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Datasheet for the decision of 27 August 2014

Case Number: T 0161/11 - 3.3.08

Application Number: 99927599.3

Publication Number: 1088057

IPC: C12N5/073

Language of the proceedings: EN

Title of invention:
METHOD AND MEDIUM FOR IN VITRO CULTURE OF HUMAN EMBRYOS

Patent Proprietor:
Adelaide Research & Innovation Pty Ltd
Hamberger, Lars

Opponent:
STRAWMAN LIMITED

Headword:
GM-CSF for embryo culture/ADELAIDE RESEARCH, HAMBERGER

Relevant legal provisions:
EPC Art. 56, 56, 83

Keyword:
Main request - requirements of the EPC met (yes)
Art. 54 EPC - new ground of opposition - not admitted

Decisions cited:
G 0005/83, G 0002/88, G 0009/91, T 1119/05

Catchword:

Europäisches Patentamt
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Case Number: T 0161/11 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 27 August 2014

Appellant: (Opponent)	STRAWMAN LIMITED 34 Lovedon Lane Winchester, Hampshire, SO23 7NU (GB)
Representative:	Dean, John Paul Withers & Rogers LLP 4 More London Riverside London SE1 2AU (GB)
Respondent: (Patent Proprietor 1)	Adelaide Research & Innovation Pty Ltd 1st floor, 10-20 Pulteney Street Adelaide, S.A. 5000 (AU)
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Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 9 December 2010 concerning maintenance of the European Patent No. 1088057 in amended form.**

Composition of the Board:

Chairman M. Wieser
Members: B. Stolz
J. Geschwind

Summary of Facts and Submissions

I. The appeal lies against the decision of the opposition division dated 9 December 2010 to maintain European patent No. 1 088 057 in amended form.

II. The opposition was filed on the grounds of Articles 100(a) EPC in conjunction with Article 56 EPC, 100(b) and 100(c) EPC. The opposition division decided that the main request did not meet the requirements of Article 123(2) EPC but that the auxiliary request filed on 20 October 2010 met the requirements of the EPC.

III. With its grounds of appeal, the opponent (appellant) submitted new evidence ("slides") entitled "Preimplantation embryo development" (document D32) and "Analysis of D2 Results" (documents D33 a-d).

IV. With their reply to the statement of grounds of appeal, the patent proprietors (respondents) resubmitted document D26 and submitted new documents D34 to D55.

V. In response to the respondents' submissions, the appellant submitted new documents D56 to D60.

VI. The parties were summoned to oral proceedings. A communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) annexed to the summons, informed them of the preliminary non-binding opinion of the board on some of the issues of the appeal proceedings.

VII. The appellant informed the board that it would not attend the oral proceedings.

VIII. In response to the board's communication, the respondents, with a letter dated 5 June 2014, filed a new auxiliary request.

IX. Oral proceedings, scheduled for 24 July 2014, were cancelled.

X. Claim 1 of the main request (claims as maintained in opposition proceedings) reads:

"1. Use of human GM-CSF for preparing a medium for propagating early stage human embryos to blastocyst stage in an IVF program."

Dependent claims 2 to 12 specify further features of the culture medium, while dependent claims 13 to 20 refer to steps of cultivation of a human embryo.

XI. The following documents are referred to in this decision:

D1: Gardner & Lane (1997) Human Reproduction, Update 3, 367-382

D2: de Moraes & Hansen (1997) Biology of Reproduction, 57, 1060-1065

D3: WO 95/24469 (Immunex Corporation; Lyman)

D11: Kane et al. (1997) Human Reproduction, Update 3, 137-157

D13: Robertson et al. (1991) The Molecular and Cellular Immunobiology of the Maternal-Fetal Interface. Oxford University Press, New York, p. 191-206

D14: Hill et al. (1987) Journal of Immunology 139, 2250-2254

D15: Haimovici et al. (1991) Biol. Reprod. 44, 69-75

D23: Park et al. (2001) Korean J Fertil Steril. 28(2), 161-168

D24: Novacek (2001) Current Biology 11(14), R573-R575

D57: Brännström et al. (1994) Biol. Reprod. 50, 88-94

D58: Robertson et al. (1996) Biol. Reprod. 54, 183-196

D59: Robertson and Seamark (1994) Critical Rev. Immun. 14(3&4), 239-292

D60: Robertson and Seamark (1990) Reprod. Fertil. Dev. 2, 359-368

XII. Appellant's arguments, as far as relevant for the decision, can be summarized as follows:

The documents entitled "Summary of D2 results table" and "Critical prior art timeline", which were not admitted by the opposition division, should be admitted into the appeal proceedings.

Article 54 EPC

The term "for propagating" in claim 1 had to be interpreted as "suitable for propagating". Consequently, the subject matter of claim 1 referred merely to the use of human GM-CSF for preparing a medium. This subject matter lacked novelty over Document D3 which disclosed an extra corporeal cell

culture kit including GM-CSF. This novelty objection was extremely simple and the opposition division was wrong not to admit it into the procedure.

Article 53(a) EPC

The invention did not relate to a method of medical treatment but to a method of growing human cells using human GM-CSF in the medium. No disease was treated and no suffering or pain was relieved. The conclusion of the opposition division that claim 1 had to be construed as a second medical use claim was incorrect.

Article 83 EPC

The term "early stage embryo" was not specifically defined. All of the experiments of the patent showing improved blastocyst development used frozen 2 to 4 cell embryos. There was no evidence that the use of GM-CSF at any other early developmental stage would have the desired results.

Claim 1 covered the use of GM-CSF at any concentration, also at concentrations known to be toxic. The skilled person could not be required to undertake unnecessary experiments with human embryos to determine toxic levels.

Only the use of recombinant human GM-CSF was disclosed. In respect of non-recombinant human GM-CSF, the disclosure was insufficient.

Article 56 EPC

The closest prior art, document D1 related to the use of blastocyst stage human embryos in IFV programs. The

technical problem was seen in the provision of an alternative solution to the problem of low numbers of human embryos developing to the blastocyst stage for use in an IVF program. Document D1 proposed the addition of growth factors to culture medium which provided a motivation to combine the disclosures of documents D1 and D2. Document D2 showed positive effects of GM-CSF on the developmental potential of bovine embryos in culture. Document D14 did not show negative effects of GM-CSF because it was not clear that GM-CSF was used at all and because the concentration used was not clear. Document D15 was not relevant because it related only to possible effects of GM-CSF downstream of the developmental period covered by the claim. Any negative effect at this later stage had no bearing on the claimed subject matter. The results of document D13 showed the influence of GM-CSF on embryo development from the 8 cell stage onward. This document proposed the use of GM-CSF for enhancing the implantation rates of human as well as livestock embryos. As for the relevance of animal models, documents D24 and D25, disclosing phylogenetic studies, were less relevant than the declaration by Dr Meintjes from which it was clear that bovine models would have been more relevant than mouse models.

XIII. The arguments of the respondents, as far as relevant for the present decision, can be summarized as follows:

Article 54 EPC

The novelty objection on the basis of document D3 represented a fresh ground of opposition which should not be admitted into the proceedings.

Article 53(a) EPC

In opposition proceedings, the opponent only objected to claim 13. Any objection under this Article against claim 1 represented a fresh ground of opposition which should not be admitted.

Article 83 EPC

The objection against the term "early stage embryo" was an inadmissible objection under Article 84 EPC. Moreover, there was no scientific reason, let alone evidence, for assuming that the method would only work with 2 to 4 day embryos.

As regards suitable concentrations of GM-CSF, the description at page 6 and the examples provided sufficient guidance to the skilled person.

The objection that the invention was only sufficiently disclosed as far as it related to the use of recombinant human GM-CSF, but not to the use of any other form of human GM-CSF, was not supported by any evidence.

Article 56 EPC

Starting from document D1 as closest prior art, the problem to be solved consisted in providing an improved method for propagating early stage human embryos to blastocyst stage in an IVF program, such that the improvement increased the developmental potential of the blastocysts. Starting from document D1, it was not obvious to arrive at the claimed solution because the further prior art related to animal embryos. No extrapolation between species could be made and no prior art suggested a beneficial effect of GM-CSF on

human embryos. The prior art relating to animal embryos was, at best, contradictory and mentioned potentially detrimental effects of GM-CSF. Document D2 clearly taught adverse effects of GM-CSF on the developmental competence of the bovine blastocysts obtained. Documents D13 and D15 referred to the use of GM-CSF at different stages of embryo development. Their results could therefore not be compared. Document D14 clearly demonstrated a negative effect of increasing concentrations of GM-CSF on mouse embryo development. Further negative effects of GM-CSF on mouse embryos could also be found in document D16.

XIV. The appellant requested that the decision under appeal be set aside and the patent be revoked.

XV. The respondents requested that the appeal be dismissed or in the alternative, that the patent be maintained on the basis of the auxiliary request filed with letter of 5 June 2014. Objections against claim 1 under Articles 53(c) and 54 EPC represented fresh grounds for opposition and should not be admitted. Oral proceedings were requested, should the board not be minded to allow respondents' main request.

Reasons for the Decision

Fresh Grounds for Opposition

Article 54 EPC

1. The only objection raised in the opposition brief on the ground of Article 100(a) EPC referred to a lack of inventive step (Article 56 EPC).

At the oral proceedings before the opposition division, the opponent requested that an objection of lack of novelty under Article 54 EPC be admitted as a new ground of opposition. After deliberation, the opposition division dismissed this request (cf. Minutes of the oral proceedings, points 11 to 13).

2. With its grounds of appeal, the appellant raised again an objection under Article 54 EPC. The appellant requested that novelty not be admitted as a ground of opposition.

3. As stated in decision G 009/91 (OJ 1993, 408), "[t]he purpose of the appeal procedure inter partes is mainly to give the losing party a possibility to challenge the decision of the Opposition Division on its merits. It is not in conformity with this purpose to consider grounds for opposition on which the decision of the Opposition Division have not been based. Furthermore, in contrast to the merely administrative character of the opposition procedure, the appeal procedure is to be considered as a judicial procedure, as explained by the Enlarged Board in its recently issued decisions in the cases G 7/91 and G 8/91 (see point 7 of the reasons). Such procedure is by its very nature less investigative than an administrative procedure. Although Article 114(1) EPC formally covers also the appeal procedure, it is therefore justified to apply this provision generally in a more restrictive manner in such procedure than in opposition procedure. In particular with regard to fresh grounds for opposition, for the above reasons the Enlarged Board considers that such grounds may in principle not be introduced at the appeal stage. However, an exception to the above principle is justified in case the patentee agrees that a fresh ground for opposition may be considered".

4. In view of the above and the respondents' request that Article 54 EPC not be admitted as a ground for opposition, the board decides not to admit objections on the ground of Article 100(a) EPC in conjunction with Article 54 EPC.

Article 53(a) EPC

5. An objection under this provision was raised by the opponent for the first time at the oral proceedings before the opposition division when the auxiliary request was examined in respect of inventive step.

According to point 18 of the **minutes** of the oral proceedings, the opponent raised an objection under Article 53(a) EPC against **claim 1**. According to point 15.3 of the **decision** of the opposition division the objection was raised against **claim 13**. The opposition division decided "that no objection under Art. 53(a) EPC arises".

6. The respondents requested that an objection under Article 53(a) EPC not be admitted into the appeal proceedings.

7. The statement of grounds of appeal did not contain an objection under Article 53(a) EPC. In point 4, under the header "Patentability", the appellant merely commented ("we would comment generally as follows") on point 15.3 of the decision under appeal as follows:

"Strictly speaking the invention underlying the European patent is not a method of medical treatment. It is a method of growing human cells using human GM-CSF in the medium. No disease is treated and there is no

relief of pain or suffering for the cells/embryo. The invention is probably a non-medical method. In the circumstances the OD was wrong to conclude that [...] claim 1 has to be construed as an appropriate second medical use claim."

From this comment, the board can only derive that the appellant disagrees with the examining division's interpretation of claim 1 as being in the second medical use format. There is however no substantive argument based on appellant's conclusion.

8. Since the appellant has not substantiated its objection under Article 53(a) EPC in its statement setting out the grounds of appeal, this issue does not form part of the appeal procedure.

Admissibility of documents

9. The appellant requests that the documents labelled "The critical prior art" and "Summary of D2", which were not admitted into opposition proceedings, be admitted into appeal proceedings.

10. If the way in which a department of first instance has exercised its discretion on a procedural matter is challenged in an appeal, it is not the function of a board of appeal to review all the facts and circumstances of the case as if it were in the place of the department of first instance, and to decide whether or not it would have exercised such discretion in the same way as the department of first instance. A board of appeal should only overrule the way in which a department of first instance has exercised its discretion if the board concludes it has done so according to the wrong principles, or without taking

into account the right principles, or in an unreasonable way (T 640/91, OJ 1994, 918; see also T 182/88, OJ 1990, 287; T 986/93, OJ 1996, 215; T 237/96 and G 7/93, OJ 1994, 775).

11. Both documents were filed only two days before the oral proceedings. The patent proprietor requested that none of them be admitted. The opposition division, in the decision under appeal, gave the following reasons why it did not admit these documents:

"12.2 The document "The critical prior art" is a modified version of the timeline table sent by the opponent with the letter of 18.08.2010. It appears that that some further information or comments are given in addition to the dates mentioned in the document "Timeline of critical prior art". The opposition division, in line with the patentee, considers that this document provides new informations or evidence that the patentee did not have the possibility to take into account with sufficient time before the oral proceedings. Reference is made to the Decision T1122/01, wherein a Power-point presentation during oral proceedings was not allowed. Consequently, the document is not admitted into the procedure.

12.3 The document "Summary of D2" was not admitted into the procedure since said document allegedly refers to the data derived from D2. If it would be the case, a direct reference to D2 is possible and is preferable. This document cannot be more relevant than D2 itself. To the contrary, any misinterpretation of the results of D2 would add additional information, which can not be admitted at this stage of the procedure."

12. The board decides that the opposition division took its decision on the basis of the right principles and in a reasonable way, and that this exercise of discretion should therefore not be overturned (cf. point 3.2 of decision T 1119/05 of 8 January 2008). The two documents are therefore not admitted into the appeal procedure.

13. In response to the patent proprietors' response to appellant's grounds of appeal, the appellant submitted documents D57 to D60 to document the general knowledge. The board decided to admit them into the proceedings.

Articles 123(2), 123(3) and 84 EPC

14. Claims 1 to 20 of the main request correspond to claims 1 to 20 of Auxiliary request 1 on the basis of which the patent was maintained in opposition proceedings. The appellant did not raise any objections under the provisions of Articles 123(2), 123(3) and 84 EPC and the board has no reason to raise any of its own.

Claim interpretation

15. Claim 1 refers to the use of human GM-CSF for preparing a medium for propagating early-stage human embryos to blastocyst stage in an IVF program."

16. The respondents considered this claim to be in the "swiss type" format for a second or further medical use.

17. According to point 23 of decision G 005/83 (OJ 1985, 64), it is legitimate in principle to allow claims directed to the use of a substance or composition for

the manufacture of a medicament **for a specified new and inventive therapeutic application**, even in a case in which the process of manufacture as such does not differ from known processes using the same active ingredient.

18. According to the respondents' submissions an increased proportion of human embryos reaches blastocyst stage and hatching as a result of the new therapeutic application of the culture medium.

19. The board does not agree. "Propagating" early stage human embryos to blastocyst stage merely stands for "culturing" the embryos for the amount of time required for achieving blastocyst stage. Claim 1 lacks any indication of a therapeutic intervention, (in the sense of curing or preventing a disease state). It is therefore not in a "swiss type" claim format but represents a non-medical use claim.

20. A claim of the type "use of human GM-CSF for preparing a medium", is equivalent to a claim to "a method for preparing a medium comprising the use of human GM-CSF" (cf. point 5.1 of decision G 002/88 (OJ 1990, 93)). The product of this method is the medium for propagating early stage human embryos to blastocyst stage. According to established case law, the statement of a purpose of use of a product is to be interpreted as meaning that the product is suitable for the stated purpose (Case Law of the Boards of Appeal, 7th Edition, p. 161, I.C.6.3.3).

21. Claim 1 refers therefore to the use of human GM-CSF for preparing a medium **suitable for** propagating early-stage human embryos to blastocyst stage in an IVF program.

22. Contrary to appellant's submissions in point 3.1 of its statement of grounds of appeal, the feature "suitable for propagating early-stage human embryos to blastocyst stage in an IVF program" is not meaningless but implies certain technical/chemical properties of the medium which render it suitable for use in an IVF program. At the same time, this feature excludes the addition of certain compounds, such as e.g. animal sera, which would render the medium unsuitable for human IVF use.

23. The board notes in this context that, since claim 1 is a non-medical use claim, dependent claims 13 to 20, due to their dependency on claims 1 to 12, merely specify features relating to the properties of the medium resulting from the process of manufacture (e.g. according to claim 13, the medium has to be suitable for propagating embryos in vitro for a time and under conditions to increase the proportion of transfer-ready blastocysts). These claims do however not specify steps of a method for culturing human embryos.

Article 83 EPC

24. The appellant argued that the patent only disclosed an effect of recombinant human GM-CSF at a concentration of 2 ng/ml on the development of 2 to 4 cell embryos. Therefore, as far as the cultivation of embryos from other early cell stages was concerned, and as far as the claims related to the use of non-recombinantly produced human GM-CSF, the claimed subject matter was insufficiently disclosed.

25. These two objections are allegations not substantiated by any verifiable facts.

26. The appellant submitted furthermore that 2 ng/ml was the only GM-CSF concentration sufficiently disclosed for the envisaged purpose. Certain concentrations of GM-CSF were however known to be toxic and the skilled person should not be required to undertake unnecessary experiments with human embryos to establish toxic levels of GM-CSF.

27. The description of the patent refers to a concentration range of 0,01 to about 5 ng/ml for achieving the desired effect ([0029] of the patent in suit). The appellant did not provide and the board did not find any conclusive evidence of toxic concentrations of GM-CSF within this range.

28. The board is therefore satisfied that the skilled person is in a position to readily carry out the claimed invention and that the main request meets the requirements of Article 83 EPC.

Article 56 EPC

29. Document D1, entitled "Culture and selection of viable blastocysts: a feasible proposition for human IVF?", represents the closest prior art. It discloses culture media suitable for propagating early stage embryos to blastocyst stage.

30. Based on document D1, the technical problem is seen in the provision of a culture medium for the propagation of early stage human embryos to blastocysts with improved developmental potential.

31. As a solution, the patent proposes the preparation of a culture medium comprising human GM-CSF.

32. The data summarized in Tables 3 to 5 of the patent in suit show that a higher fraction of embryos cultured in the presence of GM-CSF reached blastocyst stage faster and comprised a higher total cell number than embryos cultured without GM-CSF. This effect is considered as an indicator of improved developmental potential (cf. document D1, page 378, paragraph bridging the left and right columns). The board is therefore satisfied that the proposed solution indeed solves the above mentioned problem.

33. It remains to be established whether the claimed solution involves an inventive step.

34. Appellant's main argument was that the claimed solution was obvious in view of documents D1 and D2. In appellant's view, document D1 suggested the addition of growth factors to a culture medium, which provided an incentive to try the addition of GM-CSF. Document D2 showed the same positive effects of GM-CSF on bovine embryos as the patent showed in relation to human embryos. There was therefore a reasonable expectation of success.

35. The focus of document D1 is on the propagation of human early stage embryos to the blastocyst stage with the aim of improving success rates in IVF. It suggests that media for embryo culture need to be more complex and reflect the environment of the female reproductive tract (page 369, left column, bottom). It discusses a number of additives to embryo culture media, such as carbohydrates (page 371), amino acids (pages 371 to 375), chelators (page 376) and serum (pages 376 to 377). When discussing the effects of the addition of serum to culture medium, it mentions that serum is of different origin than oviduct fluid and that negative

effects in sheep embryos (page 376, right column) are known.

The only mention of growth factors at all is in the discussion of the effects of the addition of serum on embryo development. Growth factors in serum are mentioned as potentially inducing altered patterns of development, and the use of serum itself is questioned. To avoid potential problems resulting from the use of serum, the use of serum albumin or hyalorunate is considered (page 377, right column).

36. Contrary to appellant's submissions, the board could not find a single reference in document D1 to the addition of any growth factor to a culture medium, let alone to the addition of GM-CSF. While document D1 suggests that there is room for improvement of culture media for human embryo propagation, it does neither provide any motivation nor any incentive to add GM-CSF.

Thus, the claimed solution was not obvious on the basis of document D1 alone.

37. On the other hand, several documents disclose the use of GM-CSF for the production of blastocysts from bovine embryos (document D2), and mouse embryos (documents D11, D13, D14, D15).

38. Document D2 is concerned with the use of GM-CSF for increasing blastocyst production rates in serum free culture systems of bovine embryos. Both parties made extensive submissions regarding the data presented in Tables I and II of this document.

39. The appellant submitted that the data in Table I of document D2 demonstrated a positive effect of GM-CSF on

the percentage of bovine oocytes developed to blastocyst stage, to expanded blastocysts, and to hatched blastocysts. In its view, the data showed the increased developmental potential of the blastocysts and this conclusion was supported by the authors of document D2 stating that "*GM-CSF may play a role in the early development of bovine embryos and might be a useful molecule for increasing blastocyst production rates in serum-free culture systems*" (abstract of document D2, last sentence).

40. The respondents agreed that the data in table I showed an increased percentage of oocytes that had developed to blastocysts in the presence of GM-CSF at days 7 or 9 after insemination but pointed out that the percentage of expanded blastocysts at day 7 was reduced. Furthermore, the increased percentage in the presence of GM-CSF of expanded blastocysts at day 9 was not helpful because the percentage of hatching or hatched blastocysts at day 9 was reduced in the presence of GM-CSF. Similar results were shown in Table II. Thus, while the data for GM-CSF showed an increase in the number of blastocysts at days 7 and 9, their developmental potential was reduced as shown by the reduced percentage of expanding and hatching embryos.

41. The board notes that the authors of document D2, based on the data from Tables I and II, observed a tendency for blastocysts from GM-CSF treated cultures to be less advanced in development because a smaller proportion of blastocysts reached the expanded state on day 7 and a smaller proportion of blastocysts had hatched on day 9 (page 1063, right column, first paragraph). The authors considered these data to indicate that GM-CSF might allow more developmentally delayed embryos to undergo blastocoel formation which might adversely affect the

quality of blastocysts if GM-CSF promoted blastocyst development in retarded embryos that would otherwise not become blastocysts. Bovine embryos developing to blastocysts later in culture had however been reported to be less likely to establish pregnancy after transfer to recipients than more rapidly developing embryos (page 1064, left column, penultimate paragraph).

42. Therefore, the board comes to the conclusion that the skilled person, based on document D2, did not have a reasonable expectation of achieving a positive effect on the developmental potential of early human embryos through the use of a culture medium comprising human GM-CSF.

43. Document D11 has its focus on the role of a variety of growth factors in preimplantation development. It discusses limitations of the mouse embryo as a model organism and mentions that the mouse embryo is not the most promising model in which to study the effects of growth factors. It points to other model organisms such as rabbit, sheep and cattle (page 138, right column, 1st paragraph). Table I summarizes evidence for the presence of many different growth factor ligands and receptors in mouse oviduct, uterus and preimplantation embryos, Table II for the presence of growth factor ligands and receptors in human oviduct, uterus and preimplantation embryos, and Tables III and IV summarize corresponding evidence in rabbits, rats, skunks, non-human primates, cows, sheep, pigs and horses. Tables I and II refer *inter alia* to further documents relating to the presence of GM-CSF ligands and/or receptors in the mouse and human uterus (Tables I and II), but provide no references to documents relating to the presence of GM-CSF or its receptor in early mouse or human embryos. Commenting on Tables I

and II, the authors state that "there are an enormous number of possible mechanisms controlling embryonic development" (page 142, left column). It is furthermore mentioned that GM-CSF, when added before the morula stage, had a negative effect on embryo development but a positive effect when added after the morula stage (page 147, right column, penultimate paragraph). According to the authors of document D11, the most promising growth factors for embryo culture were CSF-1, FGF-4, IGF-I/IGF II, TGF-a/EGF and LIF ("Conclusions", second paragraph). The document concludes with a reference to a possible role of non-peptide growth factors in early embryo development.

44. Document D14 reported a negative effect of GM-CSF on mouse blastocyst development. Similarly, document D15 reported a negative effect of GM-CSF on the attachment of hatched mouse blastocysts, i.e. on embryos at a later developmental stage than blastocyst.

45. Document D13, on the other hand, referring to the negative results of document D14, presents results of further experiments to determine any negative effects of GM-CSF on early mouse embryo development. It reports a positive effect of GM-CSF on the attachment of hatching embryos (cf. Table 13.7) but no effect, neither negative nor positive, on the embryo development up to the blastocyst stage (cf. Table 13.8).

46. In conclusion, the prior art relating to mouse embryo development (documents D11, D13 to D15) is inconclusive about the effect of GM-CSF on the development to blastocyst stage. Even document D13 only demonstrated a positive effect on embryo implantation but not on embryo development up to the blastocyst stage.

47. Thus, the skilled person, taking into consideration documents D11 and D13 to D15, would not have expected to achieve a positive effect on early stage human embryo development through the addition of human GM-CSF to the culture medium.

48. The appellant furthermore referred to documents D57 to D60 to support its argument that the use of GM-CSF for the propagation of early stage human embryos was obvious. These documents refer to a role of GM-CSF in the induction of ovulation associated vascular changes and in the breakdown of the rat follicular wall (document D57, page 93, left column, last paragraph), in tissue remodeling and changes in immunological competence of the murine uterus (document D58, final paragraph), an immune modulatory role in the murine uterus (document D59, page 244, left column), and a role in the priming of the murine uterus for implantation (document D60, final sentence of "Abstract"). They do however not suggest any effect of GM-CSF on early stage embryo development in vitro.

49. It follows that the claimed solution is neither obvious in view of any of documents D2, D11, D13 to D15 or D57 to D60 alone nor in view of document D1 in combination with any of these documents.

The board arrives at this conclusion on the basis of the disclosures of the cited documents, leaving aside any considerations whether the mouse model or the bovine model represented a more suitable model of human embryonic development, and irrespective of whether the skilled person considered animal models to represent a suitable starting point for predictions concerning human embryonic development at all.

50. Finally, the appellant submitted that claim 1 lacked an inventive step over document D3 which referred to kits comprising cellular growth media and a composition containing growth factors such as GM-CSF.

51. The question to be answered is whether the skilled person would have considered, in an obvious way, the kits disclosed in document D3 to be suitable for the propagation of early stage human embryos to the blastocyst stage.

52. The kits disclosed in document D3 are described as suitable for the in vitro propagation of stem cells in general and of hematopoietic stem cells in particular (page 3, lines 30 to 32; page 8, lines 31 to 35). Also mentioned is the use of the kit to expand genetically modified cells for gene therapy (page 8, line 14). There is however no mention or hint that the kit could be used for the propagation of human embryos, let alone for the propagation of early stage human embryos to the blastocyst stage, which the skilled person would not consider to be encompassed by the term stem cells.

53. Thus, document D3, which addresses a different technical problem than the patent or document D1 (and which therefore is not a candidate for the closest prior art document), does not contain any information that would have led the skilled person in an obvious way to the solution of the technical problem underlying the present invention (see point 30 above).

54. As a consequence the board decides that the subject-matter of claim 1, and of dependent claims 2 to 20 of the main request, is based on an inventive concept and meets the requirements of Article 56 EPC.

55. Since the main request is allowable and since the appellant had announced that it was not going to attend oral proceedings (cf. item VII, above), there was no need to hold any (cf. item XV, above).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Wolinski M. Wieser

Decision electronically authenticated