ES cells, including human ES (hES) cells, from cells isolated from early stage embryos by techniques analogous to PIGD. Thus, evidence was on file showing that hES cells could be isolated from single blastomeres taken from blastocyst stage embryos without requiring the necessary destruction of embryos - such as Y. Chung et al., 2006 and 2008, and I. Klimanskaya et al., 2006 - and that hES cell lines could also be derived from isolated blastocysts.

To acknowledge the outcome of case C-34/10 of the CJEU, it was necessary to take into account the final decision of the BGH in case X ZR 58/07 which held that a cell taken from a blastocyst was not an "*embryo*" for the purposes of Directive 98/44/EC, in particular Article 6(2)(c) of this Directive, and by extension to Rule 28(c) EPC in view of Rule 26 EPC. Consequently,

the objection raised by the examining division in connection with Rule 28(c) EPC and Article 53(a) EPC was not relevant.

2) Availability of deposited hES cell lines to the public

Although, as cited in the application as filed, the derivation and creation of hES cell lines was reported in prior art documents describing primate pluripotent stem (pPS) cells, including hES cells, the invention could also be practised with established hES cell lines available from a variety of cell banking sources. A large body of evidence was filed at the first instance proceedings to show that deposited hES cell lines were available to the public at the filing date of the application. The use of established hES cell lines as sources of suitable materials for the practice of the invention was explicitly cited in the application as filed. Already in 1998, Thomson et al. reported the first established hES cell lines, which were fully described in the prior art and available to the skilled person, as shown by the evidence on file. Some of these hES cell lines were used in the present application.

The appellant had thus provided a large body of evidence showing that established hES cell lines (and improved culture conditions for them) were fully characterized and publicly available - without any restrictions on their dissemination or use - at both the priority (7 December 2001) and the filing date (6 December 2002) of the present application. Since the application referred to the use of established hES cell lines which were capable of maintaining their pluripotent phenotype in continuous culture, the invention could be practised without destroying a human

embryo. In clear distinction to the case underlying decision G 2/06 (*supra*), the invention claimed in the present application was made, and as of the priority date could be practiced, using established and publicly available hES cell lines. The present application did not relate to an invention which at the filing date necessarily involved the destruction of a human embryo and thus, no objections could be raised in view of the reasoning applied in decision G 2/06 (*supra*). Consequently, no objections could be raised under Article 53(a) EPC and Rule 28(c) EPC. The public availability of established hES cell lines was also of relevance with regard to the provisions of Article 83 EPC.

Auxiliary Requests 1 and 2

These auxiliary requests had been amended to include disclaimers in accordance with the provisions of decision G 1/03 (OJ EPO 2004, page 413). The disclaimers removed the subject-matter objected by the examining division under Article 53(a) EPC and Rule 28(c) EPC.

In point 2.1 of the Reasons of decision G 1/03 (*supra)*, it was stated that a disclaimer was allowable in order to disclaim subject-matter which was excluded from patentability under Articles 52 to 57 for non-technical reasons. The disclaimers introduced into Auxiliary Requests 1 and 2 addressed an objection raised under Article 53(a) EPC. These disclaimers also satisfied the requirement set out in point 2.2 of the Reasons of decision G 1/03 (*supra*) regarding the breadth of the disclaimers. The disclaimers in Auxiliary Requests 1 and 2 did not remove more than what was necessary, they only disclaimed subject-matter excluded from

patentability for non-technical reasons. These disclaimers further satisfied the requirement set out in point 2.4 of the Reasons of decision G 1/03 (*supra*) regarding the clarity and conciseness of disclaimers according to the terms of Article 84 EPC. Thus, the disclaimers in Auxiliary Requests 1 and 2 satisfied all the requirements set out in decision G 1/03 (*supra*).

In the decision G 2/10 (OJ EPO 2012, page 376) further guidance was provided on the admissibility of disclaimers according to the "remaining subject-matter" test. The disclaimers introduced into Auxiliary Requests 1 and 2 served the sole purpose of removing subject-matter which, according to the examining division, was allegedly not eligible for patent protection pursuant to Article 53(a) EPC and Rule 28(c) EPC. The disclaimers did not relate to, or convey, any new technical teaching. Auxiliary Requests 1 and 2 had also been amended by introduction of new claims directed to a culture medium and to a system of the invention comprising various defined differentiation factors. None of the claims of Auxiliary Requests 1 and 2 could be objected to under Article 53(a) EPC or Rule 28(c) EPC, since their implementation did not require the necessary destruction of a human embryo.

Auxiliary Requests 3 and 4
Article 53(a) EPC, Rule 28(c) EPC

The claims of these auxiliary requests were directed to a culture medium and to a system of the invention comprising various defined differentiation factors. None of these claims could be objected to under Article 53(a) EPC or Rule 28(c) EPC, since their implementation

did not necessarily require the destruction of a human embryo.

XIV. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the Main Request filed on 8 November 2010 or, in the alternative, on the basis of any of Auxiliary Requests 1 to 4 filed with the statement of Grounds of Appeal.

Reasons for the Decision

Main Request

1. The Main Request is identical to the request on which the examining division decided to refuse the present application.

Article 53(a) EPC, Rule 28(c) EPC

2. The method of claim 1 for obtaining polypeptide-secreting cells requires the use of a culture of primate pluripotent stem cells (pPS) which, according to the description of the application, includes human embryonic stem (hES) cells (cf. page 6, lines 19 to 20 of the application as filed). In the decision G 2/06 (*supra*), the Enlarged Board of Appeal considered that "(*b)efore human embryonic stem cell cultures can be used they have to be made*" and that, if the "*only teaching of how to perform the invention to make human embryonic stem cell cultures is the use (involving their destruction) of human embryos, this invention falls under the prohibition of Rule 28(c) EPC*" (cf. G 2/06, *supra*, point 22 of the Reasons). The Enlarged Board of Appeal further decided that the argument of the appellant that, for the assessment of patentability of these inventions, "*all the steps preceding an*

invention for the purposes of Rule 28(c) EPC" should not be taken into account, was not relevant. Thus, the Enlarged Board decided that these steps had to be considered (cf. G 2/06, *supra*, point 23 of the Reasons).

3. At the relevant date of the patent in suit, the known and practised method for achieving cultures of hES cells, i.e. the starting material of the method of claim 1, included preceding steps that involved the destruction of human embryos. These destructive methods are not excluded from the scope of claim 1. Thus, in accordance with decision G 2/06 (*supra*), the board decides that the Main Request is not allowable under Article 53(a) EPC and Rule 28(c) EPC.

Admissibility of Auxiliary Requests 1 to 4 and of the new documentary evidence

Auxiliary Requests 1 to 4

4. Auxiliary Requests 1 to 4 were filed at the earliest stage of the present appeal proceedings, namely with the appellant's statement of Grounds of Appeal.

4.1 In its decision C-34/10, the CJEU referred back the underlying case to the BGH and required it to assess whether stem cells obtained from a human embryo at a blastocyst stage were within the concept of a "*human embryo*" for the purpose of the application of Article 6(2)(c) of the Directive 98/44/EC which corresponds to Rule 28(c) EPC. The board agrees with the appellant that this assessment is of relevance for the present appeal proceedings.

Although the Boards of Appeal are only bound by the European Patent Convention and the Implementing Regulations as part of the Convention according to Article 23(3) EPC, the decisions taken by the CJEU and the Supreme Courts of EPC Contracting States on the interpretation of shared or common legislative terms and concepts are certainly of relevance for, and may be considered by, the Boards of Appeal to arrive at their decisions.

In the present case, the board accepts appellant's argument that the reasons of the BGH in the decision X ZR 58/07 were not available to the appellant during the first instance proceedings. The filing of Auxiliary Requests 1 to 4 with its Grounds of Appeal was thus the earliest opportunity to take into account the reasons of the BGH in the decision X ZR 58/07.

4.2 The board also accepts appellant's argument in relation to the opposition proceedings on European patent 1 040 185, now pending as T 1808/13 before this board in a different composition. In view of the matter of this European patent, which concerns non-tumorigenic cells obtained from mammalian (human) embryonic stem cells, the board agrees with the appellant that the parties' submissions and the decision of the opposition division in that case are also of relevance for the present case.

4.3 The disclaimers introduced into Auxiliary Requests 1 and 2 (cf. points IX and X *supra)* are a direct reply to the reasons given by the examining division for the refusal of the present application in the decision under appeal and they are an attempt to take into account the reasons given by the BGH in its decision X ZR 58/07. The subject-matter of the additional claims

introduced into these requests was derived from an essential feature of the methods claimed in the Main Request and thus, already present in the Main Request although in an implicit manner. Auxiliary Requests 3 and 4 have been restricted to this subject-matter, namely to the specific culture media on which pPS cells are cultured in the method for obtaining polpypeptide-secreting cells of claim 1 of the Main Request.

5. In view of the above situation, the board does not see that these requests could have been presented at an earlier stage (in the first instance proceedings) and does not object to their admissibility into the appeal proceedings (Article 12(4) RPBA).

New documentary evidence

6. The new documentary evidence, namely the scientific publications Verlinsky et al. (2001), Chung et al. (2006), Klimanskaya et al. (2006) and Chung et al. (2008) (*supra*), were also filed at the earliest stage of the appeal proceedings, namely with the appellant's statement of Grounds of Appeal.

6.1 Although all these publications were published before 18 September 2012, the date on which the summons to attend oral proceedings pursuant to Rule 115(1) EPC were issued by the examining division, their filing, only now in appeal proceedings, is considered to be in direct reply to the reasons given by the examining division for the refusal of the present application in the decision under appeal. The filing of these publications is also a reaction to the reasons of the BGH in its decision X ZR 58/07 and supports the appellant's argumentation set out in its statement of Grounds of Appeal.

7. In view thereof, the board admits this evidence into the appeal proceedings (Article 12(4) RPBA).

Auxiliary Request 1

8. Claims 1 and 5 of Auxiliary Request 1 contain a disclaimer that excludes methods involving the destruction of human embryos, reading: "*... wherein said pPS cells are not obtained by means of a process in which human embryos are destroyed*" (cf. point IX *supra*). This disclaimer intends to overcome the objection raised against the Main Request (cf. points 2 and 3 *supra*).

9. The criteria for allowability of disclaimers have been laid down in the decisions of the Enlarged Board of Appeal G 1/03 (*supra*, see in particular point 2.4.1 of the Reasons) and G 2/10 (*supra*). According to decision G 2/10 (*supra*), the subject-matter remaining in the claim after the introduction of the disclaimer must be - explicitly or implicitly - directly and unambiguously disclosed to the skilled person using common general knowledge, in the application as filed (cf. G 2/10, *supra*, Headnote answer to question 1(a)). In fact, this is "*the overriding principle for any amendment to be allowable under Article 123(2) EPC ... that applies equally to the subject-matter of a claim the scope of which is determined by a disclaimer*", be it an undisclosed or a disclosed disclaimer (cf. G 2/10, *supra*, point 4.7 of the Reasons).

10. In the present case, the subject-matter remaining in claims 1 and 5 of Auxiliary Request 1 after the introduction of the disclaimer, namely a method for obtaining polypeptide-secreting cells which includes

the culture of hES cells derived only and exclusively from non-destructive methods, was not available at the priority date of the application (7 December 2001) and thus, was not directly and unambiguously disclosed to a skilled person as required by decision G 2/10 (*supra*). The board does not consider this "remaining subject-matter" to be disclosed in the application as filed. For the board to arrive at this decision, the following points are relevant:

10.1 According to the appellant, a single hES cell could be obtained from a human pre-implantation embryo by using methods developed in 2000 for pre-implantation genetic diagnosis (PIGD) of *in vitro* fertilised (IVF) embryos. Document Verlinsky et al. (2001) has been filed in order to show that a single blastomere cell could be obtained from day 3 cleaving embryos without destroying the embryo. This evidence allegedly supports the availability of hES cells at the priority date of the application by methods that do not involve the destruction of human embryos.

10.2 However, for carrying out the methods of claims 1 and 5, it is not enough to be in possession of single hES cells but it is further necessary to culture these cells in order to obtain an established culture of hES cells or a hES cell line, i.e. *in vitro* culturing and expansion of hES cells (derivation).

It is acknowledged that derivation methods of embryonic stem cells from mice and from some primates were known and available to a skilled person at the priority date of the application, as shown by the bibliographic references in the application as filed cited by the appellant (cf. page 6, third full paragraph and page 8, first and second full paragraphs of the application as

filed). However, none of these derivation methods has been successfully used with hES cells.

Indeed, document Klimanskaya et al. (2006) states that the derivation of hES cells "*currently requires the destruction of ex utero embryos*" (cf. page 481, left-hand column, lines 1-2). Only by using a new method disclosed in this document, it was for the first time possible to obtain two hES cell lines (cf. page 481, right-hand column, last paragraph to page 482, left-hand column, first paragraph). In document Chung et al. (2008), this method is referred to as being highly inefficient (cf. page 1, middle column, first paragraph). Incidentally, Chung et al. (2008) also states that "*(t)o date, the derivation of all human embryonic stem cell (hSEC) lines has involved destruction of embryos*" (cf. page 1, left-hand column, lines 1-3).

10.3 It is worth noting that the derivation method disclosed in document Klimanskaya et al. (2006) is based on a co-culture of hES cells with green fluorescent protein (GFP)-positive hES cells (cf. page 482, left-hand column, first paragraph). The source of these GFP-positive hES is not mentioned in this document but, in view of the comments made in all these post-published documents (cf. point 10.2 *supra*), these hES cells were also obtained by methods involving the destruction of human embryos. It is thus only the derivation method disclosed by Chung et al. in **2008**, seven years after the priority date of the present application (7 December 2001), which for the first time has allowed the provision of hES cultures (cell lines) without destroying a human embryo in any production step.

11. Appellant's further argument based on the public availability of established hES cell lines cannot be followed by the board, since these cell lines were also originally obtained using methods that, at some preceding step, involved the destruction of a human embryo (cf. point 2 *supra*, last sentence). This has not been contested by the appellant and there is no evidence on file to demonstrate the contrary.

In this respect, appellant's attention has also been drawn to decision T 2221/10 (*supra)* (cf. point V *supra*). In this decision, this board in a different composition considered methods using commercially or otherwise publicly available hES cell lines, including most of the hES cell lines referred to by the appellant in the present case (*inter alia*, Thomson et al., 1998). Although methods using these hES cell lines did not require *de novo* destruction of human embryos, the board concluded that all these hES cell lines were initially derived from a process which had destroyed human embryos.

Therefore, the board, following the criteria established in decision G 2/06 (*supra*), decided that "*(i)nventions which make use of publicly available human embryonic stem cell lines which were initially derived by a process resulting in the destruction of the human embryos are excluded from patentability under the provisions of Article 53(a) EPC in combination with Rule 28(c) EPC*" (cf. T 2221/10, *supra*, Headnote and points 10 to 29 of the Reasons).

Accordingly, the board dismissed the appeal against the decision of the examining division to refuse European patent application No. 03 751 238.1 claiming the priority dates of 7 October 2002 and 19 February 2003,

i.e. almost one year after the priority date of the present application (7 December 2001).

12. Thus, the board does not accept appellant's argument that the application discloses a method for obtaining polypeptide-secreting cells which uses hES cultures or cell lines produced without involving the destruction of a human embryo, in a manner sufficiently clear and complete for it to be carried out - without undue burden or inventive skill - by a person skilled in the art. Rather the methods available to the skilled person at the relevant date all included, at some point in time, the destruction of a human embryo.

13. In view thereof, the board does not consider it necessary to examine whether the disclaimer introduced into claims 1 and 5 of Auxiliary Request 1 fulfils the other criteria established in decision G 1/03 (*supra*), such as for instance whether the disclaimer is complete, i.e. whether it actually excludes all subject-matter not allowable under Article 53(a) EPC in combination with Rule 28(c) EPC (see in this respect the disclaimer introduced into Auxiliary Request 2, points 15 to 17 *infra*).

14. In conclusion, the board considers the disclaimer introduced into claims 1 and 5 of Auxiliary Request 1 not to be allowable since the application as filed does not disclose the "remaining subject-matter" of the invention (a method which includes the culture of hES cells derived, only and exclusively, from non-destructive methods). Only with information available seven years after the claimed priority date, a skilled person would have been in a position to put into practice this "remaining subject-matter" (cf. point 9 *supra*).

Auxiliary Request 1 does not meet the requirements of Article 123(2) EPC.

Auxiliary Request 2

15. Claims 1 and 5 of Auxiliary Request 2 contain a disclaimer reading: "*... wherein the method does not involve use of a human embryo for industrial or commercial purposes*" (cf. point X *supra*).

16. Without entering into the question whether this disclaimer overcomes the objection raised against the disclaimer introduced into Auxiliary Request 1 (cf. points 10 and 11 *supra*), the board considers the disclaimer in Auxiliary Request 2 not to be clear and to be contradictory in itself. The fact that industrial protection is sought for the claimed subject-matter, i.e. a method comprising culturing pPS cells, already indicates that a human embryo is used for industrial or commercial purposes. Thus, claims 1 and 5 of Auxiliary Request 2 are not clear and contravene the requirements of Article 84 EPC.

17. If it is the aim of the introduced disclaimer to restrict the later use of the differentiated pPS cells produced by the claimed method, namely to be used exclusively for the embryo (or the human being derived therefrom) which was used for obtaining the starting material of the claimed method, then the disclaimer is directed to subject-matter which is not covered by the claim. Such disclaimer does not meet the requirements of Article 123(2) EPC is not allowable (cf. T 1836/10 of 9 April 2013, points 11 and 13 of the Reasons).

Auxiliary Requests 3 and 4
Article 111 EPC

18. The requirements of patentability for the subject-matter of the claims of these requests have never been examined by the first instance. Accordingly, no comments or reasons concerning it can be found in the decision under appeal. In view thereof, the board considers that a remittal to the department of first instance is the most appropriate course of action in the present circumstances.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution based on the Auxiliary Requests 3 and 4 filed with the appellant's statement of Grounds of Appeal.

The Registrar: The Chairman:

A. Wolinski M. Wieser

Decision electronically authenticated