

THE PATENTS ACT, 1970
Section 15

In the matter of an application for
Patent No.1435/DELNP/2006
dated the 16th March, 2006.

BOARD OF REGENTS OF THE
UNIVERSITY OF TEXAS SYSTEM APPLICANT

HEARING HELD ON 9th July, 2009 at 3.00PM

Present :-

Mr. Shukadev Khuraijam
REMFRY & SAGAR

Agents for the Applicant

Mrs. Reena

Examiner of Patents & Designs

ORDER

1. M/s. BOARD OF REGENTS OF THE UNIVERSITY OF TEXAS SYSTEM, a body corporate organized under the laws of United States of America, 201 West 7th Street. Austin, TX 78701, U.S.A. through their agent M/s REMFRY & SAGAR filed the application No. 1435/Delnp/2006 dated 16th March, 2006 for their invention related to "A METHOD OF ENHANCING THE BLASTOCYST SIZE, THE INNER CELL MASS OR THE TROPHOBLASTIC SIZE OF A MOUSE OR HUMAN BLASTOCYST". A request for examination of the said application was filed by their agent on 24th May, 2006. This application was published under the provisions of Section 11(A) of the Patents Act, 1970 as amended in 2005 (Hereinafter referred as 'Act') in the Patent Office Journal dated 3rd August 2007. This application was examined by the Office and First Examination Report thereof was as issued on 21st May, 2008 which inter alia communicated following objections:

1. Subject matter of claims 1-16 do not constitute an Invention u/s 2(1)(j) of the Patents Act 1970 as amended by Patents (Amendment) Act 2005 as claims lacks inventive step in view of document US 6100 249c and US 5 096 822.
2. Claims are not clear in respect of where indicated therein.
3. Claims are not clearly worded.

4. Claims do not sufficiently define the invention.
 5. Title is inconsistent with description and claims.
 6. Title should be given in the abstract.
 7. Claims (10 and 11) relate(s) to an invention Distinct from claim – 1.
2. The agent for the applicant in their reply on 12th March, 2009 amended the claims as follows (amendment given in bold):

1. A method of enhancing the blastocyst size, the inner cell mass or the trophoctoderm size of a mouse or human blastocyst, comprising:
 - (a) obtaining an in vitro fertilization pre-blastocyst embryo comprising at least two cells;
 - (b) growing said embryo in vitro to form a blastocyst in a culture medium that is supplemented **with 0.001-1 uM** prostaglandin or prostaglandin analog **between 24-42 hours and/or 42-72 hours after said embryo is placed in culture;** and
 - (c) **obtaining from step (b) a blastocyst with-at least one of enhanced blastocyst size, enhanced inner cell mass and enhanced trophoctoderm size, compared to a mouse or human blastocyst not obtained by this in vitro method.**

And submitted as follows

With respect to paragraph 1, it is respectfully submitted that the instant invention is inventive over the referred cited documents US 5,096,822 (hereinafter referred as D1) and US 6,100,249 (hereinafter referred as D2). In this regard, it is submitted that cited document D1 does not describe in vitro treatment method instead appears to describe in vivo treatment (for example, col.3, lines 24-28). The cited document D2 appears to describe only bovine embryo culture, whereas the amended claims are directed to mouse and human embryo culture. Neither of the cited documents disclose or suggest the method of treatment of pre-blastocyst human or mouse embryos in vitro with a prostaglandin or prostaglandin analog, including prostacyclin, prostaglandin E2 (PGE2), iloprost, or prostaglandin E1 (PGE1) to enhance blastocyst size, inner cell mass or trophoctoderm size. In view of this, the objection may kindly be reconsidered and withdrawn.

Regarding paragraph 2 to 4, claims have been thoroughly amended so as to define the subject invention in a clear and sufficiently manner. The

amended set of claims is in consistency with our practice. In light of this, the said objections may be withdrawn.

3. This case was further examine and a report was sent on 9th April, 2009 which inter alia states that

1. Objection raised in paragraph 1 of FER dated 21 May still stands.
2. Revised Claim(s) 1-12 fall(s) within the scope of such clauses (i) and (j) of section 3 of Patents Act 1970 as amended by Patents (Amendment) Act 2005.
3. Claims are not allowable under section 3(d) as it relates to new use of prostaglandins for enhancing development of mammalian embryos ref US 5096822.

4. In their reply dated 15th May, 2009 the agent for applicant reiterated the stand taken by them earlier. The examiner maintained the objections of paragraph 1-3 of office letter dated 12nd March,2009. In view of the outstanding objections and the request of the agent for giving an opportunity to be officially heard by the Controller before any adverse order on the application is passed, a hearing was fixed on 9th July, 2009 under section 14 of the Act and this matter was heard.

5. Applicant's agent submissions during hearing

- (a) The agent for the applicant contended that subject matter of claims do not fall under the purview of Section 2(1)(j) of the Act as the claims are not anticipated by US Patent No. 5096822 and 6100249 stating same reasons as given above.
- (b) The agent for the applicant further stated that the present claim does not fall under section 3(d) as these claims goes beyond a mere new use because the amended claims required a affirmative step (c) that is not taught or suggested by the cited documents
- (c) The agent for the applicant submitted that the method present invention being not an essentially biological method or process does not come under the purview of section 3(j). They contended that present invention is a method for in vitro culturing of embryo in a medium supplemented with a prostaglandin.

6. Findings and conclusions

The issue before me was to decide whether the claims lack inventive step under section 2(1)(j) and whether the claims fall within the scope of section 3(d).

(a) Citations given by the Examiner

- (i) Rosenkrans, Jr. et al (US 5096822) This citation teaches method for culturing bovine (mammalian) embryos comprising using a culture medium including substances necessary to support the embryo (abstract). Such beneficial components include prostaglandins (col. 7 line 17-26).
- (ii) Macnamee (US 6100249). This citation teaches that prostaglandins have been shown to assist embryo implantations in animal models (col.2 line 15-25).

Other Citations based on ISA report.

- (i) Chan (Prostaglandins. 42(4): 321-36, 1991) teach administering PGE2 and PGF2a to the embryos (p. 323, In vitro Treatment).
- (ii) Huang et al. (Human Reprod., 18(1);2582-2589,2003,IDS). This citation teaches the culturing of 2-cell mouse embryos with iloprost (see p. 2583, Harvest and Culture of Mouse Embryos) and teaches an increase in the hatching of mouse embryos (p.2587, 1st col. and Figure 4).

7. I shall deal with first objection that Claim(s) are anticipated by cited documents and thus does not meet the requirement of inventive step and therefore not allowed under section 2(1) (j).

- (a). The claimed invention is directed to an *in vitro* method of enhancing the development of a mammalian embryo to at least the blastocyst stage, comprising obtaining an *in vitro* fertilization embryo comprising at least two cells; growing said embryo in a culture medium supplemented with an amount of a prostaglandin or a prostaglandin analog effective for enhancing the quality of a resulting blastocyst. Further embodiments are directed to the qualities to be enhanced, such as increasing the blastocyst size, increasing the ICM of the blastocyst and increasing the trophectoderm size of the blastocyst.
- (b) I shall deal with first objection that '(Amended) Claims 1-11 lack an inventive step as being obvious over Rosenkrans, Jr. et al (US 5096822). This citation teaches method for culturing bovine (mammalian) embryos comprising using a culture medium including substances necessary to support the embryo (abstract). Such beneficial components include prostaglandins (col. 7 line 17-26). Further Macnamee (US 6100249)

teaches that prostaglandins have been shown to assist embryo implantations in animal models (col.2 line 15-25). I do agree with the agent for the applicant that both of these document does not specifically teaches a method for enhancing in vitro development of mammalian embryos utilizing the claimed steps, but these citation does discloses that prostaglandins have been shown to assist embryo implantations in mammalian embryos. Therefore, it would have been obvious to one of ordinary skill in the art to practice the claimed method using prostaglandins, since they were well known to assist in such development, as disclosed by Rosenkrans and Macnamee.

(c) Additionally, Chan (Prostaglandins. 42(4): 321-36, 1991) teach administering PGE2 and PGF2a to the embryos (p. 323, In vitro Treatment). Chan teach that treatment of blastocysts with PGE2 resulted in an enhanced outgrowth of trophoblast and an increase in spreading area (p. 326. Results). Further Huang et al. (Human Reprod., 18(1);2582-2589,2003,IDS).discloses method of the isolation of 2-cell mouse embryos and the incubation of these embryos in iloprost (p.2583, 2nd col., Harvest and Culture of Mouse Embryos). Iloprost is a stable PG₁₂ analogue also statedATED in description page 3 line14-15 of the present specification (see Abstract). It also discloses that iloprost enhanced the hatching of mouse blastocysts (p.2587, 1st col., 1st and Figure 4). It is the cardinal principle of properties of chemical compositions that products of identical chemical composition cannot have mutually exclusive properties. Thus a chemical composition and its properties are inseparable. It is therefore clear that if the prior art teaches the identical chemical structure and its uses (in this case use of prostaglandin or prostaglandin analog) to achieve the claimed results and the claimed invention also pertain to achieve the same, there is no inventive step involved. In other words where the properties applicant discloses and/or claims are inherently present in the said compounds it cannot be claimed as inventive. Accordingly, claims are not inventive in view of Chan and Huang also.

(d) I shall now deal with second objection that Claim (s) fall(s) within the scope of section 3 (d). Section 3 states that following are not inventions within the meaning of this Act. Sub section (d) states that

the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least a new reactant.

Explanation.- For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy;

- (e) I shall now examine whether the present invention relates to a mere new use of known substance. To know that I shall first ascertain whether the claimed invention relates to *the mere new use for a known substance*. In the present case substance in question is a prostaglandin or a prostaglandin analog and its use is its effectiveness in enhancing the quality of the resultant blastocyst. To answer the first question I shall examine whether the compound prostaglandin or a prostaglandin analog is known and then examine whether this said compound is known to be effective for enhancing the quality of the resultant blastocyst when used in culture medium for growing embryos.
- (f) Following citation clearly indicate that compound prostaglandin or a prostaglandin analog is known and it is also known that such compound is effective for enhancing the quality of the resultant blastocyst when used in culture medium for growing embryos.
 - (i) Rosenkrans, Jr. et al (US 5096822) This citation teaches method for culturing bovine (mammalian) embryos comprising using a culture medium including substances necessary to support the embryo (abstract). Such beneficial components include prostaglandins (col. 7 line 17-26).
 - (ii) Macnamee (US 6100249). This citation teaches that prostaglandins have been shown to assist embryo implantations in animal models (col.2 line 15-25).
 - (iii) Chan (Prostaglandins. 42(4): 321-36, 1991) teach administering PGE2 and PGF2a to the embryos (p. 323, In vitro Treatment).
 - (iv) Huang et al. (Human Reprod., 18(1);2582-2589,2003,IDS). This citation teaches the culturing of 2-cell mouse embryos with iloprost (see p. 2583, Harvest and Culture of Mouse Embryos) and teaches an increase in the hatching of mouse embryos (p.2587, 1st col. and Figure 4).
- (g) I shall consider the submission of the agent for the applicant given above. I do not agree with reasons given by the agent for the applicant that the claims goes beyond a mere new use because the amended claims required a affirmative step (c) that is not taught or suggested by the cited documents, as the so called affirmative step c is in fact not a step but a routine procedure of obtaining the blastocyst so resulted

from the growing embryo in the culture medium supplemented with prostaglandin or its analog. The agent for applicant has admitted that the *in vivo* process of treatment of pre-blastocyst culture is known as per the disclosure in US (US 5096822) and US (6100249). What is not known is the use of prostaglandin or its analog for culturing embryos *in-vitro*.

- (i) The claims method is use of culture medium supplemented with prostaglandin or its analog for growing embryo *in vitro* conditions. This clearly indicates that it is a clear case new use of same substance which is known to be useful in culturing bovine (mammalian) embryos *in vivo*. There is nothing in the specification which suggests that there has been increased efficacy when the same compound is use for culturing embryos *in vitro*. Therefore the use of prostaglandins or its analog is mere new use of the same substance which is not patentable under section 3(d).

- (h) Additionally, Claims 1 fall under section 3(d) as Chan (Prostaglandins. 42(4): 321-36, 1991) discloses the similar method and use of prostaglandins or its analog. Chan also teaches the recovery of embryos, including blastocysts from mice (p.322, last): they teach treatment of the embryos with the prostaglandins PGE2 and PGF2a to the embryos (p. 323, *In vitro* Treatment). Chan teach that treatment of blastocysts with PGE2 resulted in an enhanced outgrowth of trophoblast and an increase in spreading area (p. 326, Results). With regard to the particular limitations of claim 1, Chan teaches a blastocyst, which is an embryo that comprises at least 2 cells. They further teach growing the blastocyst in a media comprising a prostaglandin (PGE2 or PGF2a) that results in a blastocyst with increased size and increased trophectoderm size. Similarly, Huang teach the culturing of 2-cell mouse embryos with iloprost (see p. 2583, Harvest and Culture of Mouse Embryos) and teach an increase in the hatching of mouse embryos (p.2587, 1sr col., 1st). Therefore , I am convinced that this invention is a clear case of a new use of known substance.

- (i) I am convinced with the teachings of the citations mentioned above and infer that when culturing embryos with media supplemented with factors that are known to increase implantation rates were known in the art, growing such embryos *in vitro* is merely a new use of known substance thus not patentable u/s 3 (d). Therefore, where the use of a compound for the treatment of embryos is known *in vivo*, the treatment of the embryos with the same compound constitutes a new use even if it is used *in vitro*. I am of the opinion that the alleged invention relates to

new use /second use of the known substance and hence is not patentable under section 3(d) on this count also.

Having considered all the submissions made by the agent for the applicant during the hearing including all the documents on record and in view of my above findings and conclusions and in exercise of the powers vested in me under Section 15 of the Patents Act 1970, it is hereby ordered that the application No.1435/DELNP/2005 shall be refused.

Dated this 24th day of September, 2009.

(D.P.S. Parmar)
Deputy Controller of Patents & Designs.