

Filed on behalf of XY, LLC.

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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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ABS GLOBAL, INC.,  
Petitioner

v.

XY, LLC,  
Patent Owner

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Case IPR2017-02184  
Patent No. 7,208,265

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**XY, LLC'S PRELIMINARY RESPONSE**

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**LISTING OF EXHIBITS PURSUANT TO 37 C.F.R. § 42.63(e)**

<b>Exhibit</b>	<b>Description</b>
Ex. 2001	Farmers Weekly, July 3-July 9, 1998

## **I. Introduction**

In accordance with 37 C.F.R. § 42.107, patent owner XY, LLC submits this preliminary response to the Petition filed by ABS Global, Inc. requesting *inter partes* review of claims 1-4, 8-20, 22, and 26-28 of U.S. Patent No. 7,208,265 (“the ’265 Patent”). Patent Owner requests that the Board deny institution of *inter partes* review as to both proposed grounds in the Petition.

The ’265 Patent relates to a method for cryopreserving non-human mammalian sperm cells that comprises a complex combination of processing steps, each of which can kill or injure delicate sperm cells. Though some of the individual processing steps may be present in the prior art, it would not have been obvious to combine all of those injurious and potentially fatal processing steps into a single method, as the ’265 Patent requires. Indeed, at the time of the invention, Genus, Petitioner’s parent company and a real party-in-interest to in these proceedings, publicly criticized the ’265 Patent’s approach. According to Genus, sex-selecting sperm cells with a flow cytometer and centrifuging them –just two of the multiple damaging processing steps required by ’265 Patent—is enough to render those sperm “unsuitable for freezing.” The ’265 Patent, though, has proven those statements to be wrong, and Petitioner’s attempt to reverse course on that position 20 years later is precisely the kind of hindsight that has no place in an obviousness analysis.

Petitioner requests institution on two grounds, both of which are inadequately supported in the Petition. First, Petitioner argues that the '265 Patent is rendered obvious by XY's own U.S. Patent 7,195,920 to Seidel (Ex. 1005), which discloses a method of sorting sperm cells at high speed, combined with two chapters on freezing conventional, unsexed sperm cells from a book by Salisbury (Ex. 1006) and U.S. Patent 5,021,244 to Spaulding (Ex. 1031), which is directed to a method of distilling special proteins from sperm cells. Second, Petitioner argues that the '265 patent claims are obvious in light of Fugger (Ex. 1007), which discusses an infertility study in humans using sex-selected sperm cells, and Salisbury (Ex. 1006). But Petitioner has failed to demonstrate that a person of ordinary skill would have been motivated to combine these references in the particular manner claimed in the '265 Patent, and that the skilled artisan would have a reasonable expectation of success in doing so.

Patent Owner further requests that the Board exercise its discretion under 35 U.S.C. § 325(d) to refuse to revisit arguments about the Salisbury reference that were already fully considered during the original prosecution of the '265 Patent.

## **II. Background**

### **A. The Parties**

XY ("Patent Owner") is a Delaware limited liability company with its principal place of business in Navasota, Texas. XY is the true and correct owner of



the '265 patent, which is the subject of the instant Petition for *Inter Partes* Review.

Petitioner, ABS Global, Inc (“Petitioner”) is a corporation organized under

Delaware law, and its principal place of business is in DeForest, Wisconsin.

Petitioner’s parent company is Genus, plc, and has been identified as a real party-in-interest in these proceedings. Petition at 1.

## **B. Sperm Sorting**

XY’s patented technology, which is used for gender selection of non-human mammalian offspring, is most commonly used in bovines (cattle). Because the dairy industry generally seeks female offspring while the beef industry seeks males, gender selection is a crucial technology. An efficient way to select the gender of offspring is to fertilize the embryo with sperm of a particular gender, i.e., only sperm bearing the X chromosome (producing a female) or only sperm bearing the Y chromosome (producing a male). But it is difficult to separate sperm cells of a particular type into an identifiable subpopulation. Sperm cells are tiny and delicate, and the difference in DNA content between “X” and “Y” sperm cells is small. (Ex. 1005, '920 patent, 2:30-3:3.) Further, a commercially viable selection process must separate the cells at a high rate of speed, but high-speed sorting may stress or even kill the cells. (Ex. 1005, '920 patent, 3:43-50.)

XY was able to develop a high-speed sperm sorting process for which it filed a disclosure on December 31, 1997. The '920 patent (Ex. 1005) discloses and

claims a high-speed sperm sorting process that includes “cushioning” the cells. To fully commercialize the sperm sorting process, XY commenced its pursuit of methods to cryopreserve sorted sperm cells--the next vital step toward commercialization of semen sorting for livestock management purposes:

The ability to select sperm based on sex-type or any other desirable characteristic provides an important tool for accelerating genetic progress, increasing production efficiency, and achieving greater flexibility in livestock management. Full exploitation of this tool, however, depends on the ability to freeze and store selected sperm.

(Ex. 1001, '265 patent, 1:42-48 (emphasis added).)

After two years of research and development, XY filed a provisional application on the process for successfully freezing viable sex-selected sperm cells for fertilization in 1999.

### **III. The '265 Patent**

#### **A. Background**

The '265 Patent relates generally to a method for cryopreserving sex-selected sperm cells. But the '265 Patent goes well beyond simply freezing sex-selected sperm and requires multiple additional processing steps, including (i) sorting the sperm cells “without the presence of protective compounds in seminal plasma”, which encompasses centrifuging the sperm cells before sorting, (ii) cooling the selected sperm sample; and (iii) suspending the sperm cells in a particularly dilute concentration. *See* Ex. 1001,32:27-54. At the time of the

invention, processing sperm cells in the manner claimed in the '265 Patent was viewed as highly detrimental to the sperm cells. Indeed, the senior veterinarian for Petitioner's parent company, Genus, is on record as saying that sperm cells that have been "knocked about by a centrifuge" and sorted via flow cytometry—just two of the multiple processing steps required by every challenged claim—renders those sperm cells "unsuitable for freezing." Ex. 2001 at 3. The '265 Patent, though, requires not just knocking sperm cells about with a centrifuge, sorting them with a flow cytometer, and freezing them, but also cooling them (and risking potential "cold shock"—*see* Salisbury, Ex. 1006 at 446) and diluting them in a final extender (known to depress sperm motility/fertility—Salisbury, Ex. 1006 at 446).

Piling these damaging processing steps, one on top of the other, is what makes the '265 Patent an important, non-obvious advance in the field of livestock management. Sex-selected sperm used in reproductive procedures has managed to increase the production of offspring having desirable traits and increasing livestock production efficiency and quality. Ex. 1001 at 2:56-67.

## **B. The Disputed Claims**

Petitioner challenges claims 1-4, 8-20, 22, and 26-28 of the '265 Patent. Claim 1 is the sole independent claim and is reproduced below ('265 Patent, Ex. 1001 at 32:26-41.

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.

The remaining challenged claims all depend from claim 1, either directly or indirectly. Each is directed to one or more additional features, such as a method specific to bovine or equine cells (claim 2); methods involving the isolation of sex-selected sperm cells (claims 3-4); a method of cooling the sex-selected sperm cells (claims 8-9); methods for extending the sperm sample (claims 10-20, 22); methods for equilibrating the sperm cells prior to freezing (claims 26-27); and methods for freezing particular numbers of sperm cells (claim 28). Ex. 1001 at 32:42-34:53.

### **C. Related Prosecution**

Two applications claiming priority to the application that matured into the '265 Patent are currently pending. U.S. Patent Application No. 12/807,555 was filed on September 7, 2010, and U.S. Patent Application No. 13/752,082 ("the '082

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Application”) was filed on January 28, 2013. The Fugger reference, which ABS relies on for Ground 2 of its Petition, has been asserted by the Examiner in both applications. The Salisbury reference, which ABS relies on for both Ground 1 and Ground 2 of its Petition, has been asserted by the Examiner in the ’082 Application.

#### **D. The Proceedings on the ’425 Patent**

The ’265 Patent is related to U.S. Patent No. 7,820,425 (“the ’425 Patent”), which is the subject of an *inter partes* review (IPR2014-01550) that is currently on appeal to the Federal Circuit. The appeal is not concluded and so issue preclusion has not attached as to any decisions by the Board in the underlying IPR proceeding. 37 C.F.R. 42.73(d); *SDI Techs., Inc. v. Bose Corp.*, IPR2014-00343, Paper 32 at 8-9 (P.T.A.B. Jun. 11, 2015) (holding that estoppel does not attach until all appeal rights have terminated). That said, the issues raised in this Preliminary Response are unique to the ’265 Patent and arise from claim limitations not found in the ’425 Patent. Patent Owner’s arguments here relate primarily to a number of sperm-damaging processing steps not present in the claims of the ’425 Patent, including performing sex-selection procedures “without the presence of protective compounds in seminal plasma,” “isolating a number of bovine sperm cells,” and “suspending said sex-selected sperm cells in an extender to provide a concentration of sperm cells of about 5 million per milliliter to about 10 million per milliliter of

extender.” Thus, even if the ’425 IPR appeal becomes final before the Board decides whether to institute IPR on the ’265 Patent, the Board need not give consideration to any matters of issue preclusion.

#### **IV. Claim Construction**

In an IPR, claims must be given their broadest reasonable construction in light of the specification. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016). The proper interpretation of a claim term is the one that “corresponds with what and how the inventor describes his invention in the specification.” *In re Smith Int’l, Inc.*, 871 F.3d 1375, 1383 (Fed. Cir. 2017).

##### **A. Petitioner’s Claim Constructions**

Petitioner proposes a number of claim constructions in its Petition, including constructions of the terms “sorting” (Petition at 18-19), “based on sex-type to provide a collection of sex-selected sperm cells obtained using flow cytometry or fluorescence-activated cell-sorting” (Petition at 21-22), “extender” (Petition at 22), “about 5 million per milliliter of extender to about 10 million per milliliter of extender” (Petition at 22-23), and “freezing” (Petition at 23-24). Some of these constructions are incorrect and others are inconsequential, but the Board can deny institution without construing any of them. That said, Patent Owner reserves the right to challenge any and all of Petitioner’s proposed constructions if *inter partes* review proceedings are instituted.

**B. “without the presence of protective compounds in seminal plasma”**

Every challenged claim requires that the sex-selection process occur “without the presence of protective compounds in seminal plasma.” Petitioner construes this term to explicitly encompass “the technique of removing nearly all of the seminal plasma through centrifugation.” Petition at 20-21. Patent Owner does not dispute this construction. The fact that this claim term encompasses the highly-damaging centrifuging process is critical to understanding both the non-obviousness of combining multiple sperm-damaging processing steps, and the direct connection between the ’265 Patent’s claims and the disparaging remarks made by Petitioner’s parent company at the time of the invention.

**C. “isolating”**

The cryopreservation method of dependent claims 3 and 4 both require a step of “isolating” a particular number of bovine sperm cells. During prosecution of the ’265 Patent, the patentee expressly stated that he “acted as his own lexicographer and explicitly defined the term ‘isolating sperm’” in the portion of the specification entitled “Isolation of Sperm Cells from the Selected Sperm Sample.” Ex. 1002 at 258-59. Two notable features of the patentee’s definition are relevant to the instant Petition. First, “isolating” requires separating the sperm cells from some portion of the suspension—such as through centrifugation, filtration, or sedimentation—a process that necessarily involves concentrating the

sperm cells. '265 Patent, Ex. 1001 at 8:1-24 (“Any of a variety of methods suitable for recovering cells from a suspension can be used to isolate the sperm, including for example, filtration, sedimentation, and centrifugation.”). Second, the “isolating” step of claims 3 and 4 occurs after sorting, but prior to suspension in the final extender and freezing. '265 Patent, Ex. 1001 at 8:27-29 (“After isolation, the sperm are pooled, if desired, and extended with final extender to an appropriate concentration for freezing.”).

**D. The Cooling, Isolation, And Final Extension Steps Are Performed in That Order**

The '265 Patent specification also prescribes a specific order for performing the claimed steps. After the sex-selection procedure is performed, the sperm cells are cooled. If, as in claims 3 and 4, a particular number of sperm cells are to be isolated, that step is performed after the sperm cells are cooled, and before the sperm cells are suspended in a final extender. The sperm cells are then frozen.

This required order is readily discerned from the specification. “The first step in the cryopreservation method of the invention encompasses obtaining a previously selected sperm sample, as well as subjecting a source sample to any suitable selection method.” Ex. 1001 at 3:64-67. The specification goes on to identify sex-selection via flow cytometry as a “preferred method” of performing this first step. Ex. 1001 at 4:20-46. “The second step in the cryopreservation method entails cooling the selected sperm sample.” Ex. 1001 at 7:47-48. The



“isolating” step is then performed on the already-cooled cells: “During the isolation step, the cooled sperm should generally be kept cold.” Ex. 1001 at 8:7-8. “After isolation, the sperm are pooled, if desired, and extended with final extender to an appropriate concentration for freezing.” Ex. 1001 at 8:27-29. The specification does not describe the cryopreservation method of the invention in any other order. Accordingly, the only reasonable reading of the challenged patent claims requires the cooling, isolation, and final extension steps to be performed in that order.

## **V. The Asserted Prior Art**

### **A. Seidel 1997**

Petitioner’s Seidel 1997 reference is a U.S. patent (U.S. 7,195,920), assigned to Patent Owner, that names the inventor of the ’265 Patent, John Schenk, as a co-inventor. While Seidel 1997 generally relates to using flow cytometry to sex-select mammalian sperm cells, the reference differs from the claimed invention of the ’265 Patent in a number of critical ways. Most critically, Seidel 1997 does not disclose freezing of sex-selected sperm cells; rather, Seidel merely chills his sorted samples (to 5°C). Ex. 1005 at 14:12, 15:37-38. Seidel 1997 also differs from the ’265 Patent in that Seidel cools the sperm cells after final extension, *see* Ex. 1005 at 14:11-12 (“After this last extending...[T]his sample may then be cooled...”), whereas the cryopreservation method of the ’265 Patent performs these steps in the

opposite order. Ex 1001 at 3:64-67 (“The first step in the cryopreservation method of the invention encompasses obtaining a previously selected sperm sample, as well as subjecting a source sample to any suitable selection method.”) and 7:47-49 (“The second step in the cryopreservation method entails cooling the selected sperm sample...”).

## **B. Salisbury**

The disclosure of the Salisbury reference (Ex. 1006) also differs significantly from the invention of the '265 Patent. Salisbury contains two chapters from a book entitled “Physiology of Reproduction and Artificial Insemination of Cattle.” Ex. 1006. The first chapter, Chapter 16, deals entirely with “Extenders and Extension of Unfrozen Semen.” Ex. 1006 at 442-493 The second chapter, Chapter 17, explains techniques for freezing semen. Ex. 1006 at 494-554. It also explains that freezing semen comes with extraordinary physical and chemical consequences— “[a]t least 50 percent of the sperm from an unselected population of bulls are killed or rendered immotile during freezing and thawing.” Ex. 1006 at 495.

Although Salisbury describes general methods for freezing sperm cells, Salisbury does not disclose whether or how the techniques it describes could be applied to sex-selected sperm cells, which is the essential invention of the '265 Patent. To the contrary, the sole mention of sex-selected sperm in the Salisbury

reference is a two-sentence dismissal of claims that any meaningful sex-selection can be accomplished. Ex. 1006 at 479 (“[N]o experimental data have been found to support claims by commercial concerns that they are able essentially to guarantee the sex of the calf produced.”).

### **C. Spaulding**

Spaulding is a U.S. Patent (No. 5,021,244) that discloses a very different method than the one claimed in the '265 Patent. At a high level, Spaulding attempts to achieve sex-selection by immunizing females with sex-specific proteins or using the sex-specific proteins to inactivate sperm cells of a particular sex. *See* Ex. 1031 at 4:19-23, 25:21-26, and 25:43-45. Spaulding uses flow cytometry as an intermediate step in this process to obtain populations of sperm cells that were skewed only slightly toward one sex or the other. Ex. 1031 at 9:65-67 (“we simultaneously collected two viable subpopulations enriched for X- or Y-sperm, respectively. Each subpopulation had an enrichment of at least 68%”). Unlike the sex-selected sperm of the '265 Patent, the slightly sex-skewed sperm cells of Spaulding are not cooled, suspended at a concentration of about 5-10 million cells/mL, or frozen. Instead, the sperm cells are highly processed to remove either sperm plasma membranes or sex-associated membrane proteins from the sperm cells. *See* 1031 at 10:14-54; 10:58-14:30. These additional processing steps

strongly indicate that Spaulding did not consider flow cytometry, by itself, to be a suitable sex-selection method.

#### **D. Fugger**

The Fugger reference (Ex. 1007) also differs significantly from the invention of the '265 Patent. Generally, Fugger reports on the results of the use of sex-selected human semen in two types of procedures: IVF/ICSI procedures where fertilization occurs outside the body and intrauterine insemination ("IUI") procedures where fertilization occurs inside the body. As described below, Fugger omits key elements of the claimed invention of the '265 Patent, and provides discouraging results as to the process it actually discloses.

##### **1. Fugger Omits Key Elements of the '265 Patent**

Every challenged claim of the '265 Patent requires cooling the sperm cells after sorting and before final extension. *See* Claim Construction, Section IV(D), above. Fugger does not disclose the required cooling step. Fugger also does not teach "isolating" sex-selected sperm cells—such as via centrifugation—after sorting and prior to final extension, which is a requirement of claims 3 and 4 of the '265 Patent. *See* Claim Construction, Section IV(C), above. Instead, Fugger describes sperm cells going straight from the flow cytometer to final extension without any intermediate cooling or "isolation" steps. Ex. 1007 at 2368 ("Sorted specimens to be frozen were extended. It is undisputed that Fugger does not

disclose the cooling step. *See* Petition at 48 (failing to identify a cooling step or isolation step in Fugger); Pace Dec., Ex. 1003 at ¶ 248 (same).

Fugger also does not teach “suspending 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,” which is required by every challenged claim of the ’265 Patent. Petitioner explicitly admits that Fugger does not disclose this claim limitation. *See* Petition at 49 (“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”).

Finally, Fugger relates solely to techniques involving human sperm cells, whereas the claims of the ’265 Patent are limited to non-humans sperm cells (and further limited to bovine/equine sperm in challenged claims 2-4). Again, it is undisputed that Fugger discloses only techniques related to human sperm cells. Petition at 47 (“Fugger discloses the step of obtaining sperm from a human male.”).

## **2. Fugger’s Discouraging Results**

Fugger does not report on the final results of using frozen sex-selected semen. This leaves the reader with significant questions as to whether the frozen sex-selected semen generated by Fugger’s procedures is usable. Fugger reports using frozen, sex-selected semen in one set of procedures—namely IVF/ICSI, in

which fertilization occurs outside the body—while using non-frozen semen in an entirely different procedure—intrauterine insemination (“IUI”), in which fertilization occurs inside the body. This is evident from Fugger’s detailed description of the processes used. In the section entitled “Post-sort specimen cryopreservation,” Fugger first indicates that only some of the sex-selected specimens were earmarked for freezing, suggesting that other sex-selected sperm specimens remained unfrozen. Ex. 1007 at 2368 (“Sorted specimens to be frozen were extended...”). Further, Fugger describes preparing frozen sex-selected semen only for IVF/ICSI procedures, and appears to indicate that only some of the IVF/ICSI procedures used frozen sexed semen. Ex. 1007 at 2368 (“Frozen specimens used for IVF or ICSI were thawed at room temperature, centrifuged, and resuspended...”). The paper contains no description of preparing frozen sexed semen for IUI. The clear implication is that Fugger used frozen, sex-selected semen only in IVF/ICSI procedures, and used only unfrozen sex-selected semen in the IUI procedures.

The difference in how Fugger utilizes frozen and unfrozen sex-selected semen means that the reported results cast serious doubt on the usability of frozen sex-sorted semen. Fugger reports normal births only for the non-frozen semen, remaining silent as to the ultimate result of using frozen sex-selected semen. Specifically, in the summary paragraph, Fugger says there have been a “significant

number of individual normal births” using Fugger’s sex-selection approach. Ex.

1007 at 2369. Fugger is less enthusiastic, however, in describing the results of using frozen, sex-selected sperm cells, stating only that “[p]regnancies have also been attained with the use of frozen sorted sperm cells.” Ex. 1007 at 2369.

Notably, Fugger does not say that “normal births” have been obtained with frozen sex-selected sperm cells—Fugger reports only on “pregnancies” in those instances.

*Id.* Moreover, the pregnancy data Fugger presents gives even more cause for concern. Of the 17 pregnancies for which final results were reported, 7 resulted in spontaneous miscarriages and one was an ectopic pregnancy. Thus, 8 out of 17 reported pregnancies—i.e., 47%—did not result in a normal pregnancy carried to full-term. *Id.*

## **VI. Petitioner Has Not Met Its Burden of Demonstrating a Reasonable Likelihood that the Challenged Claims are Obvious**

The claimed invention of the ’265 Patent is a complex and lengthy combination of many individual processing steps, each of which is potentially fatal or injurious to uniquely fragile sperm cells. While each of the references that make up Petitioner’s grounds may contain some subset of the claimed processing steps, the ’265 Patent requires sperm cells to endure the rigors of all of the claimed processing steps. This distinct combination of multiple damaging and stressful processing steps is what makes the invention of the ’265 Patent unique and not obvious. Despite bearing the burden of doing so, Petitioner does not identify the

requisite motivation to combine one set of potentially fatal/injurious processing steps with still more potentially fatal/injurious processing steps. Petitioner has presented no argument or evidence to support a finding that one of skill in the art at the time of the invention would have expected that the claimed combination of damaging and stressful processing steps would be successful. To the contrary, evidence from the time of the invention shows that Petitioner's own parent company did not believe that the claimed processing method of the '265 Patent would work.

**A. The Standard for Instituting an *Inter Partes* Review**

The Board's authority to institute *inter partes* review is limited only to those circumstances where "the information presented in the petition . . . and any response . . . shows that there is a reasonable likelihood that petitioner would prevail with respect to at least one of the claims challenged in the petition." 35 U.S.C. § 314(a); *see also* 37 C.F.R. § 42.108(c). The Petitioner bears the burden of showing that this statutory threshold has been met. *See, e.g.*, Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756 (Aug. 14, 2012) ("The Board . . . may institute a trial where the petitioner establishes that the standards for instituting the requested trial are met . . .").

The combinations of references Petitioner relies on in its Petition do not render obvious the method claimed in the '265 Patent. "A patent composed of



several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR Int’l Co v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). Instead, the Petitioner must demonstrate not just that the elements were known in the prior art, but also “that a skilled artisan would have been motivated to combine the teachings of the prior art...and that the skilled artisan would have had a reasonable expectation of success in doing so.”

*Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359 (Fed. Cir. 2016). As shown below, Petitioner has not met its burden of demonstrating the requisite motivation to combine the prior art in the manner claimed in the ’265 Patent, nor that the skilled artisan would have reasonably expected such a combination to be successful.

### **B. Sperm Cells Are Uniquely Fragile Cells**

The challenged claims of the ’265 Patent are a combination of sperm processing steps, each of which damages or otherwise stresses the sperm cells being processed. This is a critical fact because sperm cells are uniquely fragile. As the ’265 Patent explains, “processing of sperm cells presents unique challenges because sperm are incapable of DNA repair and because of sperm morphology. Each sperm has an acrosome overlying the head and a tail, which are important for fertility and which are relatively susceptible to physical injury.” ’265 Patent, Ex. 1001 at 1:46-50. Petitioner’s own asserted references further demonstrate the

fragility of sperm cells and the importance of maintaining the sperm cell's integrity. For example, Seidel 1997 explains that "[i]n addition to the delicateness of the process, it has always been known that the sperm themselves are extremely delicate cells. ...The sensitivities range from dilution problems and the flow cytometer's inherent need to isolate and distinguish each cell individually as well as the pressure and other stresses..." Ex. 1005 at 2:45-59. The fragility of sperm cells is an important factor in analyzing the invention of the '265 Patent because, as Petitioner's Salisbury reference explains, "[s]permatozoa must be alive to be fertile" and "[t]he integrity of the genetic material in the sperm chromatin must also be preserved in order for normal embryo development to take place after fertilization." Ex. 1006, Salisbury at 442.

Moreover, predicting the degree of damage to sperm cells during processing is difficult, if not impossible, prior to using the sperm cells in some form of reproductive procedure. According to Petitioner's Salisbury reference, "there is no test of semen quality prior to use that can predict how well the genetic material is maintained." Ex. 1006 at 442. Petitioner's Seidel 1997 reference elaborates further, explaining that "this may also represent a unique factor for sperm cells because it appears that even though the sperm cell may appear to pass through the flow cytometer and be sorted with no visually discernible side-effects, in fact, the

cells themselves may have been stressed to the point that they perform less than optimally in the insemination process.” Ex. 1005 at 2:61-67.

**C. Each of the Claimed Steps Imposes Stresses on the Sperm Cells**

The '265 Patent contains a series of processing steps, each of which imposes new stresses on sperm cells, many of which are fatal to a large number of the processed sperm. The stresses attending each of these processing steps are explained below.

**1. Pre-sort removal of protective compounds in seminal plasma imposes stress on sperm cells**

Every challenged claim requires sorting sperm cells “without the presence of protective compounds in seminal plasma.” '265 Patent, Ex. 1001 at 32:30-31.

There is no dispute that this claim term includes “the technique of removing nearly all of the seminal plasma through centrifugation.” Petition at 20-21. Removing seminal plasma in this manner prior to sorting imposes severe stresses on sperm cells, and this is evident from both the '265 Patent and the prior art. The '265 Patent describes centrifugation processes that could result in losing up to half of the sex-selected sperm cells. '265 Patent, Ex. 1001 at 8:16-21. Others have also recognized the injurious nature of centrifugation. At the time of the invention, the senior veterinarian for Petitioner’s parent company, Genus, stated publicly that sperm cells that have “been knocked about by a centrifuge” as part of the sex-selection process means those sperm are “unsuitable for freezing.” Ex. 2001 at 3.

And Petitioner's own Spaulding reference relies on the damaging nature of centrifugation for a critical component of its process, namely the completely removal of plasma membranes from the sperm cells. Ex. 1031 at 10:24-29.

## **2. The sex-selection process imposes stress on sperm cells**

Sex-selection via flow cytometry or fluorescence-activated cell sorting ("FACS") is also required by every challenged claim. '265 Patent, Ex. 1001 at 32:30-31. This sex-selection process imposes further stresses on sperm cells that go "beyond those normally encountered in standard artificial insemination or in vitro fertilization protocols." '265 Patent, Ex. 1001 at 61-63. First, the methods "involve physical stresses," which include "staining, dilution, and interrogation of cells with light." '265 Patent, Ex. 1001 at 1:52. All of these steps represent stresses that can reduce sperm viability." '265 Patent, Ex. 1001 at 4:64-65. Second, flow cytometry imposes further stresses on sperm cells simply because the process takes time, and "sperm fertility decreases with increasing time between collection and use." '265 Patent, Ex. 1001 at 1:50-51; *see also* Seidel 1997, Ex. 1005 at 2:22-29 ("sperm are time critical cells. They [lose] their effectiveness the longer they remain unused"). As a result of these physical and time-related stresses, sex-selected sperm "are typically somewhat compromised compared to non-selected cells" '265 Patent, Ex. 1001 at 1:53-54.

Petitioner's own exhibits also demonstrate that the stresses of flow cytometry can be extraordinarily harsh to sperm cells. The Fugger reference gives an example of a flow cytometry-based sex-selection process that reduces the number of motile sperm cells in a given sample by several orders of magnitude: "The retrieval rate currently can vary between 0.6% and 1.2% of the sperm cells passing through the cytometer. Sperm samples starting with  $50 \times 10^6$  or more cells generally result in ~100,000 to 300,000 motile cells..." Ex. 1007 at 2369.

### **3. Cooling imposes stresses on sperm cells**

Cooling also imposes stress on sperm cells. "Cooling too rapidly can cause cold shock, which can result in a loss of membrane integrity and cell function." '265 Patent, Ex. 1001 at 7:49-51. This is confirmed by Petitioner's own evidence. For example, Petitioner's Salisbury reference explains that "[w]hen mammalian sperm cells are cooled to 5°C they are subject to cold shock, which causes leakage of intracellular enzymes, potassium, lipoprotein, ATP, and other materials from the cells." Salisbury, Ex. 1006 at 446, § 16-2.9. As sperm cells are cooled, "motility is decreased and the flagellum may become bent." *Id.* Although it is known that cooling steps can damage sperm cells, the amount and way in which sperm can become damaged is not necessarily predictable. "The precise mechanisms of damage are unknown, but presumably changes occur at unequal rates on the

surface and internal portions of spermatozoa during cooling, and both physical and chemical damage may result.” Ex. 1006 at 446.

**4. Post-sort isolation of sperm cells imposes stress on sperm cells**

Claims 3 and 4 of the '265 patent include an additional step of “isolating” a number of sperm cells prior to freezing. This isolation step can be performed using a “variety of methods” that result in a more concentrated sperm sample, including by way of centrifugation. '265 Patent, Ex. 1001 at 8:10-14. Isolating sperm cells, however, “exposes already somewhat compromised sperm to additional physical stresses.” '265 Patent, Ex. 1001 at 2:2-4. These stresses can be severe: in the centrifugation process described in the '265 Patent specification as an example of the “isolating” step can result in the loss of up to 50% of the sex-selected sperm cells. '265 Patent, Ex. 1001 at 8:16-21.

**5. Final extension of sperm cells further imposes stress on sperm cells**

The claimed addition of a final extender results in dilution of the concentrated sperm sample, and further compromises the cells. '265 Patent, Ex. 1001 at 1:54-56 (“Fertility may be further reduced if the selection technique involves significant dilution.”). The '265 Patent claims particular final concentrations of about 5-10 million cells per milliliter of extender. Ex. 1001 at 32:37-40. Storage at these final concentrations can have a deleterious effect on

the sperm cells. In fact, experiments described in the specification demonstrate that storing sperm cells at the dilute concentrations claimed in the '265 Patent "resulted in a substantial reduction in the percentage of motile sperm." *See* Ex. 1001, Example 1 13:21-67 (comparing motility of sperm cells stored at  $20 \times 10^6$  cells/mL (31% motile cells) versus  $10 \times 10^6$  cells/mL (20% motile cells).

## **6. Freezing damages sperm cells**

Freezing also indisputably damages sperm cells. '265 Patent, Ex. 1001 at 2:5-6 ("The freezing of sperm also invariably reduces fertility, motility, and/or viability."). Petitioner's own Salisbury reference quantifies the damage, stating that "[a]t least 50 percent of the sperm from an unselected population of bulls are killed or rendered immotile during freezing and thawing." Ex. 1006 at 495, § 17-2.1. The '265 Patent explains one particular mechanism by which freezing is known to damage cells, namely through dehydration: "freezing is accompanied by an increase in solute concentration in the medium surrounding the sperm. The increase in solute concentration draws water out of the cells, which increases intracellular electrolyte concentration." Ex. 1001 at 5:64-6:3. Petitioner's own Salisbury reference confirms the '265 Patent's explanation and provides even more detail concerning the damage due to freezing. "The damage is caused 1) by internal ice crystal formation that affects the structure of the spermatozoa, 2) by the solute concentration that results as pure water is withdrawn from suspension media

both inside and outside the cells, and 3) by the interactions of these two physical factors.” Salisbury, Ex. 1006 at 495, § 17-2.1.

**D. Petitioner Does Not Provide a Sufficient Motivation to Combine**

Petitioner does not demonstrate the requisite motivation to combine multiple processing steps that are known to cause damage to fragile sperm cells, and so the Petition must be denied in its entirety. Obviousness requires demonstrating a motivation “to combine the references to arrive at the claimed invention.” *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1366 (Fed. Cir. 2012).

This means that Petitioner is required to do more than just provide a motivation to create cryopreserved sex-selected sperm. Instead, Petitioner must demonstrate that there was a motivation to freeze sex-selected sperm AND perform the sex-selection procedure in the absence of protective compounds in seminal plasma AND cool the sex-selected sperm cells after sorting AND dilute the isolated sperm cells to a particular concentration prior to freezing. Ex. 1001 at 32:26-50. At best, Petitioner merely identifies a commercial motivation to create cryopreserved sexed semen. See Petition at 24 and 46 (claiming a motivation “to freeze sorted sperm” because of the commercial benefit of using frozen sperm at different times and different locations). This is insufficient because it does not provide a motivation to combine all of the particular processing steps claimed in the ’265 Patent, and that failure is reason alone to deny institution of the requested IPR.



Even the purported commercial motivation Petitioner provides for freezing sex-selected sperm points away from subjecting frozen, sex-selected sperm cells to additional processing steps that can injure or kill the sperm cells. These additional processing steps reduce the fertility of the sex-selected semen and increase the risk of abnormal embryo development. *See* Salisbury, Ex. 1006 at 442 (“Spermatozoa must be alive to be fertile,” and “[t]he integrity of the genetic material in the sperm chromatin must also be preserved in order for normal embryo development to take place after fertilization.”). Decreases in fertility and/or increased risks of abnormal embryos would plainly run contrary to the goals of a commercial cattle breeder.

The importance of maximizing fertility and minimizing stresses on sperm cells is abundantly described in Petitioner’s asserted prior art. For example, Petitioner’s Salisbury reference repeatedly emphasizes the primacy of sperm fertility. *See* Ex. 1006 at 475 (“Semen should be processed in a manner that will insure maximum fertility”) and 532 (“The end fertility level is the ultimate test of superiority of any semen.”). This is further supported by other references submitted by Petitioner which explicitly seek to minimize stresses on sperm cells and/or increase fertility levels. *See* Seidel 1997, Ex. 1005 at 4:48-51 (“An object of the invention is thus to achieve better sorting for substances such as sperm cells. A goal is to minimize the impact the sorting function itself has on the cells...”);

Ex. 1026 (U.S. Patent No. 4,007,087, directed to “a method for reducing the loss in the fertility of semen”).

Even aside from fertility concerns, commercial motivations point toward simplifying the process of producing commercial sexed semen and making it more efficient. *See* Seidel 1997, Ex. 1005 at 2:31-44 (“Thus, for commercial production and success in this field, improvements which might only represent an increase in efficiency may still be significant...In this regard, it has been desired to simplify the process...”). These concerns for efficiency and simplicity counsel against adding more processing steps and increasing the complexity of the process of cryopreserving sex-selected semen.

In light of these commercial motivations and the teachings of the prior art, the burden is on Petitioner to show why one of skill in the art would combine the asserted references in a way that (1) adds processing steps that negatively affect the sperm cells’ viability and fertility and (2) increases the complexity of the cryopreservation process. Petitioner has not done so. The Petition, in its entirety, should therefore be denied.

**E. No Expectation of Success in Combining All of the Claimed Stress-Imposing Steps in the Claimed Manner**

Petitioner has also failed to demonstrate the required “expectation of success” in combining the asserted prior art to achieve the claimed invention. *See Senju Pharm. Co. v. Lupin Ltd.*, 780 F.3d 1337, 1341 (Fed. Cir. 2015) (“In addition

to showing a reason to combine the elements in the manner claimed, a defendant must also demonstrate that a person of ordinary skill would have a reasonable expectation of success in combining the elements.”). The Petition’s sole discussion of the “expectation of success” is directed only to whether one of skill in the art would expect to be able to successfully freeze sex-selected sperm cells. Petition at 25, 47 (“[A] skilled person would have expected success...Individuals had been freezing animal sperm since the 1950’s and numerous individuals had reported successfully freezing separated animal sperm.”). This minimal explanation is insufficient because it is directed only to whether one of skill in the art would expect success in the combination of some elements of the claimed invention. Petitioner provides no explanation of why one of skill in the art would expect to successfully combine not just sex-selection and freezing, but also the additional claimed processing steps of (i) performing the sex-selection procedure in the absence of protective compounds in seminal plasma, (ii) cooling the sex-selected sperm cells after sorting, (iii) isolating a particular number of sperm cells,<sup>1</sup> and (iv) diluting the isolated sperm cells to a particular concentration prior to freezing. Neither the Petitioner, the Petitioner’s expert, nor the prior art references themselves provide any explanation as to why one should expect to successfully

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<sup>1</sup> The “isolation” step is required by claims 3 and 4, and is discussed in more detail in the Claim Construction section above.

cryopreserve sex-selected semen by combining multiple damaging and stressful processing steps, one after another.

Indeed, contemporaneous evidence shows that senior personnel at Petitioner's own parent company, Genus, did not expect anyone to be successful at cryopreserving sex-selected sperm processed in the manner claimed by the '265 Patent. In a 1998 article entitled "Sexing Claims Dismissed," Genus's scientists dismissed the possibility of successfully cryopreserving sperm cells that have been centrifuged and sex-selected using flow cytometry. Ex. 2001, *Sexing Claims Dismissed*, FARMER'S WEEKLY (July 3, 1998).<sup>2</sup> In the article, Genus's senior veterinarian, Stuart Revell, expressed his conclusion that sperm cells sex-selected by flow cytometry are "unsuitable for freezing" because of the low output of flow cytometers and because the sperm cells have "been knocked about by a centrifuge." Ex 2001 at 3. In other words, Petitioner's parent company, at the time of the invention, was highly skeptical that one could successfully combine just some of the processing steps claimed in the '265 Patent—namely, flow-cytometric

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<sup>2</sup> The Farmer's Weekly article was raised in the '425 IPR as evidence of secondary considerations. Here, the article is direct evidence of the lack of a reasonable expectation of success.

sex-selection, centrifugation,<sup>3</sup> and freezing—to say nothing of adding more harmful processing steps, such as cooling the sperm cells or diluting them to a concentration of about 5-10 million cells per milliliter. The Petition completely ignores consider these contemporaneous statements from a real party-in-interest, despite the recent reminder of them during the IPR proceeding on the '425 Patent. *See, e.g.*, IPR2014-01550, Paper 15 at 44 (P.T.A.B. July 15, 2015). Petitioner's failure to demonstrate an expectation of success in making the particular combination claimed by the '265 Patent and its complete failure to take into account contrary statements made by its parent company mean that this Petition should be denied.

**F. Secondary Considerations Demonstrate the Non-Obviousness of the Claimed Invention**

Petitioner's obviousness analysis also fails to guard against hindsight in combining the prior art. An evaluation of objective evidence at the time of the invention, however, guards against such hindsight and demonstrates that the

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<sup>3</sup> Every challenged claim requires sorting to be done without the presence of protective compounds in seminal plasma, and centrifuging the sample prior to sorting is one way to achieve that. Further, claims 3 and 4 require isolating a particular number of sperm cells prior to final extension and freezing. This can also be achieved through centrifugation. See Claim Construction section, above.

combination of processing steps is not actually obvious. “Objective evidence of nonobviousness is an important component of the obviousness inquiry because evidence of secondary considerations may often be the most probative and cogent evidence in the record. It may often establish that an invention appearing to have been obvious in light of the prior art was not.” *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1349 (Fed. Cir. 2012) (quotations omitted). “[W]hen secondary considerations are present, though they are not always dispositive, it is error not to consider them.” *In re Huai-Hung Kao*, 639 F.3d 1057, 1067-68 (Fed. Cir. 2011). Objective evidence that may shed light on the non-obviousness of a claimed invention includes “teaching away” by others, the failure of others, and unexpected results created by the claimed invention. *Ecolochem, Inc. v. S. California Edison Co.*, 227 F.3d 1361, 1376-80 (Fed. Cir. 2000). These secondary considerations are addressed below and demonstrate the non-obviousness of the ’265 Patent.

### **1. Teaching Away by Others**

Genus’s statement that sperm cells sex-selected by flow cytometry are “unsuitable for freezing” (Ex. 2001 at 3) is a clear “teaching away” that demonstrates that the invention of the ’265 Patent was not obvious. A reference teaches away “when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in

a direction divergent from the path that was taken by the applicant.” *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1327 (Fed. Cir. 2009).

Teaching away can include criticizing, discrediting, or otherwise discouraging investigation into the claimed invention. *Id.*

Genus’s statements in the FARMER’S WEEKLY article are a classic case of teaching away. Genus specifically criticizes combining the ’265 Patent’s claimed processing steps of (i) centrifuging, (ii) sex-selection via flow cytometry, and (iii) freezing. Ex. 2001 at 3. These processing steps correspond perfectly to claim elements 1(b) and 1(d) in the ’265 Patent, which are required by every challenged claim. According to Genus, the stresses of the first two steps are just too high. Sex-selection via flow cytometry yields a low number of viable sperm cells (“output from the system was about 12% which had to be halved for the sex required. ‘Only 6% is available...’”) and centrifuging results in the sperm cells being “knocked about.” Ex. 2001 at 3. Combining these two processing steps alone was enough for Genus to conclude that the resulting sperm cells were “unsuitable for freezing.”

Genus’s criticism was not just a mere soundbite: Genus itself was, in fact, actually discouraged from following the approach taken in the ’265 Patent. After criticizing the combination of flow cytometry, centrifuging, and freezing, the article goes on to describe Genus’s evaluation of an alternate sex-selection

technology that does not involve flow cytometry. Ex. 2001 at 3 (“Genus believes flotation or filter methods of sexing semen offer a much greater chance of achieving a commercially viable system.”).

## **2. Failure of Others**

The same FARMER’S WEEKLY article also demonstrates that others in the industry had tried and failed to achieve the results of the ’265 Patent. Dr. McGuirk, the head of Genus’s R&D department, summarized the industry’s dim view of the flow cytometry-based sex-selection method being tested at Cogent: “The technique heralded by Cogent as a breakthrough has already been trialed by several international AI organizations and been abandoned.” Ex. 2001 at 3. Thus, at a time when others in the industry had given up development of flow cytometry as a sex-selection tool, XY and its partners were still pushing the technology ahead.

## **3. Unexpected Results**

Finally, the ’265 Patent’s nonobviousness is evident from the unexpected results achieved by the invention. Despite being directly involved in the research of one of Petitioner’s principal prior art references (Seidel 1997), the inventor himself was surprised by the unexpectedly good results of the claimed procedure. “[The] result was surprising because of the well-documented fragility of sperm” and because “[p]rior researchers had demonstrated that the stresses associated with



various selection methods or with cryopreservation resulted in significant losses in fertility and/or viability.” ’265 Patent, Ex. 1001 at 2:48-53.

The unexpected nature of the ’265 Patent’s results become even more clear when compared with the results of less complex procedures that include fewer processing steps. For example, the experiment in Fugger did not involve cooling sperm cells prior to final extension, isolating sperm cells prior to final extension, or diluting sperm cells to a concentration of about 5-10 million cells per mL. *See* Section V(D)(1), above. Despite this simpler procedure, which should impose fewer stresses on the sperm cells, Fugger’s results were not encouraging. Fugger did not report any “normal births” resulting from the use of frozen sex-selected semen, and reported only a 21.2% clinical pregnancy rate. Ex. 1007 at 2368-69.<sup>4</sup> In comparison, the ’265 Patent reports on a number of field trials occurring in 1997 and 1998 (including some that plainly pre-date the Fugger reference), with notably better results. *See, e.g.*, Ex. 1001 at 25:22-50 (Table 9). The pregnancy rates reported by the inventor when frozen sex-selected semen was used ranged from 33% on the low end all the way up to 68% on the high end. Ex. 1001, Field Trial #2, Col. 28, Table 11 and Col. 31, Table 21. Moreover, the inventor of the ’265 Patent was able to report on a number of field trials that resulted in actual birthed

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<sup>4</sup> A more detailed analysis of Fugger’s discouraging results is provided above in Section V(D)(2).

calves (*see, e.g.*, Ex. 1001 at Col. 28, Table 12), and reported that those calves “appear to be normal” and that “the population of calves produced to date from sexed semen appears to be no different from the population of controls.” Ex. 1001 at 31:62-67 and 32:6-7.

## **VII. Petitioner Fails to Demonstrate that the Prior Art Discloses the “Isolating” Step of Claims 3 and 4**

The Board can deny the Petition with regard to dependent claims 3 and 4 of the ’265 Patent for an additional, independent reason: the Petition does not demonstrate that the asserted prior art—and specifically the Salisbury and Seidel 1997 references that Petitioner relies on—discloses the “isolating” step of those claims. The patentee acted as his own lexicographer in defining the term “isolating,” and that definition requires a step of concentrating the sperm sample—such as through centrifugation—after sorting and cooling, but prior to final extension. *See* Claim Construction, section IV(C), above. Neither Salisbury nor Seidel 1997 disclose an “isolating” step as the patentee defines it. Instead, as explained in more detail below, the purported disclosure of the “isolating” step that Petitioner relies on in both references relates to dilution steps (not concentration steps) in preparing artificial insemination doses at some point well after final extension of the sperm cells.

**A. Salisbury Does Not Disclose the “Isolating” Step**

Petitioner alleges that a three-page spread of Salisbury discloses the isolation step of claims 3 and 4 (see Petition at 31-32, citing Ex. 1006 at 476-478), but these pages are taken wildly out of context. The numbers listed on these pages do not describe the number of sperm cells isolated from a sexed sperm sample after sex-selection, prior to final extension and freezing, as required by claims 3 and 4. Instead, pages 476-478 describe the number of unfrozen, un-sexed sperm cells used in an artificial insemination procedure. The chapter Petitioner cites to is explicitly entitled “Extenders and Extension of Unfrozen Semen” (emphasis added). *See* Ex. 1006 at 477. In some cases, the samples are not only unfrozen, they are not even cooled. *See* Ex. 1006 at 478, Table 16-12 (providing numbers for total sperm at “Ambient” temperature). In addition, each study described in the cited three-page spread relates to numbers of sperm at the insemination stage, not at some earlier pre-extension, pre-freezing stage. *See e.g.*, Ex. 1006 at 78, Table 16-12 (entitled “Fertility of unfrozen semen with different numbers of spermatozoa per insemination”) (emphasis added). Petitioner provides no explanation of how these numbers of un-sexed, unfrozen/uncooled sperm cells used in an artificial insemination procedure disclose or render obvious the isolation of different numbers of sperm cells that have undergone far more stresses (*i.e.*, removal of

seminal plasma, sorting, cooling) and will undergo additional stresses (i.e., from isolation, extension, and freezing).

**B. Seidel 1997 Does Not Disclose the “Isolating” Step**

Petitioner asserts that the “isolation” steps of claims 3 and 4 are disclosed by Seidel 1997. Petition at 31-32. This is not correct. First, the ’265 Patent requires the isolation step of claims 3 and 4—exemplified by the centrifugation process described in Ex. 1001 at 8:1-24—to occur after cooling and prior to any final extension. *See* Claim Construction, Section IV(D), above. Seidel 1997 describes a different procedural order wherein uncooled sperm cells are centrifuged immediately after sex-selection (Ex. 1005 at 56-64), followed by final extension of the sample (Ex. 1005 at 13:64-14:10), which is then cooled (Ex. 100 at 14:12-14). Second, Seidel 1997 does not disclose isolating between 300,000 and 3,000,000 cells before final extension (required by claim 3) or “no more than about 1,000,000 cells” before final extension (required by claim 4). Petitioner points to a statement in Seidel 1997 stating that after final extension, “3 to 5 million sperm per ml (for bovine species) may result.” Petition at 31, citing Ex. 1005 at 14:11-12. This is not a disclosure of isolating a particular number of sperm cells, but rather a disclosure of diluting a sample to a particular concentration.

Petitioner then assumes that this finally extended sample is placed in a straw of a particular volume. Petition at 31 (“0.25 milliliter containers are commonly

used (e.g., “straws”), resulting in a sample of 1.25 million sperm at the higher concentration.”). This assumption is belied by Seidel 1997’s actual disclosure. For horses, Seidel 1997 discloses using the semen directly, without placing it in a straw. Ex. 1005 at 14:14-16 (“In the equine species the sample may then be used in oviductal or other insemination processes...”). Meanwhile, Seidel 1997’s description of preparing a straw for use with cattle (Petition at 31, citing Ex. 1005 at 14:16-22) does not disclose the concentrating isolation step of claims 3 or 4. Instead, Seidel 1997 describes further diluting a finally extended sample to prepare an artificial insemination dose after the centrifugation, final extension, and cooling steps have already been completed. Ex. 1005 at 14:16-26. And as with the Salisbury reference, Petitioner provides no explanation of how the preparation of an artificial insemination dose renders obvious the isolation of a number of sperm cells that will still be subjected to additional damaging processing steps.

### **VIII. The Board Should Decline to Readjudicate the Teachings of Salisbury**

The Salisbury reference was directly at issue during the original prosecution of the ’265 Patent, and Petitioner uses Salisbury in exactly the same way that was rejected during original prosecution. The Board can and should exercise its discretion under 35 U.S.C. § 325(d) to refuse to revisit these issues and deny institution of *inter partes* review with regard to claims 3 & 4 on both Grounds 1 and 2, as well as for all challenged claims under Ground 2.

**A. The Board’s Discretion to Deny Institution Under 35 U.S.C. § 325(d)**

In reviewing a petition for *inter partes* review, 35 U.S.C. § 325(d) permits the Board to “take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.” The Board recently designated three “informative” decisions in which the Board exercised its discretion to deny institution where the same prior art and/or arguments were at issue during the original prosecution of the challenged patents. *See Cultec, Inc. v. Stormtech LLC*, No. IPR2017-00777, Paper 7 at 13 (P.T.A.B. Aug. 22, 2017) (informative) (denying institution under Section 325(d) because “the same or substantially the same prior art or arguments as are presented in the Petition previously were presented to the Office”); *Hospira, Inc. v. Genentech, Inc.*, No. IPR2017-00739, Paper 16 at 17–19 (P.T.A.B. July 27, 2017) (informative) (denying institution under Section 325(d) because the petitioner’s priority challenge was already considered by the Patent Office); *Unified Patents Inc. v. Berman*, No. IPR2016-01571, Paper 10 at 12 (P.T.A.B. Dec. 14, 2016) (informative) (denying institution on certain claims because “the Petition relies on the same or substantially the same prior art and arguments presented previously to the Office” and further noting that institution “would not be an efficient use of Board resources in this matter”).

**B. Salisbury Was Already Considered During Original Prosecution**

**1. The “isolating” step was fully considered**

Petitioner uses Salisbury for the purported disclosure of two key elements. First, for both requested grounds, Petitioner claims that Salisbury discloses the “isolating” steps of claims 3 and 4. Petition at 31-32, 51-52. This position was already considered and rejected by the Patent Office during original prosecution. The original set of claims presented in the patent application contained the limitation “isolating sperm from said selected sperm sample.” Ex. 1002 at 58-62. In examining these claims, the Examiner evaluated Salisbury but found that it did not teach the isolating step, stating “Salisbury does not teach to specifically isolate the sperm using centrifugation.” Ex. 1002 at 201. The Examiner remained consistent on this point throughout prosecution, and at no point did the Examiner ever assert that Salisbury discloses any form of “isolating” step, whether via centrifugation or otherwise. Petitioner provides no explanation as to why Salisbury needs to be re-reviewed on this point, and it would not be an efficient use of the Board’s resources to do so. Accordingly, the Board should refuse to consider Salisbury as disclosing the “isolating” step of claims 3 and 4.

**2. The concentration limitation was fully considered.**

For proposed Ground 2,<sup>5</sup> Petitioner relies on Salisbury for a second key element, namely for the purported disclosure of the limitation “suspending said sex-selected sperm cells in an extender to provide a concentration of sperm cells of about 5 million per milliliter to about 10 million per milliliter of extender.” This ground relies on the same reference in the same way as has already been considered by the Patent Office, and so the Board should exercise its discretion to deny institution of Ground 2 under 35 U.S.C. § 325(d). Specifically, application claim 38, which became issued claim 1, was amended during prosecution to add the 5-10 million cells/mL concentration limitation. The Examiner rejected this amended claim 38 as unpatentable under §103 over Salisbury in view of Spaulding and Shrimpton. Ex. 1002 at 433. In response, the patentee submitted a declaration of the inventor, John Schenk, who examined Salisbury and explained that Salisbury does not teach the 5-10 million cells/mL concentration limitation:

After reviewing each of the Salisbury reference, Spaulding reference, and Shrimpton reference, I do not find that any of them teach or even suggest all of the elements of independent claim 38. For example, claim 38 is distinguished from these references through the inclusion of the elements of sorting the sperm cells without the presence of protective compounds in seminal plasma and suspending at dilutions

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<sup>5</sup> Perhaps tellingly, Petitioner does not rely on Salisbury for disclosure of the concentration limitation in Ground 1.



of at least about 5 million per milliliter of extender to at least about 10 million per milliliter of extender.

Ex. 1002 at 496, ¶ 12 (emphasis added).

In response to Mr. Schenk's declaration, the Examiner did not dispute Mr. Schenk's conclusion that Salisbury lacks the claimed concentration limitation, and took issue only with whether the concentration limitation was adequately disclosed in the specification. Ex. 1002 at 700-01. The patentee subsequently directed the Examiner to the portions of the specification supporting the concentration limitation (Ex. 1002 at 746-47) and reiterated the argument that the Salisbury reference does not disclose suspending sorted sperm cells at about 5-10 million cells/mL (Ex. 1002 at 749). The Examiner again did not dispute the fact that Salisbury lacks the claimed concentration limitation, and the claims issued shortly thereafter (Ex. 1002 at 778-784). Thus, because Salisbury's disclosure of the claimed concentration limitation was fully considered during original prosecution, the Board should decline to readjudicate the same prior art and arguments in the Petition, and deny institution on Ground 2 for all of the challenged claims.

## **IX. CONCLUSION**

For at least the reasons discussed in this preliminary response, Petitioner has not shown a reasonable likelihood of prevailing on either of its proposed grounds for any of the challenged claims, and accordingly, the Petition should be denied in its entirety.

IPR2017-02184  
Patent No. 7,208,265  
Date: January 18, 2018

Respectfully submitted,

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**CERTIFICATE OF SERVICE**

The undersigned hereby certifies that a copy of the foregoing XY, LLC's Preliminary Response was served on counsel of record on January 18, 2018, by filing this document through the End-to-End System, as well as delivering a copy via electronic mail to the counsel of record for the Petitioner at the following address:

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IPR2017-02184

Patent No. 7,208,265

**CERTIFICATE OF COMPLIANCE PURSUANT TO 37 C.F.R. § 42.24**

This paper complies with the type-volume limitation of 37 C.F.R. §42.24.

The paper contains 9,802 words, excluding the parts of the paper exempted by §42.24(b).

This paper also complies with the typeface requirements of 37 C.F.R. §42.6(a)(2)(ii) and the type style requirements of § 42.6(a)(2)(iii) & (iv).

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