Paper No. 1

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ABS GLOBAL, INC.,
Petitioner

v.

XY, LLC,
Patent Owner

Patent No. 7,208,265
Issued: April 24, 2007
Filed: January 5, 2000
Inventor: John L. Schenk

Title: METHOD OF CRYOPRESERVING SELECTED SPERM CELLS

Inter Partes Review No. IPR2017-02184

PETITION FOR *INTER PARTES* REVIEW

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I. COMPLIANCE WITH REQUIREMENTS FOR A PETITION FOR INTER PARTES REVIEW

A. Certification that the Patent May Be Contested by Petitioner

ABS Global, Inc. ("Petitioner") certifies it is not barred or estopped from requesting *inter partes* review of U.S. Patent No. 7,208,265 ("the '265 patent") (Ex. 1001). Neither Petitioner, nor any party in privity with Petitioner: (1) has filed a civil action challenging the validity of any claim of the '265 patent; or (2) has been served a complaint alleging infringement of the '265 patent more than a year prior to the present date. Also, the patent has not been the subject of a prior *inter partes* review or a finally concluded district court litigation involving Petitioner. Petitioner therefore certifies that the '265 patent is available for *inter partes* review.

B. Fee for Inter Partes Review (37 C.F.R. § 42.15(a))

The Director is authorized to charge the fee specified by 37 C.F.R. § 42.15(a) to Deposit Account No. 50-1597.

C. Mandatory Notices (37 C.F.R. § 42.8(b))

1. Real Party in Interest (§ 42.8(b)(1))

The real parties in interest are Petitioner ABS Global, Inc., located at 1525 River Road, DeForest, Wisconsin 53532; and Genus plc, located at Belvedere House, Basing View, Hampshire RG21 4DZ, United Kingdom.

2. Other Proceedings (§ 42.8(b)(2))

The '265 patent is the subject of pending litigation in the United States District Court for the Western District of Wisconsin (No. 3:17-cv-00446), which names ABS Global, Inc. and Genus plc, among others, as defendants. The '265 patent is also the subject of pending litigation in the United States District Court for the District of Colorado (*XY, LLC et al. v. Trans Ova Genetics, LC*, No. 1:17-cv-00944), which was transferred from an earlier filed case in the United States District Court for the Western District of Texas between the same parties (No. 6:16-cv-00447).

3. Lead and Backup Lead Counsel (§ 42.8(b)(3))

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D. Service on Petitioner

Service on Petitioner may be made by e-mail (IPRNotices@sidley.com) or by mail or hand delivery to: Sidley Austin LLP, 1501 K Street, N.W.,

Washington, D.C. 20005. The fax number for Lead Counsel Jeffrey P. Kushan and Backup Lead Counsel Paul J. Zegger is (202) 736-8711.

E. Proof of Service (37 C.F.R. §§ 42.6(e) and 42.105(a))

Proof of service is provided in Attachment A.

II. INTRODUCTION

The Board previously found unpatentable all claims of U.S. Patent No. 7,820,425 ("the '425 patent") (Ex. 1033), a patent sharing the same specification and priority date as the '265 patent being challenged in this petition and, more significantly, also directed to methods of freezing sex-selected sperm cells. *See ABS Global, Inc. v. XY, LLC*, IPR2014-01550, Final Written Decision, Paper 25 (P.T.A.B. Apr. 15, 2016) ("'425 IPR FWD"). The '265 patent claims, like the '425 patent claims, are unpatentable.

In the '425 patent IPR, the Board found all of the claims at issue unpatentable as obvious on one or more of three grounds: (1) Seidel in view of Salisbury; (2) Fugger; and (3) Fugger in view of Salisbury. '425 IPR FWD, 29. As the Board previously held, the prior art taught techniques for sorting sperm for sex-selection in both humans and non-humans. '425 IPR FWD, 4-5. The Board further found the prior art taught techniques for freezing sperm. *Id*. And, the Board found the combination of successfully sorting and freezing human sperm was known and

that sorting and freezing non-human sperm would have been obvious. '425 IPR FWD, 5, 17-18.

Compared to the claims of the '425 patent, the sole independent claim of the '265 patent, claim 1, recites two additional steps. First, it specifies "sorting" the sperm cells "without the presence of protective compounds in seminal plasma." Second, it specifies suspending the sperm cells in an extender "to provide a concentration of sperm cells of about 5 million per milliliter of extender to about 10 million per milliliter of extender." Both steps, however, were known, conventional steps in the sorting and handling of sperm cells, and would have been considered obvious variations of the techniques described and suggested by the prior art, consistent with the reasoning employed by the Board in its decision in the '425 patent IPR.

Therefore, for the reasons discussed in detail below, Petitioner requests that the Board institute trial as to each of the challenged claims and cancel all of these claims on the Grounds asserted.

III. IDENTIFICATION OF CLAIMS BEING CHALLENGED

Claims 1-4, 8-20, 22, and 26-28 of the '265 patent ("the challenged claims") are unpatentable as obvious under pre-AIA 35 U.S.C. § 103(a), based on two different Grounds:

(1) Each of the challenged claims would have been obvious based on U.S. Patent No. 7,195,920 ("Seidel 1997") (Ex. 1005) in view of Salisbury *et al.*, "Physiology of Reproduction and Artificial Insemination of Cattle," 2nd Ed. (1978) ("Salisbury") (Ex. 1006) and further in view of U.S. Patent No. 5,021,244 ("Spaulding") (Ex. 1031); and

(2) Each of the challenged claims would have been obvious based on Fugger *et al.*, "Births of normal daughters after MicroSort sperm separation and intrauterine insemination, in-vitro fertilization or intracytoplasmic sperm injection," Human Reproduction, Vol. 13, No. 9, 2367-2370 (1998) ("Fugger") (Ex. 1007) in view of Salisbury (Ex. 1006).

The first Ground is based on Seidel 1997, which in view of Spaulding, establishes that the sorting of semen without seminal plasma using flow cytometry was known in the prior art, and in further view of Salisbury, which teaches the use of sperm freezing techniques that correspond to the freezing elements of the claims.

The second Ground, which relies upon Fugger as the primary reference, is not redundant of Ground 1 because Fugger expressly discloses the freezing of sorted semen, which addresses a potential argument Patent Owner may make that no single reference discloses both sorting of sperm cells without the presence of seminal plasma and subsequently freezing the sorted sperm cells. Salisbury

teaches that the specific elements in the claims relating to freezing were well-known.

The two Grounds address sets of issues that are linked to those potential arguments, and thus advance alternative and non-redundant bases for finding the challenged claims unpatentable for obviousness. Petitioner submits that these two alternative Grounds are thus "rational, narrowly targeted, and not burdensome." *Great W. Casualty Co. v. Transpacific IP I Ltd*., No. IPR2015-01912, Paper 10 at 18 (P.T.A.B. Mar. 22, 2016). Petitioner therefore respectfully requests that trial be instituted on both Grounds and the arguments advanced herein.

Petitioner's proposed construction of the challenged claims, the evidence relied upon, and the precise reasons why these claims are unpatentable are provided in §§ IV and V, below. A list of evidence relied upon in support of this petition is set forth in Attachment B.

IV. NO PROHIBITION BASED ON 35 U.S.C. § 325(d)

Patent Owner may contend that actions taken during prosecution of the '265 patent warrant denial of institution of this petition under 35 U.S.C. § 325(d). In particular, Patent Owner may argue that the Examiner found the Spaulding reference inoperable based on a declaration of the named inventor John Schenk.

But, as discussed below, the statements in the Schenk declaration about inoperability relate to an antibody method of separating sperm cells, not the use of

the flow cytometry technique described in Example 1 of the Spaulding reference, which is the portion of Spaulding being relied upon in this petition. *See* Ex. 1002 ('265 File History), 496-497 (Jan. 5, 2000 Schenk Decl. ¶ 14), 783 (Dec. 5, 2006 Notice of Allowability, 3); *see also* Ex. 1003 (Declaration of Dr. Marvin M. Pace) ¶ 160. As explained below, the Examiner erred in eliminating all of Spaulding as a § 103 reference. Additionally, the Examiner did not have the benefit of Dr. Pace's detailed expert testimony addressing the two Grounds and Spaulding in particular. The Board should therefore reject any argument that the Patent Owner may advance under § 325(d) that the Examiner considered the grounds being advanced in this petition during prosecution. *See, e.g.*, *Amneal Pharmaceuticals LLC v. Purdue Pharma L.P.*, IPR2016-01413, Paper 9 at 23 (P.T.A.B. Jan. 18, 2017) (rejecting a § 325(d) challenge because "[t]he Petition presents additional arguments and evidence beyond what was already considered by the Examiner, including those presented in the [Expert's] Declaration").

V. RELEVANT INFORMATION CONCERNING THE CONTESTED PATENT

The title of the '265 patent is "Method of Cryopreserving Selected Sperm Cells." Ex. 1001, 1:1-2; Ex. 1003 (Pace Decl.), ¶ 75. The patent relates to freezing sperm after separating X chromosome containing sperm from Y chromosome containing sperm. Ex. 1001, 1:17-21; Ex. 1003, ¶¶ 76, 80-99. Claim 1 of the '265 patent -- the only independent claim -- appears in the chart below:

'265 patent, Claim 1
A method of cryopreserving sex-selected sperm cells, comprising:
a. obtaining sperm cells from a species of a non-human male mammal;
b. sorting said sperm cells, without the presence of protective compounds in seminal plasma, and based upon sex-type to provide a collection of sex-selected sperm cells obtained using flow cytometry or fluorescence-activated cell sorting;
c. cooling said sex-selected sperm cells;
d. suspending said sex-selected sperm cells in an extender to provide a concentration of sperm cells of about 5 million per milliliter of extender to about 10 million per milliliter of extender; and
e. freezing said sex-selected sperm cells in said extender.

Ex. 1001, 32:26-41.

As discussed below, these were all well-known process steps in the sorting and handling of sperm cells, and cannot simply through their combination, impart patentability.

A. Background of the Technology

1. Methods of sorting sperm were well known

Methods of separating (or selecting) sperm were well known before the earliest filing date of any application to which the '265 patent claims priority, *i.e.*, November 24, 1999. '425 IPR FWD, 9; Ex. 1003, ¶¶ 18-29, 78-79. Indeed, in the "Background of the Invention" section, the '265 patent itself acknowledges that "advances in selection of mammalian sperm based on slight differences in physical characteristics has made it possible to separate sperm based on sex-type, that is, to select for cells containing either the X or Y chromosome." Ex. 1001, 1:31-42; Ex. 1003, ¶¶ 22, 78. The patent also recognizes that "[a] variety of methods are available for selecting cells" and that flow cytometry is "a particularly efficient selection method . . . for sorting sperm by sex-type." Ex. 1001, 1:49-50, 1:59-64; Ex. 1003, ¶ 79.

U.S. Patent No. 5,135,759 ("Johnson 1992") (Ex. 1008) provides a summary of how sperm cells are sorted by flow cytometry. Ex. 1008, 3:4-6; Ex. 1003, ¶¶ 25-26, 86, 108. Sperm are stained with a fluorochrome stain; the stained sperm are then passed through a laser beam, and the flow cytometer measures and analyzes the amount of fluorescent light given off by the cells passing through the laser. Ex. 1008, 3:4-6; Ex. 1003, ¶¶ 25-26. Because "the X chromosome is larger and contains slightly more DNA than does the Y chromosome," X chromosome

bearing sperm cells can be separated from Y chromosome bearing sperm cells based on "relative DNA content." Ex. 1008, 1:60-62, 2:64-67; Ex. 1003, ¶ 26.

2. Methods of freezing sperm were well known

Methods of freezing sperm were also well known before November 24, 1999. '425 IPR FWD, 11 ("Salisbury describes principles and techniques of freezing non-human spermatozoa . . . ."); Ex. 1003, ¶¶ 30-41. Indeed, the '265 patent recognizes that "techniques for freezing unselected sperm are well-known" and that "advances in the cryopreservation and storage of sperm have facilitated widespread distribution and commercialization of sperm intended for artificial insemination or in vitro fertilization." Ex. 1001, 1:24-32, 2:5-11; Ex. 1003, ¶¶ 70-71, 77. Accordingly, the '265 patent instructs that "any standard freezing method can be employed" in the claimed invention. Ex. 1001, 10:54-56; Ex. 1003, ¶ 81.

3. Methods of freezing sorted sperm were well known

As it did during prosecution, Patent Owner may argue here that the named inventor of the '265 patent was the first to freeze separated sperm. *See* Ex. 1002, 221. But, as explained below and in the declaration of Dr. Pace, the facts do not support such an argument. Ex. 1003, ¶¶ 50, 68, 101.

For example, Fugger reports the separation of X chromosome bearing sperm from Y chromosome bearing sperm using flow cytometry, freezing the sorted

sperm, and thereafter using the separated sperm to achieve pregnancies. Ex. 1007, 2367-2368; Ex. 1003, ¶¶ 57, 167, 172; '425 IPR FWD, 5 ("Fugger disclose[s] a method of sorting and freezing human sperm to produce 'normal and healthy' human babies.").

Likewise, in 1999, Seidel *et al.* published "Insemination of Heifers with Sexed Frozen or Sexed Liquid Semen," in Vol. 51, No. 1 of Theriogenology: An Int'l J. of Animal Reproduction ("Seidel 1999") (Ex. 1016). Seidel 1999 reports separation of X chromosome bearing sperm from Y chromosome bearing sperm, freezing the sperm, and thereafter using it in artificial insemination. Ex. 1016, 400; Ex. 1003, ¶ 58.

Indeed, at least nine other prior art references also report freezing sperm subjected to separation procedures. Ex. 1018 (U.S. Patent No. 3,854,470); Ex. 1019 (U.S. Patent No. 4,092,229); Ex. 1020 (U.S. Patent No. 4,083,957); Ex. 1021 (U.S. Patent No. 4,362,246); Ex. 1022 (A.A. Luderer, "Separation of Bovine Spermatozoa by Density on Water Insoluble Newtonian Gels and Their Use for Insemination," Bio. of Repro., Vol. 26, 813-824 (1982) ("Luderer 1982")); Ex. 1023 (U.S. Patent No. 4,474,875); Ex. 1024 (Beal, W.E., *et al.*, "Sex Ratio after Insemination of Bovine Spermatozoa Isolated using a Bovine Serum Albumin Gradient," 58 J. Anim. Sci., 1432-1436 (1984)); Ex. 1025 (Foote, "Normal Dev. Of Fetuses Resulting from Holstein Semen Processed for Sex Separation,"

Theriogenology, Vol. 24, No. 1, 197-202 (1985) ("Foote 1985")); Ex. 1026 (U.S. Patent No. 4,007,087); *see also* Ex. 1003, ¶¶ 56, 59-67.

B. Detailed Description of the Prior Art

1. Detailed description of Seidel 1997

Seidel 1997 qualifies as prior art to the '265 patent pursuant to pre-AIA 35 U.S.C. § 102(e). Seidel 1997 discloses a technique for sorting non-human sperm for sex-selection. Ex. 1005, 1:62-2:4, 6:12-30; '425 IPR FWD, 4.

Specifically, Seidel 1997 discloses a process in which collected sperm is stained with a fluorescent dye and then sorted using flow cytometry. Ex. 1005, 15:21-27; Ex. 1003, ¶¶ 128-131. Seidel 1997 explains that flow cytometry is a technique "which is well understood." Ex. 1005, 1:45-47; Ex. 1003, ¶ 132. In fact, both Seidel 1997 and the '265 patent credit the earlier pioneering work of Larry Johnson in developing the flow cytometry technique for sorting sperm cells. Ex. 1001, 4:40-57; Ex. 1005, 1:61-2:13; *accord*, '425 IPR FWD, 9.

Seidel 1997 further discloses that, after the sperm has been separated, the sperm can be concentrated to about 3-5 million sperm cells per milliliter through the use of centrifugation to remove fluid. Ex. 1005, 13:61-64.

Seidel 1997 discloses that the concentrated sperm can then be extended using either a 20% egg yolk citrate extender or other extender. Ex. 1005, 13:64-66. Seidel 1997 also discloses that the extender may contain antibiotics. *Id.*, 12:6-

12. Seidel 1997 discloses that after the last extension, there may be 3-5 million sperm per milliliter. *Id.*, 14:11-12.

Additionally, Seidel 1997 discloses that the "sample may then be cooled to slow the sperm's metabolism and to permit use over longer periods of time." Ex. 1005, 14:12-14. Seidel 1997 specifically discloses cooling the sperm to 5° C over 75 minutes. *Id.*, 15:37-39.

Finally, Seidel 1997 discloses that, if desired, the sperm can be further processed to result in a dose of 300,000 sperm per 0.184 milliliter. Ex. 1005, 14:16-22.

2. Detailed description of Salisbury

Salisbury, which qualifies as prior art to the '265 patent pursuant to pre-AIA 35 U.S.C. § 102(b), was, and remains, one of the most respected texts in the field of artificial insemination of cattle and gives a detailed description of the state of the art as of the time it was published. Ex. 1006, 1, 442-443; Ex. 1003, ¶¶ 144-152. Salisbury contains an entire chapter, chapter 17, devoted to "Principles and Techniques of Freezing Spermatozoa." Ex. 1006, 494-554. Salisbury notes that since the discovery that glycerol protected sperm, "freezing has been the preferred method of preserving spermatozoa." *Id.*, 494.

Salisbury also explains the basic components of extenders for freezing bull sperm, which include: (1) substances to maintain osmolality and to buffer the pH

of the medium, such as sodium citrate; (2) organic materials with the capacity to prevent cold shock, such as egg yolk; (3) cryoprotective agents such as glycerol; (4) simple sugars for an energy source; and (5) antibiotics to control microbial growth. Ex. 1006, 498-507. Salisbury further specifies that penicillin and streptomycin antibiotics are particularly effective at preventing bacterial growth in egg yolk extenders. *Id.*, 445, 464, 469-472.

Salisbury also teaches that sperm should be cooled to 5° C before freezing "for maximum livability of the cells." Ex. 1006, 509. In addition, Salisbury recommends slow cooling to avoid deleterious effects of "cold shock." *Id.*, 508-509. More specifically, Salisbury reports that post-thaw motility was maintained significantly longer in semen that was cooled for four hours before freezing than in semen cooled for only one hour. *Id.*, 510. And, the data reported by Salisbury included sperm concentrations of 5-10 million sperm per milliliter prior to freezing. *Id.*, 517-518; Ex. 1003, ¶ 157.

Salisbury also teaches that a wide range of sperm concentrations can be used successfully to inseminate animals such as cattle. Ex. 1006, 476-478; Ex. 1003, ¶ 158. Specifically, Salisbury notes that one study showed that insemination with four million motile sperm "gave initial high fertility" and that when the number was decreased to two million "fertility changed little." Ex. 1006, 477. Even

insemination with as few as 500,000 sperm was shown to result in 32% and 46% conception rates. *Id.*

3. Detailed description of Spaulding

Spaulding is prior art to the '265 patent claims under 35 U.S.C. § 102(b). Spaulding describes a method to separate living sperm cells using flow cytometry. Ex. 1031, 4:24-34, 7:43-10:9; Ex. 1003, ¶ 159. Specifically, Spaulding describes in Example 1, "Sorting Sperm by Flow Cytometry," using the Hoechst 33342 fluorescent dye to distinguish between the X chromosome bearing sperm and Y chromosome bearing sperm. Ex. 1031, 4:24-34, 7:43-10:9. Example 1 describes the "preparation of the sperm" prior to sorting. *Id.*, 9:15-36. As part of the preparation, the sperm was washed three times and then centrifuged to remove the seminal plasma. *Id.*, 9:25-27 ("We centrifuged the cells at 483Xg for 20 minutes and resuspended them to remove seminal plasma proteins."). This preparation process would have removed all, or nearly all, of the seminal plasma prior to sorting. Ex. 1003, ¶ 159. Spaulding reports that "[t]he objective was to match the refractive indices between sheath and sample fluid." Ex. 1006, 9:35-36.

After removal of the seminal plasma and addition of the dye, the sperm was sorted using a flow cytometer. Ex. 1031, 9:38-10:8. After sorting, two viable subpopulations enriched for X- or Y- sperm, respectively, were obtained. *Id.*, 9:65-67.

During prosecution, the Examiner allowed the '265 patent claims and cited in the reasons for allowance that "the declaration of Dr. Schenk filed January 20, 2006, proves that [Spaulding was] inoperable and thus cannot be used in a 35 U.S.C. § 103 rejection against the claims." Ex. 1002, 783 (Dec. 5, 2006 Notice of Allowability, 3). This, however, was error, because the Schenk's statements about inoperability of Spaulding relate to a different technique of using antibodies as a way of discriminating between X chromosome bearing and Y chromosome bearing sperm cells, not the sorting of sperm by flow cytometry of Spaulding's Example 1. *Compare* Ex. 1002, 496-497 (Jan. 5, 2006 Schenk Decl. ¶ 14), with Ex. 1003, ¶ 160.

4. Detailed description of Fugger

Fugger was published in September 1998, more than a year before the filing date of any application from which the '265 patent claims priority, and therefore qualifies as prior art under pre-AIA 35 U.S.C. § 102(b). Ex. 1007, 2367. Ex. 1003, ¶¶ 161-162. As the Board found in the earlier IPR of the related '425 patent, Fugger discloses "a method of sorting and freezing human sperm." '425 IPR FWD, 5; *see also* Ex. 1007, 2367; Ex. 1003, ¶¶ 57, 163.

Specifically, Fugger reports that "fresh or frozen semen specimens were provided for sorting." Ex. 1007, 2367. The sperm to be sorted was "extended, centrifuged, resuspended, [and] filtered." Ex. 1007, 2367. For these centrifugation

steps, Fugger cites a paper by Johann *et al*. ("Johann 1989") (Ex. 1032), which further describes the centrifugation conditions (including 750 x g for 15 minutes). Ex. 1007, 2367. These centrifugation conditions would have resulted in removal of all, or nearly all, of the seminal plasma. Ex. 1003, ¶ 165.

In the Fugger process, the sperm were treated with a solution of Hoechst 33342 fluorescent dye and then sorted using known flow cytometry techniques. Ex. 1007, 2367; Ex. 1003, ¶ 166. Fugger reports that the "enriched fraction of the sorted sample was collected." *Id.*, 2367-2368. Thereafter, sorted specimens were extended with TEST yolk buffer freezing medium and then frozen. *Id.*, 2368. Fugger notes that "[p]regnancies have also been obtained with the use of frozen sorted sperm cells." *Id.*, 2369.

C. Prosecution History and Effective Filing Date of the '265 Patent

1. Prosecution of the '265 patent

During prosecution, the applicant repeatedly informed the Patent Office that the named inventor was the first to obtain viable separated, frozen sperm in order to overcome prior art rejections. *E.g.*, Ex. 1002, 221 (June 25, 2001 Response, 3); *see also* Ex. 1003, ¶ 101. As discussed above, and as the Board found in the '425 patent IPR, those statements are incorrect. '425 IPR FWD, 5 (finding that Fugger discloses a method of sorting and freezing human sperm).

2. Effective filing date of the '265 patent

The '265 patent issued from U.S. Application No. 09/478,299 filed on January 5, 2000. Ex. 1001, cover. The patent claims priority to a provisional application, No. 60/167,423, filed on November 24, 1999. *Id.* For the purposes of this proceeding, Petitioner assumes that the patent is entitled to the benefit of the earliest filing date to which it claims priority, November 24, 1999.

D. Person of Ordinary Skill in the Art

The person of ordinary skill in the art ("skilled person") is someone with at least a bachelor's degree in the biological sciences or a relevant field of engineering, and at least three years of experience with methods of freezing sperm. Ex. 1003, ¶ 17. The Board previously accepted this standard in the IPR of the related '425 patent. '425 IPR FWD, 6-7. Further, the Board found that Dr. Pace was qualified to opine from the perspective of a skilled person. '425 IPR FWD, 7; *see also* Ex. 1004 (curriculum vitae of Dr. Pace).

E. Construction of Terms Used in the Claims

In an IPR, claims must be given their broadest reasonable construction in light of the specification. 37 C.F.R. § 42.100(b); M.P.E.P. § 2111.

1. "sorting" sperm cells

The '265 patent expressly defines the term "sorting" as "a selection method carried out using a fluorescence-activated cell sorter (FACS)." Ex. 1001, 3:27-29. That is consistent with the plain and ordinary meaning of "sort," which is "to

separate from others." Ex. 1028 (The American Heritage College Dictionary, 3rd Ed. 1997), 1299; Ex. 1003, ¶ 106.

Additionally, the '265 patent specification provides contextual support for this plain and ordinary meaning. Ex. 1003, ¶ 107. The specification defines the related term "selection" as "a method whereby a sample is subdivided based on presence or absence of a specific characteristic" and notes that a "selected sperm sample is therefore enriched, relative to the source sample, in sperm having the specific characteristic." Ex. 1001, 3:19-26. The specification further states that "advances in selection of mammalian sperm based on slight differences in physical characteristics has made it possible to separate sperm based on sex-type, that is, to select for cells containing either the X or Y chromosome." *Id.*, 1:31-40.

The specification also notes that "flow cytometry" is a preferred method for "separating cells." Ex. 1001, 4:40-60. A skilled person would have understood that flow cytometry typically results in two discrete, sorted populations of cells (*i.e.*, X chromosome bearing sperm and Y chromosome bearing sperm). Ex. 1003, ¶¶ 108-109.

Accordingly, a skilled person would have understood the term "sorting" to mean "separating." Ex. 1003, ¶ 110.

2. "without the presence of protective compounds in seminal plasma"

The '265 patent does not provide an express definition of the term "without the presence of protective compounds in seminal plasma."

Example 1B of the '265 patent disclosure describes a process in which sperm cells are centrifuged and cell supernatant is removed. Ex. 1001, 13:6-10; Ex. 1003, ¶ 111. The '265 patent notes that this process "remov[es] most of the seminal plasma" and leaves the sperm in a "pellet." Ex. 1001, 13:7-10.

The plain and ordinary meaning of "without" is "[w]ith something absent or lacking" or "[n]ot having; lacking" or "[n]ot accompanied by; in the absence of." Ex. 1028.

A skilled person would recognize that the process described in Example 1B does this -- it results in the removal of nearly all of the seminal fluid, thus yielding a sample that is not accompanied by protective compounds in seminal plasma. Ex. 1001, 13:6-10; Ex. 1003, ¶ 111. Given the absence of an explicit definition of this element of the claim, the plain meaning of the terms used in it, and the presence of an example describing a process consistent with the plain meaning of the terms, the phrase "without the presence of protective compounds in seminal plasma" must at least cover the technique of removing nearly all of the seminal plasma through centrifugation.

Accordingly, a skilled person would have understood the broadest reasonable construction of the term "without the presence of protective compounds in seminal plasma" would encompass a sample that has had nearly all of the seminal plasma removed by centrifugation. Ex. 1003, ¶ 111.

3. "based on sex-type to provide a collection of sex-selected sperm cells obtained using flow cytometry or fluorescence-activated cell-sorting"

The term "based on sex-type to provide a collection of sex-selected sperm cells obtained using flow cytometry or fluorescence-activated cell-sorting" refers to the sex-selected cells collected as a part of the flow cytometry or fluorescence-activated cell-sorting processes. Ex. 1003, ¶ 112. The '265 patent notes that flow cytometry is a preferred method for separating cells based on differential staining with fluorescent dyes. Ex. 1001, 4:40:43; Ex. 1003, ¶ 112. In addition, the patent states: "In fluorescence activated cell sorting ('FACS'), the cells are 'sorted' into different populations based on the fluorescence intensity upon irradiation." Ex. 1001, 4:43-46; Ex. 1003, ¶ 112. The '265 patent credits the Johnson 1992 patent (Ex. 1008), discussed above, for employing this strategy for sex-selection of sperm. Ex. 1001, 4:43-54; Ex. 1003, ¶¶ 23-24, 86. A skilled person would have understood that flow cytometry results in two discrete populations of cells, typically a population of X chromosome bearing sperm and a population of Y chromosome bearing sperm. Ex. 1003, ¶ 112. Accordingly, a skilled person

would have understood the term to require the "sorting" be based on sex-type to provide a collection of sex-selected sperm cells and that the sorting be accomplished using either of the recited techniques (either a flow cytometer or FACS), both of which were well known. *Id.*

4. "extender"

The '265 patent specification expressly defines "extender" as "any medium that tends to preserve sperm viability" and defines "extension" to mean "the dilution of sperm with extender." Ex. 1001, 3:30-33; Ex. 1003, ¶ 113.

Accordingly, a skilled person would have understood the term "extender" to mean "any medium that tends to preserve sperm viability." Ex. 1003, ¶ 113.

5. "about 5 million per milliliter of extender to about 10 million per milliliter of extender"

The claims recite "about 5 million per milliliter of extender to about 10 million per milliliter of extender."

The '265 patent does not provide an express definition for the term "about" in this limitation. Ex. 1003, ¶ 114. The '265 patent applicants added the limitation during prosecution and argued that Table 1 in Example 1A provided support for the values. Ex. 1002, 422 (Feb. 28, 2005 Response, 9), 449-450 (Nov. 14, 2005 Response, 9-10), 746-747 (Aug. 9, 2006 Response, 10-11); Ex. 1003, ¶ 114.

A skilled person would have understood that numerical limitations encompass a variance to take into account measurement tolerances associated with

determining sperm concentrations. Ex. 1003, ¶ 114. The typical methodologies to determine sperm cell concentrations varied by up to plus or minus 5% to 10% with sperm concentrations in the 5 to 10 million range. *Id.* Accordingly, under a broadest reasonable interpretation, the sperm cell concentration measures may vary by up to 10%. *Id.* Under these circumstances, a skilled person would have understood "about 5 million" to encompass 4.5 to 5.5 million sperm per milliliter and "about 10 million" to encompass 9 to 11 million sperm per milliliter. *Id.*

6. "freezing"

The broadest reasonable construction of the term "freezing" refers to any method for taking sperm from a liquid to a solid state by loss of heat, so long as the cells retain sufficient viability to result in pregnancy. Ex. 1003, ¶ 120.

The plain and ordinary meaning of "freeze" is to "pass from the liquid to the solid state by loss of heat" or to "preserve (foods, for example) by subjecting to freezing temperature." Ex. 1028, 543-544; Ex. 1003, ¶ 116.

The specification of the '265 patent is in accord. The specification notes that "any standard freezing method can be employed, provided the freezing rate is not too rapid." Ex. 1001, 10:54-57. Elsewhere in the examples, the '265 patent refers to sperm "frozen conventionally" or "frozen in static liquid nitrogen vapor." *Id.*, 17:2-17, 19:3-27; Ex. 1003, ¶¶ 117-119.

Accordingly, a skilled person would have understood the broadest reasonable construction of the term "freezing" to refer any known method for taking sperm from a liquid to a solid state by loss of heat, so long as the cells retain sufficient viability to result in pregnancy. Ex. 1003, ¶ 120.

VI. PRECISE REASONS FOR RELIEF REQUESTED

A. Claims 1-4, 8-20, 22, and 26-28 Are Unpatentable in View of Seidel 1997 in Combination with Salisbury and Spaulding

As stated by the Board in the '425 patent IPR, "a person of ordinary skill in the art would have been led to combine Seidel 1997's method of sorting non-human sperm, based on sex-selection, with Salisbury's method of freezing to cryopreserve the sorted sample for later use in fertilizing an egg." *See* '425 IPR FWD, 14.

First, Seidel 1997 describes the sex-sorting of sperm. Ex. 1005, 1:12-18; Ex. 1003, ¶ 130. While Seidel 1997 does not specifically teach freezing, a skilled person would have been motivated to freeze separated sperm in light of the commercial benefits to separated, frozen sperm. For example, it was well known that separated sperm allows farmers to vary the male to female offspring ratio. Ex. 1001, 1:31-35. It also was well known that female dairy cows are normally more valuable than males because only females can produce milk and because female calves have a lower incidence of difficult births (female calves tend to be smaller than male calves). Ex. 1003, ¶¶ 19, 181. And, it was well known that because

fresh sperm quickly loses viability, frozen sperm allows breeders to store sperm over long periods of time and to use it to artificially inseminate cows at the optimal time. *Id.*, ¶¶ 70, 142-143, 181. In fact, it was an established industry practice to ship sperm in a frozen state, which permitted samples to be shipped long distances and enabled producers to take advantage of the genetic attributes of bulls located far away from the cows to be impregnated. *Id.*

Second, a skilled person would have been aware of these well-known benefits before the '265 patent was filed, and would have known how to freeze sperm. Salisbury (Ex. 1006) is one of the most respected texts in the field of artificial insemination of cattle and gives a detailed description of the state of the art (including techniques for freezing sperm) as of the time it was published. Ex. 1003, ¶ 144. An earlier version of Salisbury was cited on the face of Seidel 1997, demonstrating that a skilled person would have been aware of both references. Ex. 1005, 7; Ex. 1003, ¶ 181. Thus, a skilled person would have been motivated to combine the teachings of Seidel 1997 (Ex. 1005) and Salisbury (Ex. 1006). Ex. 1003, ¶¶ 71, 181.

A skilled person also would have expected success in freezing sperm separated by the methods described in Seidel 1997. Skilled persons had been freezing sperm from non-human mammals since at least the 1950's. Ex. 1003, ¶¶ 30-37; Ex. 1009, Polge, C. and Rowson, L.E.A., "Long-term Storage of Bull

Semen Frozen at Very Low Temperatures (-79° C.)," in Report of the 2d Int'l Congress of Physiology and Pathology of Animal Reproduction and Artificial Insemination, Vol. 3 (1952). Moreover, numerous individuals had reported success in freezing sperm after it had been subjected to separation procedures. *Id.*, ¶¶ 56, 72; Ex. 1018 (U.S. Patent No. 3,854,470); Ex. 1019 (U.S. Patent No. 4,092,229); Ex. 1020 (U.S. Patent No. 4,083,957); Ex. 1021 (U.S. Patent No. 4,362,246); Ex. 1022 (Luderer 1982), 813-824; Ex. 1023 (U.S. Patent No. 4,474,875); Ex. 1024 (Beal 1984), 1432-1436); Ex. 1025 (Foote 1985), 197-202; Ex. 1026 (U.S. Patent No. 4,007,087).

Second, while Seidel 1997 does not explicitly discuss removing seminal plasma prior to sorting, Spaulding does. A skilled person would have considered the guidance in Spaulding, because it, like Seidel 1997, is directed to sorting sperm using flow cytometry. Ex. 1031, 1:16-24; Ex. 1003, ¶¶ 177-178. Spaulding discloses an obvious variant of the sorting process, namely, removing the seminal plasma through centrifugation before the sorting, rather than after the sorting, as in Seidel 1997. Ex. 1031, 3:17-30; Ex. 1003, ¶¶ 177-178.

1. Claim 1

Claim 1 specifies "a method of cryopreserving sex-selected sperm cells," comprising the recited steps in the claims, which are discussed individually below.

Seidel 1997 in combination with Salisbury and Spaulding teaches a method for cryopreserving sex-selected sperm cells, as discussed below.

a. "obtaining sperm cells from a species of a non-human male mammal"

Seidel 1997 relates to "sex selection in mammalian offspring." Ex. 1005, 1:12-15; Ex. 1003, ¶ 126. Seidel 1997 discloses the step of obtaining sperm from a non-human mammal, and specifically discusses collecting bull semen through the use of an artificial vagina. Ex. 1005, 13:17-21; Ex. 1003, ¶ 127.

b. "sorting sperm cells . . . based upon sex-type to provide a collection of sex-selected sperm cells obtained using flow cytometry or fluorescence-activated cell sorting"

Seidel 1997 teaches the use of flow cytometry sorting to separate X chromosome containing sperm from Y chromosome containing sperm. Ex 1005, 4:35-37, 5:29-32; Ex. 1003, ¶¶ 130. Seidel 1997 thus teaches "sorting" of sperm cells based upon sex-type using flow cytometry or fluorescence-activated cell-sorting to yield a collection of sex-selected sperm cells. Ex. 1005, 1:12-18, 15:18-41; Ex. 1003, ¶¶ 133-134, 176.

c. "without the presence of protective compounds in seminal plasma"

Spaulding describes a method to separate different types of living sperm cells using flow cytometry. Ex. 1031, 4:24-34, 7:43-10:9; Ex. 1003, ¶¶ 27, 159. Example 1 describes the "preparation of the sperm" prior to sorting, in which the

sperm was washed three times and then centrifuged to remove the seminal plasma. Ex. 1031, 9:25-27 ("We centrifuged the cells at 483 x g for 20 minutes and resuspended them to remove seminal plasma proteins."); *see generally id*., 9:15-36. As Spaulding itself notes, this preparation process would have removed the seminal plasma prior to sorting. *Id.*; Ex. 1003, ¶¶ 27, 159, 177. Centrifugation also is the method disclosed in the '265 patent for removing the seminal plasma. Ex. 1001, 13:6-10.

After removal of the seminal plasma, the sperm was sorted using a flow cytometer. Ex. 1031, 9:38-10:8. After sorting, "two viable subpopulations enriched for X- or Y- sperm, respectively, were obtained." *Id*., 9:65-67.

The removal of seminal plasma using centrifugation is taught by both Spaulding and Seidel 1997. Spaulding shows this step prior to sorting by flow cytometry, as discussed above. Seidel 1997 describes use of a centrifuging step after sorting, at conditions that would also remove the seminal plasma. Ex. 1005, 15:32-33 ("Collected [sorted] sperm were centrifuged at 600xg for 10 min and resuspended to 1.63 x 10^6 live sperm/ ml in CUE."); Ex. 1003, ¶¶ 177-178. Whether to remove the seminal plasma before or after sorting is a matter of process design choice and an obvious variant. Ex. 1003, ¶ 178.

In addition, Spaulding provides a motivation to remove the seminal plasma prior to sorting. Specifically, Spaulding states that one of the objectives of the pre-

sort preparation of the sperm, which included the removal of seminal plasma, was "to match the refractive indices between the sheath and sample fluid." Ex. 1031, 9:35-36; Ex. 1003, ¶¶ 159, 178.

For these reasons, it would have been obvious to a skilled person to sort sperm cells without the presence of protective compounds in seminal plasma, using flow cytometry. Ex. 1003, ¶¶ 177-178.

d. "cooling said sex-selected sperm cells"

Seidel 1997 also specifies the step of cooling the sex-selected sperm. Specifically, Seidel 1997 discloses cooling the sperm to slow the sperm's metabolism and to permit its use over longer periods of time. Ex. 1005, 14:12-14, 15:37-39; Ex. 1003, ¶¶ 140, 179.

e. "suspending said sex-selected sperm cells in an extender to provide a concentration" of "about 5 million per milliliter to about 10 milliliter of extender"

Seidel 1997 further specifies that the sorted sperm are suspended in an extender, after which the sperm is at a concentration of 3,000,000 to 5,000,000 per milliliter. Ex. 1005, 14:11-12; Ex. 1003, ¶¶ 139, 180.

f. "freezing said sex-selected sperm cells in said extender"

Seidel 1997 does not expressly teach the step of freezing the sperm after separation. However, a skilled person would have considered it obvious to do so based on the teachings of Salisbury. Ex. 1003, ¶ 181; *accord*, '425 IPR FWD, 14.

A skilled person would have been motivated to freeze the separated sperm cells because of the numerous benefits inherent in freezing sperm, such as the ability to ship sperm long distances and the knowledge that freezing was the preferred method of preserving sperm. Ex. 1003, ¶¶ 69-70. In light of the significant body of knowledge regarding freezing sperm, such as the chapter in Salisbury entitled "Principles and Techniques of Freezing Spermatozoa" that provides detailed information regarding how to freeze sperm, as well as the numerous reports that sperm subjected to separation procedures had been frozen, a skilled person would have expected that separated sperm could be successfully frozen and thereafter used in artificial insemination. Ex. 1003, ¶¶ 69, 72, 181; Ex. 1006, 494-554; Exs. 1018-1026. Indeed, even the '265 patent notes that conventional freezing methods can be used with separated sperm. Ex. 1001, 17:2-17; Ex. 1003, ¶¶ 98, 119.

Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 1. Ex. 1003, ¶¶ 173-182.

2. Claim 2

Claim 2 is dependent upon claim 1 and further specifies that the sperm cells be bovine or equine. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claim 1.

Seidel 1997 also discloses that the sperm cells are bovine or equine. Specifically, Seidel 1997 collected sperm cells from bulls. Ex. 1005, 13:17-21; Ex. 1003, ¶¶ 127, 184. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 2. Ex. 1003, ¶ 185.

3. Claim 3

Claim 3 is dependent upon claim 2 and further specifies isolating a number of bovine cells from between about 300,000 to about 3,000,000. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1 and 2.

Seidel 1997 also discloses that the insemination sample contains between 300,000 and 3,000,000 sex-selected sperm cells. Ex. 1005, 14:11-12. Specifically, Seidel 1997 discloses that separated sperm are extended to a concentration of 3,000,000 to 5,000,000 cells per milliliter. *Id.*; Ex. 1003, ¶¶ 139, 187. A skilled person would have understood that 0.25 milliliter containers are commonly used (*e.g.*, "straws"), resulting in a sample of 1.25 million sperm at the higher concentration. Ex. 1003, ¶ 187. Seidel 1997 also discloses that, if desired, the sperm can be processed to result in a dose of 300,000 sperm per 0.184 milliliter. Ex. 1005, 14:16-22; Ex. 1003, ¶ 141. And, Salisbury similarly discloses that a wide variety of amounts of bovine sperm can be successfully utilized to inseminate cows, including amounts in the 300,000 to 3,000,000 range. Ex. 1006, 476-478;

Ex. 1003, ¶¶ 157-158, 190. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 3. Ex. 1003, ¶ 188.

4. Claim 4

Claim 4 is dependent upon claim 2 and further specifies the step of isolating no more than "about 1,000,000" bovine sperm cells. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1 and 2.

Seidel 1997 also discloses that the insemination sample has no more than about 1,000,000 sex-selected sperm cells. Ex. 1003, ¶ 190. Specifically, Seidel 1997 discloses that separated sperm are extended to a concentration of 3-5 million per milliliter. Ex. 1005, 14:16-22. A skilled person would have understood that 0.25 milliliter straws are commonly used, resulting in a sample of 1.25 million sperm at the higher concentration. Ex. 1003, ¶¶ 139, 190. Seidel 1997 notes that the sperm may be further diluted to a sample of no more than "about" one million sex-selected sperm cells. Ex. 1005, 14:16-22; Ex. 1003, ¶ 190. Salisbury discloses that a wide variety of amounts of bovine sperm can be successfully utilized to inseminate cows, including amounts of no more than 1,000,000 cells. Ex. 1006, 476-478; Ex. 1003, ¶¶ 157-158, 259. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 4. Ex. 1003, ¶ 191.

5. Claim 8

Claim 8 is dependent upon claim 1 and further specifies that the step of "cooling" the sex-selected sperm cells comprises reducing the temperature of the cells to about 5° C. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claim 1.

Seidel 1997 also discloses that the step of cooling the sperm cells comprises the step of reducing the temperature to about 5° C. Ex. 1005, 14:12-14. Specifically, Seidel 1997 discloses that the sperm is reduced in temperature to 5° C. Ex. 1005, 15:37-39; Ex. 1003, ¶¶ 140, 193. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 8. Ex. 1003, ¶ 194.

6. Claim 9

Claim 9 is dependent upon claim 8 and further specifies reducing the temperature of the sex-selected sperm cells "for a period of about 60 minutes to about 240 minutes." As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1 and 8.

Seidel 1997 also discloses the step of cooling the sperm. Specifically, Seidel 1997 discloses cooling the sperm to slow the sperm's metabolism and to permit its use over longer periods of time. Ex. 1005, 14:12-14; Ex. 1003, ¶¶ 140, 196. Specifically, Seidel 1997 discloses that the sperm is reduced in temperature

to 5° C over 75 minutes. Ex. 1005, 15:37-39; Ex. 1003, ¶¶ 140, 196. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 9. Ex. 1003, ¶ 197.

7. Claim 10

Claim 10 is dependent upon claim 1 and further specifies that the extender comprise a component which maintains osmolality and buffers pH. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claim 1.

Seidel 1997 also discloses an extender comprising a component which maintains osmolality and buffers pH. Ex. 1005, 13:64-66. Specifically, Seidel 1997 discloses an extender containing sodium citrate. *Id.*, 13:66-14:10; Ex. 1003, ¶¶ 139, 199. Sodium citrate was well known in the art as a buffer that maintains osmolality and buffers pH. Ex. 1003, ¶¶ 42, 199. Indeed, the '265 patent acknowledges sodium citrate as a well-known example of a buffer that maintains pH and osmolality. Ex. 1001, 6:22-37; Ex. 1003, ¶ 199. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 10. Ex. 1003, ¶ 200.

8. Claim 11

Claim 11 is dependent upon claim 10 and further specifies that the component which maintains osmolality and buffers pH is selected from the group

consisting of a buffer comprising a salt, a buffer containing a carbohydrate, and any combination thereof. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1 and 10.

Seidel 1997 also discloses an extender which meets the additional limitations of claim 11. Specifically, Seidel 1997 discloses an extender containing sodium citrate. Ex. 1005, 13:66-14:10; Ex. 1003, ¶¶ 137, 202. Sodium citrate was well known in the art as a buffer that maintains osmolality and buffers pH, and it is also a salt. Ex. 1003, ¶¶ 42, 202. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 11. Ex. 1003, ¶ 203.

9. Claim 12

Claim 12 is dependent upon claim 10 and further specifies that the component in the extender which maintains osmolality and buffers pH is selected from a group consisting of a number of compounds, one of which is sodium citrate. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1 and 10.

As also stated above for claim 11, Seidel 1997 discloses an extender containing sodium citrate, which was well known in the art as a buffer that maintains osmolality and buffers pH, and is also a salt. Ex. 1005, 13:66-14:10; Ex. 1003, ¶¶ 42, 137, 202, 205. Thus, Seidel 1997 in combination with Salisbury

and Spaulding would have rendered obvious the method of claim 12. Ex. 1003, ¶ 206.

10. Claim 13

Claim 13 is dependent upon claims 10, 11, or 12 and further specifies that the extender has a pH range of about 6.5 to about 7.5. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1, 10, 11, and 12.

Seidel 1997 also discloses an extender with a pH in the range of about 6.5 to about 7.5. Ex. 1005, 13:66-14:10. Specifically, Seidel 1997 discloses an extender containing sodium citrate. *Id.*; Ex. 1003, ¶¶ 137, 208. Sodium citrate was well known in the art as a buffer that maintains osmolality and buffers pH. Ex. 1003, ¶¶ 42, 208. Salisbury reports that the optimal pH for a seminal extender is in the range from 6.5 to 7.5, depending upon the ions in the extender. Ex. 1006, 502. In particular, the optimal pH for citrate extender is 6.5 to 7.0. *Id.*; Ex. 1003, ¶¶ 150, 208. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 13. Ex. 1003, ¶ 209.

11. Claim 14

Claim 14 is dependent upon claim 13 and further specifies that the extender comprise a "cold shock protectant." As discussed above, Seidel 1997 in

combination with Salisbury and Spaulding renders obvious claims 1, 10, 11, 12, and 13.

Seidel 1997 in combination with Salisbury teaches the use of an extender comprising a cold shock protectant. Ex. 1003, ¶ 211. As discussed above, a skilled person would have been motivated to combine Seidel 1997's teaching of separated sperm with Salisbury's teaching of frozen sperm in light of the numerous benefits of frozen sperm and the recognition that freezing sperm was the preferred method of preserving sperm. Ex. 1003, ¶¶ 70, 181, 211.

Seidel 1997 discloses that sperm should be extended with an extender and notes that other extenders can be used. Ex. 1005, 13:64-66; Ex. 1003, ¶¶ 136, 211. Salisbury discloses that the basic components of extenders used when freezing sperm include organic materials to protect against cold shock. Ex. 1006, 498-507. A skilled person would have been motivated to use these ingredients when freezing separated sperm. Ex. 1003, ¶¶ 148, 211. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 13. Ex. 1003, ¶ 212.

12. Claim 15

Claim 15 is dependent upon claim 14 and further specifies that the cold shock protectant be selected from a group of compounds that includes egg yolk.

As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1, 10, 11, 12, 13, and 14.

Specifically, Seidel 1997 discloses the use of egg yolk in the final extender. Ex. 1005, 13:64-14:10; Ex. 1003, ¶¶ 136-137, 214. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 15. Ex. 1003, ¶ 215.

13. Claim 16

Claim 16 is dependent upon claim 14 and further specifies that the extender comprise an energy source. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1, 10, 11, 12, 13, and 14.

Seidel 1997 in combination with Salisbury teaches the use of an extender comprising an energy source. Ex. 1003, ¶¶ 148, 217. A skilled person would have been motivated to combine Seidel 1997's teaching of separated sperm with Salisbury's teaching of frozen sperm in light of the numerous benefits of frozen sperm and the recognition that freezing sperm was the preferred method of preserving sperm. Ex. 1003, ¶¶ 70, 181, 217. Salisbury discloses that the basic components of extenders used when freezing sperm include an energy source. Ex. 1006, 498-499; Ex. 1003, ¶¶ 148, 217. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 16. Ex. 1003, ¶ 218.

14. Claim 17

Claim 17 is dependent upon claim 16 and further specifies that the energy source be selected from a group that includes glucose and fructose. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1, 10, 11, 12, 13, 14, and 16.

Seidel 1997 teaches that glucose can be used in the final extender. Ex. 1005, 13:66-14:10; Ex. 1003, ¶¶ 137, 220. Salisbury likewise teaches that simple sugars such as glucose and fructose can be used for an energy source in the freezing extender. Ex. 1006, 501; Ex. 1003, ¶¶ 48, 153, 220. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 17. Ex. 1003, ¶ 221.

15. Claim 18

Claim 18 is dependent upon claim 16 and further specifies that the extender comprise an antibiotic. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1, 10, 11, 12, 13, 14, and 16.

Seidel 1997 in combination with Salisbury also teaches the use of a final extender comprising an antibiotic. A skilled person would have been motivated to combine Seidel 1997's teaching of separated sperm with Salisbury's teaching of frozen sperm in light of the numerous benefits of frozen sperm and the recognition

that freezing sperm was the preferred method of preserving sperm. Ex. 1003, ¶¶ 70, 181, 223.

Seidel 1997 discloses that sperm should be extended with an extender and notes that antibiotics can be used. Ex. 1005, 13:64-66; Ex. 1003, ¶¶ 136, 138, 223. Salisbury discloses that the basic components of extenders used when freezing sperm include organic materials to protect against cold shock, an energy source, an antibiotic, and a cryoprotectant. Ex. 1006, 498-499; Ex. 1003, ¶¶ 148, 223. A skilled person would have been motivated to use these ingredients when freezing separated sperm. Ex. 1003, ¶ 223. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 18. Ex. 1003, ¶ 224.

16. Claim 19

Claim 19 is dependent upon claim 18 and further specifies that the antibiotic be selected from a group of specific antibiotics, which includes tylosin, gentamicin, linco-spectin, penicillin, and streptomycin. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1, 10, 11, 12, 13, 14, 16, and 18.

Seidel 1997 also discloses that the extender may contain antibiotics, such as tylosin, gentamicin, and linco-spectin. Ex. 1005, 12:6-12; Ex. 1003, ¶¶ 138, 226. Salisbury discloses that antibiotics should be included in extenders used to freeze

semen and specifically teaches the use of antibiotics such as penicillin and streptomycin. Ex. 1006, 445, 464, 469-472; Ex. 1003, ¶¶ 46, 124, 226. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 19. Ex. 1003, ¶ 227.

17. Claim 20

Claim 20 is dependent upon claim 10 and further specifies that the extender comprise a cryoprotectant. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1 and 10.

Seidel 1997 in combination with Salisbury teaches the use of an extender comprising a cryoprotectant. As discussed above, a skilled person would have been motivated to combine the Seidel 1997 teaching of separated sperm with the Salisbury teaching of frozen sperm in light of the numerous benefits of frozen sperm and the recognition that freezing sperm was the preferred method of preserving sperm. Ex. 1003, ¶¶ 70, 181, 229.

Seidel 1997 discloses that sperm should be extended with an extender and notes that other extenders can be used. Ex. 1005, 13:64-66; Ex. 1003, ¶¶ 136, 138. Salisbury discloses that the basic components of extenders used when freezing sperm include a cryoprotectant. Ex. 1006, 498-499; Ex. 1003, ¶¶ 148, 229. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 20. Ex. 1003, ¶ 230.

18. Claim 22

Claim 22 is dependent upon claim 20 and further specifies that the cryoprotectant is selected from a group of compounds consisting of glycerol, 6% glycerol, between 5% to 7% glycerol, dimethyl sulfoxide, ethylene glycol, propylene glycol, and any combination thereof. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1, 10, and 20.

A skilled person would have been motivated to combine Seidel 1997's teaching of separated sperm with Salisbury's teaching of frozen sperm in light of the numerous benefits of frozen sperm and the recognition that freezing sperm was the preferred method of preserving sperm. Ex. 1003, ¶¶ 70, 181, 232. Salisbury also discloses the use of glycerol in the final extender and notes that, since the discovery of the benefits of glycerol, freezing sperm is the preferred way of preserving it. Ex. 1006, 494, 498, 500; Ex. 1003, ¶¶ 37, 146. In light of this teaching, a skilled person would have been motivated to add glycerol to the final extender when freezing sperm. Ex. 1003, ¶ 232. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 22. Ex. 1003, ¶ 233.

19. Claim 26

Claim 26 is dependent upon claim 1 and further specifies the step of equilibrating the discrete population of sperm cells in a final extender for a

duration of about 1 hour to about 18 hours. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claim 1.

As also discussed above, a skilled person would have been motivated to combine Seidel 1997's teaching of separated sperm with Salisbury's teaching of frozen sperm in light of the numerous benefits of frozen sperm and the recognition that freezing sperm was the preferred method of preserving sperm. Ex. 1003, ¶¶ 70, 181, 235. Such a person would have been well aware of Salisbury, which notes that fertility trials "clearly established the beneficial influence on the fertility of bull spermatozoa of an equilibration period of several hours" and recommends equilibrating in an extender containing glycerol for between 4 and 18 hours. Ex. 1006, 498-507, 514; Ex. 1003, ¶¶ 53, 156, 235. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 26. Ex. 1003, ¶ 236.

20. Claim 27

Claim 27 is dependent upon claim 22 and further specifies the step of equilibrating the discrete population of sperm cells in a final extender for a duration of a period not greater than six hours. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claims 1, 10, 20, and 22.

As also discussed above, a skilled person would have been motivated to combine Seidel 1997's teaching of separated sperm with Salisbury's teaching of frozen sperm in light of the numerous benefits of frozen sperm and the recognition that freezing sperm was the preferred method of preserving sperm. Ex. 1003, ¶¶ 70, 181, 238. A skilled person would have been well aware of Salisbury, which notes that fertility trials "clearly established the beneficial influence on the fertility of bull spermatozoa of an equilibration period of several hours" and recommends equilibrating in a final extender containing glycerol for between 4 and 18 hours. Ex. 1006 498-507, 514; Ex. 1003, ¶¶ 53, 156, 238. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 27. Ex. 1003, ¶ 239.

21. Claim 28

Claim 28 is dependent upon claim 1 and further specifies the step of freezing the sex-selected sperm in the extender involves freezing between about 300,000 and about 5,000,000 bovine sperm cells. As discussed above, Seidel 1997 in combination with Salisbury and Spaulding renders obvious claim 1.

Seidel 1997 also discloses that the insemination sample has between 300,000 and 5,000,000 sex-selected sperm cells. Ex. 1005, 14:11-22. Specifically, Seidel 1997 discloses that separated sperm are extended to a concentration of 3-5 million per milliliter. Ex. 1005, 14:11-12; Ex. 1003, ¶¶ 135, 139, 241. A skilled

person would have understood that 0.25 milliliter containers are commonly used, resulting in a sample of 1.25 million sperm at the higher concentration. Ex. 1003, ¶ 241. And, Salisbury similarly discloses that a wide variety of amounts of bovine sperm can be successfully utilized to inseminate cows, including amounts in the 300,000 to 5,000,000 range. Ex. 1006, 476-478, 518; Ex. 1003, ¶¶ 157-158, 241. Thus, Seidel 1997 in combination with Salisbury and Spaulding would have rendered obvious the method of claim 28. Ex. 1003, ¶ 242.

B. Claims 1-4, 8-20, 22 and 26-28 are Unpatentable in View of Fugger in Combination with Salisbury[1]

As found by the Board in the '425 patent IPR, a skilled person would have been motivated to combine Fugger (Ex. 1007) with Salisbury (Ex. 1006). *See* '425 IPR FWD, 25-26; *see also* Ex. 1003 (Pace Decl.), *e.g.*, ¶¶ 244, 304, 307. Although Fugger pertains to freezing human sperm, a skilled person looking to apply the teachings of Fugger to other animals would have recognized that the method taught in Fugger could be improved when applied to other animals by modifying that

[1] In the '425 patent IPR, the Board found unpatentable under § 103 all claims challenged based on Fugger 1998 in combination with Salisbury 1978, with the exception of claims 25-27. *See* IPR2014-01550 (Paper 25), 24-29. Claims 25-27 of the '425 patent all specify an "insemination sample," a requirement not set forth in the '265 patent claims challenged here.

method in modest respects, and would have turned to references such as Salisbury, one of the most respected texts in the field of artificial insemination of cattle, when performing that modification. Ex. 1003, ¶ 244. For example, skilled persons would have understood that a buffer other than the "TEST yolk buffer" described in Fugger might provide more optimal results when freezing and separating bovine sperm cells. Ex. 1003, ¶ 249.

Furthermore, a skilled person would have been motivated to transfer the teachings of Fugger to other sperm cells, such as bovine sperm cells, in light of the commercial benefits to separated, frozen sperm. For example, separated sperm allows farmers to vary the male to female offspring ratio and increase the percentage of milk-producing offspring, while reducing the number of difficult births in their herd. Ex. 1003, ¶ 19. And, frozen sperm allows breeders to use the sperm at the optimal time for the female while taking advantage of the attributes of bulls located far away from the heifers to be impregnated. Ex. 1003, ¶ 70. Thus, a skilled person would have been motivated to combine the teachings of Fugger and Salisbury. Ex. 1003, ¶ 244; *see* '425 IPR FWD, 25 ("Petitioner shows persuasively that a person of ordinary skill in the art would have recognized that the method taught in Fugger could be improved when applied to other animals, using the teachings of Salisbury.").

Furthermore, as discussed above, a skilled person would have expected success. *See* '425 IPR FWD, 25. Individuals had been freezing animal sperm since the 1950's and numerous individuals had reported successfully freezing separated animal sperm. Ex. 1008 (Johnson 1992); Exs. 1018-1026; Ex. 1003, ¶¶ 30, 69, 72, 244.

1. Claim 1

Claim 1 is "a method of cryopreserving sex-selected sperm cells," comprising the recited steps in the claim. Fugger discloses a method of cryopreserving sex-selected sperm cells. Ex. 1007, 2367-2368; Ex. 1003, ¶¶ 163, 243.

a. "obtaining sperm cells from a species of a non-human male mammal"

Fugger discloses the step of obtaining sperm from a human male. Ex. 1007, 2367; Ex. 1003, ¶ 164, 244. However, a skilled person would have recognized that the method taught in Fugger could have been applied to other animals. '425 IPR FWD, 25; Ex. 1003, ¶ 244.

b. "sorting sperm cells . . . based upon sex-type to provide a collection of sex-selected sperm cells obtained using flow cytometry or fluorescence-activated cell sorting"

Fugger discloses sorting sperm cells based upon sex-type. Fugger states that the "specimens were sorted by FCS [*i.e.*, flow cytometry separation] as previously described (Johnson *et al.*, 1993)." Ex. 1007, 2367; Ex. 1003, ¶ 245. Specifically,

Fugger discloses differentiating X chromosome bearing sperm cells and Y chromosome bearing sperm cells based on how those cells fluoresce in a flow cytometer, which is based on the amount of DNA contained within the cells. Ex. 1007, 2367; Ex. 1003, ¶¶ 167-168, 245. Fugger discloses that the sorted sperm was "collected." Ex. 1007, 2368; Ex. 1003, ¶¶ 169, 246.

c. "without the presence of protective compounds in seminal plasma"

Fugger also discloses that the sorting of the semen was done without the presence of protective compounds in seminal plasma. Fugger states that the "specimens to be sorted were extended, centrifuged, resuspended [and] filtered" as part of the sperm preparation and prior to the flow cytometry separation. Ex. 1007, 2367. The conditions specified by Fugger would have removed all, or nearly all, of the seminal plasma prior to the sorting. Ex. 1003, ¶¶ 165, 247.

d. "cooling said sex-selected sperm cells"

Fugger in combination with Salisbury also renders obvious the step of cooling the sperm cells. Fugger describes freezing separated human sperm. Ex. 1007, 2368. A skilled person would have understood that slightly different methods may be required when freezing sperm of other species and, if attempting to freeze bovine sperm, would have turned to Salisbury, which teaches the importance of cooling bovine sperm prior to freezing. Ex. 1003, ¶¶ 52, 146, 248.

e. "suspending said sex-selected sperm cells in an extender to provide a concentration" of "about 5 million per milliliter to about 10 milliliter of extender"

Fugger also discloses suspending sex-selected sperm cells in an extender prior to freezing. In particular, Fugger described that: "Sorted specimens to be frozen were extended in TEST yolk buffer freezing medium" and then subsequently frozen. Ex. 1007, 2368. Fugger does not specifically mention that the concentration of the sperm in the extender is about 5,000,000 per milliliter to about 10,000,000 per milliliter. However, a skilled person would have understood that slightly different methods may be required when freezing sperm of other species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶ 52, 248-249. Salisbury teaches that sperm concentrations of 5-10 million per milliliter had been frozen and subsequently used for successful inseminations. Ex. 1006, 517-518; Ex. 1003, ¶¶ 157, 249.

f. "freezing said sex-selected sperm cells in said extender"

Fugger discloses freezing the selected sperm sample. Specifically, Fugger states that separated sperm were placed into small containers such as cryotubes or straws "and subsequently frozen in a programmable rate freezer." Ex. 1007, 2368; Ex. 1003, ¶¶ 171, 250.

The claims of the '265 patent are limited to non-humans and Fugger pertains to human sperm. Ex. 1007, 2367. However, it would have been obvious to utilize the method disclosed in Fugger with non-human mammals. *See* '425 IPR FWD, 25-26; Ex. 1003, ¶ 244.

Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 1. Ex. 1003, ¶¶ 243-251.

2. Claim 2

Claim 2 is dependent upon claim 1 and further specifies that the sperm cells be bovine or equine. As discussed above, Fugger in combination with Salisbury renders obvious claim 1.

Fugger also teaches the use of bovine or equine sperm cells. Ex. 1007, 2367. As noted above, a skilled person would have understood that the method described in Fugger 1988 could be utilized with bovine sperm. *See* '425 IPR FWD, 25; Ex. 1003, ¶¶ 245, 253. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 2. Ex. 1003, ¶ 254.

3. Claim 3

Claim 3 is dependent upon claim 2 and further specifies isolating a number of bovine cells between about 300,000 and about 3,000,000. As discussed above, Fugger in combination with Salisbury renders obvious claims 1 and 2.

Fugger in combination with Salisbury also teaches the step of isolating between 300,000 and about 3,000,000 sex-selected sperm. Fugger describes the separation and subsequent use of separated human sperm to achieve fertilizations. Ex. 1007, 2368-2369; Ex. 1003, ¶¶ 28, 256. A skilled person would have understood that successful fertilizations in different species might require different amounts of sperm and, if attempting to inseminate a female using frozen bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 256.

Salisbury discloses that a wide variety of amounts of bovine sperm can be successfully utilized to inseminate cows, including amounts in the 300,000 to 3,000,000 range. Ex. 1006, 476-478; Ex. 1003, ¶¶ 157-158, 256. A skilled person would have known that 300,000 to 3,000,000 sperm could be used to inseminate cows. Ex. 1003, ¶ 256. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 3. Ex. 1003, ¶ 257.

4. Claim 4

Claim 4 is dependent upon claim 2 and further specifies the step of isolating no more than "about 1,000,000" bovine cells. As discussed above, Fugger in combination with Salisbury renders obvious claim 1 and 2.

Fugger describes the separation and subsequent use of separated human sperm to achieve fertilizations. Ex. 1007, 2368-2369; Ex. 1003, ¶¶ 28, 259. A skilled person would have understood that successful fertilizations in different

species might require different amounts of sperm and, if attempting to inseminate a female using frozen bovine sperm, would have turned to Salisbury. Ex. 1003, ¶ 259.

Salisbury discloses that a wide variety of amounts of bovine sperm can be successfully utilized to inseminate cows, including amounts of no more than 1,000,000. Ex. 1006, 476-478; Ex. 1003, ¶¶ 158, 259. A skilled person would have known that 1,000,000 sperm could be used to inseminate cows. Ex. 1003, ¶ 259. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 4. Ex. 1003, ¶ 260.

5. Claim 8

Claim 8 is dependent upon claim 1 and further specifies that the step of "cooling" the sex-selected sperm cells comprises reducing the temperature of the cells to "about 5° C." As discussed above, Fugger in combination with Salisbury renders obvious claim 1.

A skilled person would have understood that slightly different methods may be required when freezing sperm of other species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 52, 146, 262. Salisbury teaches the importance of cooling bovine sperm prior to freezing and notes that sperm can be cooled to 5° C. Ex. 1006, 509-511; Ex. 1003, ¶¶ 155, 262.

Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 8. Ex. 1003, ¶ 263.

6. Claim 9

Claim 9 is dependent upon claim 8 and further specifies reducing the temperature of the sex-selected sperm cells "for a period of about 60 minutes to about 240 minutes." As discussed above, Fugger in combination with Salisbury renders obvious claims 1 and 8.

Fugger describes freezing separated human sperm. Ex. 1007, 2367. A skilled person would have understood that slightly different methods may be required when freezing sperm of other species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 52, 146, 265.

Salisbury teaches the importance of slow cooling bovine sperm prior to freezing. Ex. 1006, 510; Ex. 1003, ¶¶ 155, 265. A skilled person, when freezing bull sperm, would have cooled it slowly to avoid "cold shock." Ex. 1003, ¶¶ 265-266. Salisbury reports benefits of cooling over a period of four hours. Ex. 1006, 509. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 9. Ex. 1003, ¶ 266.

7. Claim 10

Claim 10 is dependent upon claim 1 and further specifies that the extender comprises a component which maintains osmolality and buffers pH. As discussed above, Fugger in combination with Salisbury renders obvious claim 1.

Fugger describes the use of an extender for human sperm. Ex. 1007, 2368. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 268.

Salisbury teaches that extenders used in freezing bovine semen typically contain a component which maintains osmolality and buffers pH. Ex. 1006, 498-499; Ex. 1003, ¶¶ 40, 148, 268. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 10. Ex. 1003, ¶ 269.

8. Claim 11

Claim 11 is dependent upon claim 10 and further specifies that the component which maintains osmolality and buffers pH is selected from the group consisting of a buffer comprising a salt, a buffer containing a carbohydrate, and any combination thereof. As discussed above, Fugger in combination with Salisbury renders obvious claims 1 and 10.

Fugger in combination with Salisbury also suggests a final extender wherein the component which maintains osmolality and buffers pH is selected from the

group consisting of a buffer comprising a salt, a buffer containing a carbohydrate, and any combination thereof. Ex. 1003, ¶¶ 149, 170, 271. Fugger describes the use of an extender for human sperm. Ex. 1007, 2368. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 271.

Specifically, Salisbury discloses an extender containing sodium citrate. Ex. 1006, 499; Ex. 1003, ¶¶ 149-150, 271. Sodium citrate was well known in the art as a buffer that maintains osmolality and buffers pH. Ex. 1003, ¶¶ 42, 271. Indeed, the '265 patent identifies sodium citrate as a well-known example of a buffer that maintains pH and osmolality. Ex. 1001, 6:22-37. A skilled person would have incorporated sodium citrate when freezing bull sperm and would have known that sodium citrate is a salt. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 11. Ex. 1003, ¶ 272.

9. Claim 12

Claim 12 is dependent upon claim 10 and further specifies that the component in the extender which maintains osmolality and buffers pH is selected from a group consisting of a number of compounds, one of which is sodium citrate. As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, and 11.

Fugger describes the use of an extender for human sperm. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 274.

Salisbury teaches that sodium citrate can be used as a buffer to maintain osmolality and buffer pH. Ex. 1006, 499; Ex. 1003, ¶¶ 42, 149, 274. Indeed, the '265 patent identifies sodium citrate as a well-known example of a buffer that maintains pH and osmolality. Ex. 1001, 6:22-37. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 12. Ex. 1003, ¶ 275.

10. Claim 13

Claim 13 is dependent upon claims 10, 11, or 12 and further specifies that the extender has a pH range from about 6.5 to about 7.5. As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, 11, and 12.

Fugger describes the use of an extender for human sperm. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 277.

Specifically, Salisbury discloses an extender containing sodium citrate. Ex. 1003, ¶¶ 149, 277. Sodium citrate was well-known in the art as a buffer that

maintains osmolality and buffers pH. Ex. 1006, 499; Ex. 1003, ¶¶ 42, 277. Indeed, the '265 patent identifies sodium citrate as a well-known example of a buffer that maintains pH and osmolality. Ex. 1001, 6:22-37. Salisbury reports that the optimal pH for a seminal extender is in the range of 6.5 to 7.5, depending upon the ions in the extender. Ex. 1006, 502. In particular, the optimal pH for citrate extender is 6.5 to 7.0. *Id.*; Ex. 1003, ¶¶ 150, 277. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 13. Ex. 1003, ¶ 278.

11. Claim 14

Claim 14 is dependent upon claim 13 and further specifies that the extender comprise a "cold shock protectant." As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, 11, 12 and 13.

Fugger describes the use of an extender for human sperm. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 280.

Salisbury discloses that the basic components of extenders used when freezing sperm include organic materials to protect against cold shock, an energy source, an antibiotic, and a cryoprotectant. Ex. 1006, 498-499; Ex. 1003, ¶¶ 148, 280. A skilled person, when freezing bull sperm, would have utilized a final

extender containing these ingredients. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 14. Ex. 1003, ¶ 281.

12. Claim 15

Claim 15 is dependent upon claim 14 and further specifies that the cold shock protectant be selected from a group of compounds that includes egg yolk. As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, 11, 12, 13, and 14.

A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 283. Salisbury teaches that egg yolk is used extensively in extenders for bull sperm and that it protects against cold shock. Ex. 1006, 499; Ex. 1003, ¶¶ 45, 148-149, 283. Thus, a skilled person would have known to use egg yolk in the final extender when freezing bull sperm. Ex. 1003, ¶¶ 194-195. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 15. Ex. 1003, ¶ 284.

13. Claim 16

Claim 16 is dependent upon claim 14 and further specifies that the extender comprise an energy source. As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, 11, 12, 13, and 14.

Fugger describes the use of an extender for human sperm. Ex. 1007, 2368. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 286.

Salisbury discloses that the basic components of extenders used when freezing sperm include an energy source. Ex. 1006, 498-499; Ex. 1003, ¶¶ 148, 286. A skilled person, when freezing bull sperm, would have utilized a final extender containing these ingredients. Ex. 1003, ¶ 286. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 16. Ex. 1003, ¶ 287.

14. Claim 17

Claim 17 is dependent upon claim 16 and further specifies that the energy source be selected from a group that includes glucose and fructose. As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, 11, 12, 13, 14, and 16.

A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 289.

Salisbury teaches that extenders should contain an energy source and that simple sugars such as glucose and fructose can be used as such an energy source.

Ex. 1006, 501; Ex. 1003, ¶¶ 48, 148, 153, 289. Thus, a skilled person would have, when freezing bull sperm, used an extender containing a simple sugar such as glucose or fructose. Ex. 1003, ¶ 289. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 17. Ex. 1003, ¶ 290.

15. Claim 18

Claim 18 is dependent upon claim 16 and further specifies that the extender comprise an antibiotic. As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, 11, 12, 13, 14, and 16.

Fugger describes the use of an extender for human sperm. Ex. 1007, 2368. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 292.

Salisbury discloses that antibiotics should be included in extenders used to freeze semen and specifically teaches the use of antibiotics. Ex. 1006, 467-472; Ex. 1003, ¶¶ 148, 154, 292. And, industry standards required the use of antibiotics such as tylosin, gentamycin, and linco-spectin in frozen semen. Ex. 1003, ¶¶ 47, 292. Indeed, as the '265 patent recognizes, "substantial bacterial growth can threaten sperm viability and increase the risk of infection of the host in artificial insemination or in vitro fertilization procedures." Ex. 1001, 7:18-21. A skilled person, when freezing bull sperm, would have used an antibiotic. Ex. 1003, ¶ 292.

Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 18. Ex. 1003, ¶ 293.

16. Claim 19

Claim 19 is dependent upon claim 18 and further specifies that the antibiotic be selected from a group of specific antibiotics, which includes tylosin, gentamicin, linco-spectin, penicillin, and streptomycin. As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, 11, 12, 13, 14, 16, and 18.

Fugger describes the use of an extender for human sperm. Ex. 1007, 2368. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 295.

Salisbury discloses that antibiotics should be included in extenders used to freeze semen and specifically teaches the use of antibiotics such as penicillin and streptomycin. Ex. 1006, 445, 464, 469-472; Ex. 1003, ¶¶ 46, 154, 295. Indeed, as the '265 patent recognizes, "substantial bacterial growth can threaten sperm viability and increase the risk of infection of the host in artificial insemination or in vitro fertilization procedures." Ex. 1001, 7:18-22. And, industry standards required the use of antibiotics such as tylosin, gentamycin and linco-spectin in frozen semen. Ex. 1003, ¶¶ 47, 295. Thus, a skilled person would have utilized an

antibiotic from the claimed group when freezing bovine sperm. Ex. 1003, ¶¶ 71, 181, 269. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 19. Ex. 1003, ¶ 296.

17. Claim 20

Claim 20 is dependent upon claim 10 and further specifies that the extender comprise a cryoprotectant. As discussed above, Fugger in combination with Salisbury renders obvious claims 1 and 10.

Fugger describes the use of an extender for human sperm. Ex. 1007, 2368. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 49, 298.

Salisbury discloses that the basic components of extenders used when freezing sperm include a cryoprotectant. Ex. 1006, 498-499; Ex. 1003, ¶¶ 148, 298. A skilled person, when freezing bull sperm, would have utilized a final extender containing these ingredients. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 20. Ex. 1003, ¶ 299.

18. Claim 22

Claim 22 is dependent upon claim 20 and further specifies that the cryoprotectant be selected from a group of compounds consisting of glycerol, 6% glycerol, between 5% to 7% glycerol, dimethyl sulfoxide, ethylene glycol,

propylene glycol, and any combination thereof. As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, and 20.

Fugger describes the use of an extender for human sperm. Ex. 1007, 2368. A skilled person would have understood that different extenders could be used with different species and, if attempting to freeze bovine sperm, would have turned to Salisbury. Ex. 1006, 500; Ex. 1003, ¶¶ 49, 301.

Salisbury discloses the use of glycerol in the final extender and teaches that it was critical to freezing sperm successfully. Ex. 1006, 494; Ex. 1003, ¶¶ 43-44, 152, 301. Thus, a skilled person would have incorporated glycerol when freezing sperm. Ex. 1003, ¶ 301. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 22. Ex. 1003, ¶ 302.

19. Claim 26

Claim 26 is dependent upon claim 1 and further specifies the step of equilibrating the discrete population of sperm cells in a final extender for a duration of about 1 hour to about 18 hours. As discussed above, Fugger in combination with Salisbury renders obvious claim 1.

A skilled person would have understood that successful fertilizations in different species might require different amounts of sperm and, if attempting to inseminate a female using frozen bovine sperm, would have turned to Salisbury. Ex. 1003, ¶ 301, 304. Such a person would have been well aware of Salisbury,

which notes that fertility trials "clearly established the beneficial influence on the fertility of bull spermatozoa of an equilibration period" of several hours and recommends equilibrating for between 4 and 18 hours. Ex. 1006, 514-515; Ex. 1003, ¶¶ 156, 304. This range overlaps with the range identified in claim 26. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 26. Ex. 1003, ¶ 305.

20. Claim 27

Claim 27 is dependent upon claim 22 and further specifies the step of equilibrating the discrete population of sperm cells in a final extender for a duration of a period not greater than six hours. As discussed above, Fugger in combination with Salisbury renders obvious claims 1, 10, 20, and 22.

A skilled person would have understood that successful fertilizations in different species might require different amounts of sperm and, if attempting to inseminate a female using frozen bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 301, 307. Such a person would have been well aware of Salisbury, which notes that fertility trials "clearly established the beneficial influence on the fertility of bull spermatozoa of an equilibration period" of several hours and recommends equilibrating for between 4 and 18 hours. Ex. 1006, 514-515; Ex. 1003, ¶¶ 156, 307. This range overlaps with the range identified in claim 27.

Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 27. Ex. 1003, ¶ 308.

21. Claim 28

Claim 28 is dependent upon claim 1 and further specifies that the step of freezing the sex-selected sperm in the extender involves freezing a number of bovine sperm cells between about 300,000 and about 5,000,000. As discussed above, Fugger in combination with Salisbury renders obvious claim 1.

Fugger describes the separation and subsequent use of separated human sperm to achieve pregnancies. Ex. 1007, 2368-2369. A skilled person would have understood that successful insemination in different species might require different amounts of sperm and, if attempting to inseminate a female using frozen bovine sperm, would have turned to Salisbury. Ex. 1003, ¶¶ 301, 310.

Salisbury discloses that a wide variety of amounts of bovine sperm can be successfully utilized to inseminate cows, including amounts in the 300,000 to 5,000,000 range. Ex. 1006, 476-478, 518; Ex. 1003, ¶¶ 157-158, 310. Thus, a skilled person would have known that 300,000 to 5,000,000 sperm could be used to inseminate cows. Ex. 1003, ¶ 310. Thus, Fugger in combination with Salisbury would have rendered obvious the method of claim 28. Ex. 1003, ¶ 311.

VII. CONCLUSION

For the foregoing reasons, the Petitioner respectfully requests that trial be instituted and that claims 1-4, 8-20, 22, and 26-28 of the '265 patent be cancelled.

Dated: October 10, 2017

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

I hereby certify that this Petition complies with the type-volume limitations of 37 C.F.R. § 42.24, because it contains 13,997 words (as determined by the Microsoft Word word-processing system used to prepare the Petition), excluding the parts of the Petition exempted by 37 C.F.R. § 42.24.

Dated: October 10, 2017

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PETITION FOR INTER PARTES REVIEW

OF U.S. PATENT NO. 7,208,265

Attachment A:

Proof of Service of Petition

CERTIFICATE OF SERVICE

I hereby certify that on this 10th day of October 2017, a copy of this PETITION FOR INTER PARTES REVIEW has been served by Federal Express on the following address for patent owner(s):

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PETITION FOR INTER PARTES REVIEW

OF U.S. PATENT NO. 7,208,265

Attachment B:

List of Evidence and Exhibits Relied Upon in Petition

Exhibit No.	Reference Name
1001	U.S. Patent No. 7,208,265 ("'265 patent")
1002	U.S. Patent No. 7,208,265 File History ("'265 File History")
1003	Declaration of Dr. Marvin M. Pace ("Pace Decl.")
1004	*Curriculum vitae* of Dr. Marvin M. Pace
1005	U.S. Patent No. 7,195,920 ("Seidel 1997")
1006	Salisbury et al., Physiology of Reproduction and Artificial Insemination in Cattle, 2nd Ed. 1978 ("Salisbury")
1007	E.F. Fugger, S.H. Black, K. Keyvanfar and J.D. Schulman, "Births of normal daughters after MicroSort sperm separation and intrauterine insemination, in-vitro fertilization, or intracytoplasmic sperm injection," Vol. 13, No. 9 of Human Reproduction (1998) ("Fugger")

1008	U.S. Patent No. 5,135,759 ("Johnson 1992")
1009	Polge, C. and Rowson, L.E.A., "Long-term Storage of Bull Semen Frozen at Very Low Temperatures (-79° C.)," in "Report of The 2nd International Congress of Physiology and Pathology of Animal Reproduction and of Artificial Insemination," Vol. 111 (1952) ("Polge and Rowson 1952")
1010	LaSalle, B., "Introduction," in "The Integrity of Frozen Spermatozoa, Proceedings of a Round-Table Conference held on April 6-7, 1976," National Academy of Sciences (1978) ("LaSalle 1978")
1011	Herman, H.A. and Madden, F.W., "The Artificial Insemination of Dairy and Beef Cattle: A Handbook and Laboratory Manual" 6th Ed. (1980) ("Herman and Madden 1980")
1012	Graham, E.F., "Fundamentals of the Preservation of Spermatozoa," in "The Integrity of Frozen Spermatozoa, Proceedings of a Round-Table Conference held on April 6-7, 1976," National Academy of Sciences (1978) ("Graham 1978")
1013	Berndtson, W.E. and Pickett, B.W, "Techniques for The Cryopreservation and Field Handling of Bovine Spermatozoa," in "The Integrity of Frozen Spermatozoa, Proceedings of a Round-Table Conference held on April 6-7, 1976," National Academy of Sciences (1978) ("Berndtson and Pickett 1978")
1014	Bulletin 621, "Preservation of Bull Semen at Sub-Zero Temperatures," University of IL Ag. Exp. Station (1957) ("Bulletin 621")

1015	Doak, "CSS Implementation of New Antibiotic Combination," Proceedings of the 11th Tech. Conf. on Art. Insemination and Reproduction (1986) ("Doak 1986")
1016	Seidel et al., "Insemination of Heifers with Sexed Frozen or Sexed Liquid Semen," 51:1 Theriogenology: An Int'l J. of Reproduction, 400 (1999) ("Seidel 1999")
1017	Seidel, "Fertility of Bulls on the Edge of the Dose-Response Curve form Numbers of Sperm Per Inseminate," in Proceedings of the 17th Technical Conference on Artificial Insemination and Reproduction (1998) ("Seidel 1998")
1018	U.S. Patent No. 3,854,470 ("Augspurger 1974")
1019	U.S. Patent No. 4,092,229 ("Bhattacharya 1978")
1020	U.S. Patent No. 4,083,957 ("Lang 1978")
1021	U.S. Patent No. 4,362,246 ("Adair 1982")
1022	A. A. Luderer, "Separation of Bovine Spermatozoa by Density on Water Insoluble Newtonian Gels and Their Use for Insemination," Bio. of Repro., Vol. 26, pages 813-24 (1982) ("Luderer 1982")
1023	U.S. Patent No. 4,474,875 ("Shrimpton 1984")
1024	Beal, W.E., et al., "Sex Ratio after Insemination of Bovine Spermatozoa Isolated using a Bovine Serum Albumin Gradient," 58 J. Anim. Sci. 1432-36 (1984) ("Beal 1984")

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