UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TRANS OVA GENETICS, LC.
Petitioner,

v.

XY, LLC
Patent Owner.

Case IPR2018-00249
Patent 6,372,422 B1

Before GRACE KARAFFA OBERMANN, ROBERT A. POLLOCK, and DAVID COTTA, Administrative Patent Judges.

COTTA, Administrative Patent Judge.

DECISION
Denying Institution of Inter Partes Review
35 U.S.C. § 314(a)
I. INTRODUCTION


Institution of an inter partes review is authorized by statute only when “the information presented in the petition . . . and any response . . . shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314; see 37 C.F.R. §§ 42.4, 42.108. Upon considering the Petition, the Preliminary Response, and the cited evidence, we conclude that Petitioner has not satisfied the burden under 35 U.S.C. § 314(a) to show that there is a reasonable likelihood that it would prevail with respect to at least one of the challenged claims.

A. Related Proceedings


B. The ’442 Patent (Ex. 1001)

The ’442 patent issued April 16, 2002, identifying George Seidel, Lisa Herickhoff, and John Schenk as co-inventors. Ex. 1001 [75]. The patent “relates to systems for sorting sperm via flow cytometry for sex-specific and low dose efforts at artificial insemination.” Id. at 1:15–21.

1 Petitioner identifies Intrexon Corporation as a real party in interest. Pet. 1.
2 Patent Owner identifies Inguran, LLC as a real party in interest. Paper 3, 2.
The ’422 patent discloses that “[m]any methods have been attempted to achieve the separation of X- and Y-chromosome bearing sperm” including “gravimetric techniques,” “[e]lectrical properties,” “a combination of electrical and gravimetric properties,” “motility,” “chemical techniques,” “as well as the addition of serum components. . . .” *Id.* at 1:43–62. “While each of these techniques has been presented as if to be highly efficient, in fact at present none of those techniques yield the desired level of sex preselection.” *Id.* at 1:62–65. The ’442 patent teaches that “[a]t present, the only quantitative technique used to achieve the separation of X- and Y-chromosome bearing sperm has been that involving individual discrimination and separation of the sperm through the techniques of flow cytometry.” *Id.* at 1:66–2:3

The ’442 patent discloses that “artificial insemination with a high success rate is [a problem] of a statistical nature in which a multitude of factors seem to interplay.” *Id.* at 3:26–28. “Such factors may range from factors within the sorting or flow cytometer steps to those in the collection as well as insemination steps.” *Id.* at 3:43–45. The ’442 patent asserts “prior to the present invention it has been extremely difficult to achieve lower dosage insemination with sexed sperm.” *Id.* at 3:8–10.

The ’442 patent asserts “the present invention provides improved sheath and collector systems for sorting of sperm cells to determine their sex through a flow cytometer.” *Id.* at 4:36–38. In addition, the ’442 asserts, “the advances achieved by the present inventors in both sexed and low dose artificial insemination represent significant advances which may, for the first time, make commercial applications feasible.” *Id.* at 3:19–22.
C. **Challenged Claim**

Petitioner challenges claims 1–4, 7, 8, 10, 13, and 14 of the ’442 patent. Claim 1, the only independent claim among the claims challenged in this proceeding, is reproduced below:

1. A method of producing multiple, sexed embryos from a non-human female mammal comprising;
   a. creating superovulation in said female mammal to create at least two eggs comprising the step of using an ovulatory pharmaceutical to cause multiple eggs to be produced;
   b. determining a sex of a sperm cell of a male mammal;
   c. sorting according to said sex of said sperm cells;
   d. inserting at least a portion of said sorted sperm cells into a uterus of said female mammal after an onset of estrus; and
   e. fertilizing a plurality of said eggs to produce at least two sexed embryos of the desired sex from said female mammal.


D. **The Asserted Grounds of Unpatentability**

Petitioner challenges the patentability of 1–4, 7, 8, 10, 13, and 14 of the ’442 patent on the following grounds (Pet. 3):

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Petitioner submits the Declarations of Jonathan H. Hartnett (Ex. 1002) and Dr. David J. Miller (Ex. 1003) in support of institution of inter partes review.

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Factual indicators of the level of ordinary skill in the art include “the various prior art approaches employed, the types of problems encountered in the art, the rapidity with which innovations are made, the sophistication of the technology involved, and the educational background of those actively working in the field.” Jacobson Bros., Inc. v. U.S., 512 F.2d 1065, 1071 (Ct.  

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Cl. 1975); see also Orthopedic Equip. Co., v. U.S., 702 F.2d 1005, 1011 (Fed. Cir. 1983) (quoting with approval Jacobson Bros.). Petitioner contends that the person of ordinary skill includes:

someone with at least a Bachelor of Science degree in the animal sciences, or closely related discipline, and at least 5 years’ experience in one or more of the following areas: mammalian reproductive technologies, including egg fertilization techniques such as artificial insemination (“AI”) and in vitro fertilization (“IVF”); study of the various factors that affect fertilization success; handling of mammalian sperm, including insemination and fertilization; embryo transfer; and/or the use of flow cytometric techniques to study and/or sort sperm.

At this stage in the proceeding, Patent Owner does not challenge Petitioner’s definition. Prelim. Resp. 13 (“For the sole purposes of this preliminary response, XY will use Petitioner’s interpretation of a POSA”). Accordingly, for purposes of this Decision, we accept Petitioner’s definition, which is supported by Dr. Miller’s declaration (Ex. 1003, ¶ 18) and is consistent with the level of skill reflected in the asserted prior art references. See Okajima v. Bourdeau, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (the prior art itself can reflect the appropriate level of ordinary skill in the art).

Moreover, we have reviewed Dr. Miller’s credentials (Ex. 1004) and, at this stage in the proceeding, we consider Dr. Miller to be qualified to provide an opinion on the level of skill and the knowledge of a person of ordinary skill in the art at the time of the invention.

B. Claim Construction

The ’422 patent expires on December 31, 2017, prior to this decision on institution. Ex. 1001. “[T]he Board’s review of the claims of an expired patent is similar to that of a district court’s review.” In re Rambus, Inc., 694
F.3d 42, 46 (Fed. Cir. 2012). In this context, claim terms are generally given their ordinary and customary meaning, as understood by a person of ordinary skill in the art, at the time of the invention, taking into consideration the language of the claims, the specification, and the prosecution history of record because the expired claims are not subject to amendment. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

We construe claim terms only to the extent necessary to resolve the controversy. See, e.g., *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999). For purposes of this proceeding, we need only construe the limitations in claim 1 requiring: “determining a sex of a sperm cell of a male mammal” and “sorting according to said sex of said sperm cells.”

Petitioner proposes that the phrase “determining a sex of a sperm cell” (hereinafter, “the determining limitation”) should be construed to mean, “determining whether the sperm cell carries an X or Y chromosome.” Pet. 26–27. Petitioner further proposes that the phrase “sorting according to said sex of said sperm cells” (hereinafter, “the sorting limitation”) should be understood to mean, “separating the sperm cells according to whether the cells carry an X or Y chromosome.” Pet. 17.

Patent Owner contends that Petitioner’s construction of the determining limitation is “unreasonably broad” because it does not require determining whether an individual sperm cell carries an X or Y chromosome. Prelim. Resp. 15. Patent Owner thus proposes that the determining limitation should be construed to mean “determining whether an individual sperm cell carries an X or Y chromosome,” which, Patent Owner
asserts, can presently be accomplished only using flow cytometry. *Id.* at 15, 16. Patent Owner “does not take issue” with Petitioner’s proposed construction of the sorting limitation, but notes that it must be construed as separate from and occurring before the determining limitation. *Id.* at 16.

We agree with Patent Owner that the sorting limitation must be performed separately from and subsequent to the determining limitation. Prelim. Resp. 18. In claim 1, the word “said” appears twice in the limitation “sorting according to *said* sex of *said* sperm cells.” (emphasis added). In each instance, the word “said” refers back to the prior limitation – i.e., the determining limitation. Thus, “said sex” and “said sperm cells,” refer to the sex of the sperm cells mentioned in the previous step of “determining a sex of a sperm cell.” Put another way, “sex” and “sperm cell” in the determining limitation serve as the antecedent basis for “said sex” and “said sperm cells” in the sorting limitation. Accordingly, we agree with the Patent Owner that “as a ‘matter of logic or grammar,’ the ‘determining’ step must occur before the ‘sorting’ step, not after it or simultaneously with it.” *Id.* (citing *Altris, Inc. v. Symantec Corp.*, 318 F.3d 1363, 1369 (Fed. Cir. 2003); and *Mformation Techs. Inc. v. Research in Motion Ltd.*, 764 F.3d 1392 (Fed. Cir. 2014)).

Our determination that the sorting limitation must be performed separate from and subsequent to the determining limitation obviates the need to resolve the issue of whether the determining limitation requires “determining whether an *individual* sperm cell carries an X or Y chromosome,” as proposed by Patent Owner. We note, however, that the requirement that the determining step occur prior to the sorting step is consistent with individual determination.
C.  Ground 1: Anticipation by Hagel

Petitioner asserts that claims 1–3, 7, and 8 are anticipated by Hagel. Pet. 24–34. 10 We have reviewed Petitioner’s assertions and supporting evidence, and, for the reasons discussed below, we conclude that Petitioner has not demonstrated a reasonable likelihood of prevailing in showing that claims 1–3, 7, and 8 are anticipated by Hagel.

i.  Disclosures of the Asserted Prior Art

Hagel

Hagel studied the effect of separating bull semen into X and Y chromosome-bearing fractions on the sex ratio of resulting embryos. Ex. 1005, Title. Of particular relevance to this decision, the bull semen in Hagel was separated into X and Y chromosome bearing fractions using a “thermal convection counterstreaming sedimentation and forced convection galvanization process.” Id. at Abstract. During this process, spermatozoa were separated into X and Y chromosome bearing fractions as follows:

A sedimentation galvanization cell (17) was filled with extended ejaculate and allowed to run for one to two hours at 6ºC. Spermatozoa from ejaculates which showed spermatozoa migration into both anodic (Y chromosome-bearing) and cathodic (X chromosome-bearing) chambers of the sedimentation-galvanization cell were collected, centrifuged

10 In footnote 3, Petitioner asserts “should the PTAB deem that Hagel fails to expressly or inherently disclose each limitation of these claims, then it should hold that Hagel renders these claims obvious.” Pet. 24, n. 3. Petitioner, however, does not provide argument or evidence as to why any limitation found not to be anticipated by Hagel would have been obvious. Petitioner’s unsupported assertion of obviousness is insufficient to raise obviousness as an independent ground for finding claims 1–3, 7, and 8 unpatentable.
and washed free of the particle-free extender by centrifugation and drawing off the supernatant fluid.

Id. at 295.

ii. Analysis

Claim 1 requires the steps of “determining a sex of a sperm cell of a male mammal” and “sorting according to said sex of said sperm cells.” Ex. 1001, 20:24–25. As discussed supra, we interpret these steps to require that the determining step must occur before the sorting step, not after it or simultaneously with it. Thus, in order to meet these limitations, one must first make a determination as to the sex of sperm cells and then sort sperm cells based on that determination.

Petitioner asserts that Hagele discloses both of these limitations by disclosing a process where X and Y chromosome-bearing sperm are caused to migrate to anodic and cathodic chambers and collected. Pet. 26–28; Ex. 1005, 295. Petitioner also notes that Hagele evaluated the efficacy of this process and determined the percentage of X and Y bearing sperm cells in each fraction collected. Pet. 27–28; Ex. 1005, 295, 296. However, Petitioner does not identify, and we do not find, any disclosure in Hagele suggesting that a determination as to whether sperm cells bear X or Y chromosomes is made before they are sorted. Id. Hagele does determine the sex of sperm cells, but such determination is not made before Hagele’s separation process. See e.g., Ex. 1005, 295 (“In vitro evaluation of the separation process was attempted . . . by staining with quinacrine mustard (17) and determining the percentage of spermatozoa with (positive – male) and without (negative – female) anterior fluorescing bodies (B-bodies)”).
Moreover, Petitioner has not provided any evidence that Hagele sorts sperm based upon a prior determination of the sex of sperm cells, as required by claim 1. Ex. 1001, 20:24–25 ("determining a sex of a sperm cell . . . [and] sorting according to said sex of said sperm cells" (emphasis added)). Indeed, Petitioner treats the sorting step and the determining step identically, without differentiating between the two steps or otherwise explaining how the sorting step is based upon the determined sex. See, id. at 28 (asserting that Hagele discloses the sorting limitation because “[a]s discussed above in Claim 1(b) [i.e. the determining limitation], Hagele reported separating the sperm cells based on whether they carry an X or Y chromosome”). Because Petitioner has not provided persuasive evidence that Hagele determines the sex of sperm cells, and then sorts them based upon that determination, we are not persuaded that Hagele anticipates claim 1.

For the reasons discussed above, we determine that the information presented in the Petition does not establish a reasonable likelihood that Petitioner would prevail in showing that claim 1 of the ’422 patent is unpatentable over the Hagele. Accordingly, we decline to institute an inter partes review of claims 1–3, 7 and 8 over Hagele.

D. Grounds 2 and 3

Petitioner asserts that claims 3, 7, and 8 are obvious over the combination of Hagele and Seidel (Ground 2) and that claim 4 is obvious over the combination of Hagele, Nowshari, and Donaldson (Ground 3). Petitioner does not allege that any of these references address the deficiencies identified in connection with Ground 1. In particular, Petitioner does not explain how the additional references cited in connection with Grounds 2 and 3 would have rendered obvious a method of producing
multiple sexed embryos including the steps of “determining a sex of a sperm cell of a male mammal” and then “sorting according to said sex of said sperm cells.” Therefore, we conclude that Petitioner has not demonstrated a reasonable likelihood of prevailing in showing that claims 3, 7, and 8 would have been obvious over the combination of Hagele and Seidel and that claim 4 would have been obvious over the combination of Hagele, Nowshari, and Donaldson. Accordingly, we decline to institute on Grounds 2 and 3 for the reasons provided in connection with Ground 1.

E. Ground 4

Petitioner asserts that claims 1–4, 7, 8, 10, 13, and 14 would have been obvious over the combination of Hagele and Spaulding. We have reviewed Petitioner’s assertions and supporting evidence, and, for the reasons discussed below, we conclude that Petitioner has not demonstrated a reasonable likelihood of prevailing in showing that claims 1–4, 7, 8, 10, 13, and 14 are rendered obvious by the combination of Hagele and Spaulding.

i. Disclosures of the Asserted Prior Art

Hagele

The disclosure of Hagele is discussed supra p. 9–10.

Spaulding

Spaulding discloses “the use of . . . antibodies to modify a semen sample so that the semen sample will be enriched in X-chromosome bearing sperm cells or Y-chromosome bearing sperm cells.” Ex. 1010, 1:26–30. Spaulding relies on differences in sex-associated membrane (SAM) proteins to separate X- and Y-chromosome bearing sperm. Id. at 5:28–31; 6:34–49 (“The novel antibodies produced in these methods selectively bind to proteins on the plasma membranes of either X- or Y-sperm. As such, they
are useful in modifying semen to preselect the sex of the offspring produced by it.”).

To produce X- and Y-sperm enriched samples, Spaulding “employed the Model 752 Flow Cytometer . . . for sorting sperm.” Id. at 9:39–40. Spaulding “sorted the sperm based on total DNA content as measured with the aid of the Hoechst dye” based on the fact that “X-sperm have more total DNA content than Y-sperm.” Id. at 9:41–43. The X- and Y-sperm enriched samples produced using flow cytometry were used “for isolation and identification of the novel, enriched plasma membranes vesicles and the SAM proteins of this invention.” Id. at 10:1–5. Spaulding teaches that “the time consuming process of sorting sperm into enriched X- and Y-subpopulations need only be done for initial identification of the SAM proteins of this invention.” Id. at 6:30–33.

Spaulding discloses various unsuccessful approaches that have been tried for separating X- and Y- chromosome bearing sperm cells. Id. at 1:37–3:64. More specifically, Spaulding discloses that “investigators hoped” that the greater DNA content of X-sperm cells as compared to Y-sperm cells would allow live cell populations to be “separated by density gradient sedimentation or flow cytometry. . . . however, neither has proven to be possible.” Id. at 2:54–61. Spaulding proposes that one reason for these failures may be that

the head, tail, and plasma membranes of the sperm, its other cellular material, and its highly compact nucleus all act to mask the small DNA content differences between X-sperm and Y-sperm. Some evidence for this masking effect is the fact that cytometric separation, while not feasible for whole sperm, has been useful to prepare enriched subpopulations of denuded sperm nuclei. Using this technique, the sperm nuclei are first separated from the membranes and other material of whole
sperm. They are then stained and partially sorted using a flow cytometer (Johnson and Pinkel, 1986). The result has been nuclei subpopulations enriched for the X- and Y-chromosome. *Id.* at 3:17–30.

**ii. Analysis**

As discussed in connection with Ground 1, Petitioner has not established that Hagele anticipated a method of producing multiple sexed embryos including the steps of “determining a sex of a sperm cell of a male mammal” and “sorting according to said sex of said sperm cells.” With respect to Ground 4, Petitioner asserts, in a footnote, “should the PTAB conclude that claims 1-3 and 7-8 are not anticipated by Hagele for any reason, then these claims would nonetheless be obvious over Hagele in view of Spaulding for all the reasons discussed in Ground 1 combined with the reasons discussed in Ground 4.” Pet. 36 n. 4. Petitioner, however, does not provide discussion beyond this footnote explaining how Spaulding renders any aspect of claim 1 obvious. Instead, the argument and evidence provided in connection with Ground 4 focuses exclusively on dependent claims 10, 13 and 14. *See*, Pet. 36–50. This is insufficient to demonstrate that any of the limitations set forth in claim 1 would have been obvious over the combination of Hagele and Spaulding. *See*, 37 C.F.R. §104(b)(4).

Even if we were to consider Spaulding’s application to the steps of claim 1 that we found were not anticipated by Hagele – i.e. “determining a sex of a sperm cell of a male mammal” and then “sorting according to said sex of said sperm cells” – the current record does not support that Spaulding renders these steps obvious. In connection with the limitation of claim 10 requiring “staining sperm cells of a male mammal,” Petitioner asserts “it would have been plainly obvious for a POSA utilizing Hagele’s method . . .
to substitute the flow cytometric method of Spaulding [in which sperm cells
are stained] in place of the sedimentation galvanization technique taught by
Hagele.” Pet. 39. Petitioner, supported by the testimony of Dr. Miller,
further asserts:

Here, design incentives and other market forces—namely, the
recognized need in the art to improve the process of producing
offspring of a desired sex in agriculturally important food
animals, such as cattle—would have prompted a POSA to
experiment with Hagele’s method to look for ways of
improving upon it. Ex. 1003 ¶ 104. One obvious way would
have been to use the recent advances in flow cytometry taught
by Spaulding to produce the sample of sex-sorted sperm. Id.
The POSA also would have had a reasonable expectation of
success in using the flow-cytometry method of Spaulding in
producing multiple, sexed embryos as Spaulding discloses that
its flow-cytometry method was able to successfully sort sperm.

Id. at 40. We are not persuaded that the evidence provided by
Petitioner supports the conclusion that the combination of Hagele and
Spaulding would have rendered obvious the use of flow cytometry in
place of sedimentation galvanization.

Although Spaulding does disclose sorting sperm into X and Y
fractions using a flow cytometer, the sperm so sorted was used “for isolation
and identification of the novel, enriched plasma membranes vesicles and the
Moreover, in the Background of Invention section of its disclosure,
Spaulding states that “cytometric separation” is “not feasible for whole
sperm,” even if it is “useful to prepare enriched subpopulations of denuded
sperm nuclei.” Id. at 3:21–30; see also, id at 2:54–61 (“investigators hoped
that the respective live cell populations could be separated by density
gradient sedimentation or flow cytometry. . . . [h]owever, neither has proven
to be possible.”). To sort sperm for purposes of sex-selective fertilization, Spaulding relies on antibodies rather than flow cytometry. *Id.* at 4:16–24. Particularly in view of Spaulding’s teachings regarding flow cytometry, Petitioner does not persuasively explain why the combination of Hagele and Spaulding would have suggested to the person of ordinary skill in the art substituting flow cytometry for the sedimentation galvanization technique taught by Hagele.

For the reasons discussed above, we determine that the information presented in the Petition does not establish a reasonable likelihood that Petitioner would prevail in showing that claims 1–4, 7, 8, 10, 13, and 14 would have been obvious over the combination of Hagele and Spaulding. Accordingly, we decline to institute an *inter partes* review of claim 1–4, 7, 8, 10, 13, and 14 over the combination of Hagele and Spaulding.

**F. Grounds 5 and 6**

Petitioner asserts that dependent claims 10 and 14 would have been obvious over the combination of Hagele, Spaulding and Rens (Ground 5) and that dependent claims 13 and 14 would have been obvious over the combination of Hagele, Spaulding, and Johnson ‘92 (Ground 6). Petitioner does not allege that any of these references address the deficiencies identified in connection with Grounds 1 and 4. In particular, Petitioner does not explain how the additional references cited in connection with Grounds 5 and 6 would have rendered obvious a method of producing multiple sexed embryos including the steps of “determining a sex of a sperm cell of a male mammal” and then “sorting according to said sex of said sperm cells.” Therefore, we conclude that Petitioner has not demonstrated a reasonable likelihood of prevailing in showing that claims 10 and 14 would have been
obvious over the combination of Hagele, Spaulding, and Rens and that claims 13 and 14 would have been obvious over the combination of Hagele, Spaulding and Johnson ’92. Accordingly, we decline to institute on Grounds 5 and 6 for the reasons provided in connection with Grounds 1 and 4.

III. CONCLUSION

For the foregoing reasons, we do not institute trial as to the challenge over Hagele (Ground 1), over the combination of Hagele and Seidel (Ground 2), over the combination of Hagele, Nowshari, and Donaldson (Ground 3), over the combination of Hagele and Spaulding (Ground 4), over the combination of Hagele, Spaulding, and Rens (Ground 5), and over the combination of Hagele, Spaulding, and Johnson ’92 (Ground 6).

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is denied, and that we do not institute inter partes review of any claim of the ’422 patent based on the grounds asserted in this Petition.