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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/765,577	02/12/2013	William M.C. Maxwell	XY-20 (US) Cont 3	8213
114661 XY, LLC 22575 State Highway 6 South Navasota, TX 77868	7590 01/08/2020		EXAMINER MCNEIL, STEPHANIE A N	
			ART UNIT 1653	PAPER NUMBER
			NOTIFICATION DATE 01/08/2020	DELIVERY MODE ELECTRONIC

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte WILLIAM M.C. MAXWELL, FIONA K. HOLLINSHEAD,
JUSTICE K. O'BRIEN, and GARETH EVANS

Appeal 2018–002871
Application 13/765,577
Technology Center 1600

Before DONALD E. ADAMS, RACHEL H. TOWNSEND, and
MICHAEL A. VALEK, *Administrative Patent Judges*.

VALEK, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellant submits this appeal under 35 U.S.C. § 134(a) involving claims to a method of producing a non-human mammalian embryo.¹ We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

STATEMENT OF THE CASE

Appellant's application is directed to "semen and sperm cell processing and preservation techniques." Spec. 8. Claims 54–62, 64–67, and 69–72 are on appeal and can be found in the Claims Appendix of the

¹ We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies, XY, LLC, as the real party in interest. Appeal Br. 3.

Appeal Brief. Claim 54 is representative of the claims on appeal. It reads as follows:

54. A method of producing a non-human mammalian embryo comprising:
- thawing cryopreservd sperm cells;
 - staining the thawed sperm cells;
 - sorting the thawed sperm cells into X chromosome-bearing and/or Y chromosome bearing subpopulations by flow cytometry;
 - establishing at least one sperm sample from the sorted sperm cells;
 - cryopreserving the sorted sperm sample;
 - thawing the twice-cryopreserved sperm sample;
 - fertilizing at least one egg with thawed, twice cryopreserved sperm cells through artificial insemination or in vitro fertilization; and
 - producing a non-human mammalian embryo.

Appeal Br. 23.

Appellant seeks review of the following rejections:

- I. Claims 54–56, 64, 65, and 70–72 under 35 U.S.C. § 103 as obvious over Schenk² and Colas;³
- II. Claim 57 under 35 U.S.C. § 103 as obvious over Schenk, Colas, and Prieto;⁴
- III. Claims 58, 59, 61, 62, 67, and 69 under 35 U.S.C. § 103 as obvious over Schenk, Colas and DeBoer;⁵ and

² Schenk et al., *Cryopreservation of Flow-sorted Bovine Spermatozoa*, *Theriogenology*, Vol. 52, 1375–1391 (1999) (“Schenk”).

³ US 3,973,003, issued Aug. 3, 1976 (“Colas”).

⁴ US 6,204,431 B1, issued Mar. 20, 2001 (“Prieto”).

⁵ US 5,633,076, issued May 27, 1997 (“DeBoer”).

IV. Claims 60 and 66 under 35 U.S.C. § 103 as obvious over Schenk, Colas, DeBoer, Davidson,⁶ and Massey.⁷

The issue for each of these rejections is whether the preponderance of the evidence supports Examiner's finding that Appellant's claims are obvious over the cited prior art. Appellant does not separately argue the dependent claims, therefore those claims stand or fall with claim 54. Moreover, Appellant does not present any argument for rejections II–IV beyond those that it presents for rejection I. Accordingly, our analysis is focused on Examiner's rejection of claim 54 as obvious over Schenk and Colas.

Findings of Fact

FF1. Schenk teaches protocols for staining, sorting, and cryopreserving sorted bovine sperm. Schenk, Abstr. In particular, Schenk describes experiments in which fresh bull semen was collected, stained, bulk sorted using flow cytometry, and ultimately frozen using liquid nitrogen. *See id.* at 1376–78. “Post-thaw progressive motility of bulk-sorted spermatozoa” was then assessed. *Id.* at 1385.

FF2. Based on the experiments described therein, Schenk concludes that “the entire sorting process damages sperm.” Schenk, 1389. However, Schenk characterizes this damage as “minor compared to . . . routine cryopreservation.” *Id.* Abstr. Schenk teaches that “[b]ased on standard procedures for evaluation of sperm quality, there is no basis for assuming that fertilizing potential of these flow-sorted sperm should be severely compromised for most bulls.” *Id.* at 1389. Moreover, according to Schenk,

⁶ US 5,434,058, issued July 18, 1995 (“Davidson”).

⁷ US 5,057,420, issued Oct. 15, 1991 (“Massey”).

“[p]rocedures developed to date result in reasonable pregnancy rates for sorted, frozen sperm artificially inseminated into heifers.” *Id.*

FF3. Colas teaches a process for freezing freshly collected ram semen “for subsequent artificial insemination of ewes.” Colas, Abstr. According to Colas, the “rate of lambing . . . after artificial insemination of ewes with ram semen frozen according to [this process] under normal conditions are always higher than 50%, and can be as high as 70%.” *Id.* at 4:46–49.

Analysis

Examiner finds that Schenk “teaches a method for sorting and cryopreserving” sperm from semen collected from bulls. Ans. 3. Examiner acknowledges that “Schenk does not specifically teach sorting sperm that have previously been cryopreserved,” nor does it “exemplify inseminating females with processed sperm.” *Id.* at 4. Examiner determines Colas teaches “a method for preserving ram semen in liquid nitrogen vapor (Example 1) and . . . that sperm samples so preserved can be thawed and used for artificial *in vivo* insemination (Examples 2 and 4), implying that careful freezing and thawing does not harm the sperm sample in a functional sense” because “[w]hile some sperm cells die as a result of the freezing . . . half of them survive.” *Id.* Thus, according to Examiner, one of skill in the art “would have had a reasonable expectation of success in performing the sorting, cryopreservation, and thawing method of Schenk on sperm that had previously been collected, frozen and thawed using the method of Colas” and would have been motivated to do so “for the expected benefit of added time flexibility between the collection of sperm from a male animal and the sorting process.” *Id.*

According to Appellant, “[i]t was well-known at the time of filing that a single cryopreservation cycle kills sperm, or otherwise compromises its ability to fertilize an egg due to extensive damage.” Appeal Br. 9–10 (citing Donnelly 892).⁸ Thus, Appellant contends “one of ordinary skill in the art would not have had a reasonable expectation that the frozen-sorted-frozen sperm of claim 54 could successfully fertilize an egg.” *Id.* at 11. In addition, Appellant argues “the method of claim 54—in which cryopreserved sperm is thawed, sex-sorted . . . cryopreserved a second time, thawed and then used to fertilized an egg—surprisingly and unexpectedly produces embryos that demonstrate a higher blastocyst development rate when compared to . . . eggs fertilized with sex-sorted, once-cryopreserved sperm.” *Id.* at 12–13 (citing Declaration of Ramakrishnan Vishwanath, dated Sept. 28, 2016 (“Vishwanath Decl.”); and Spec. 17 (Table 1)). Appellant urges that this evidence of unexpected results overcomes Examiner’s prima facie showing. *See Id.* at 12–18.

We are not persuaded by Appellant’s arguments and agree with Examiner’s statement of the rejection and responses to Appellants’ arguments in both the Answer and Final Action, which we adopt and incorporate by reference. We provide the following additional comments to Appellant’s arguments.

We are unpersuaded by Appellant’s reasonable expectation argument. *See* Appeal Br. 9–12. Both Schenk and Colas teach that non-human,

⁸ Donnelly et al., *Cryopreservation of Human Semen and Prepared Sperm: Effects on Motility Parameters and DNA Integrity*, American Society for Reproductive Medicine, Fertility and Sterility, Vol. 76, No. 3, 892–900 (2001) (“Donnelly”).

mammalian embryos can be successfully produced from sperm that has undergone at least a single cryopreservation cycle. FF2, FF3. Moreover, Schenk teaches that “reasonable pregnancy rates” can be achieved from sperm that has been stained, sorted, frozen and subsequently thawed for artificial insemination, notwithstanding the damage caused by those processes. FF1, FF2. Thus, the prior art teaches that embryos can be successfully formed from sperm that has undergone all of the processing steps recited in claim 54. The only difference is that claim 54 requires the sperm to undergo one of those steps—cryopreservation/thawing—twice. Moreover, claim 54 does not recite any particular rate of embryo production. Thus, it is enough that a skilled artisan would reasonably expect that a second cryopreservation would not so damage the sperm as to wholly preclude embryo production. *See In re O’Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988) (“Obviousness does not require absolute predictability of success.”). The record here supports Examiner’s finding that one of ordinary skill in the art would have had such an expectation as cryopreservation is described as a “routine” process that damages only a fraction of the sperm in a sample, while leaving the rest viable for fertilization. FF2. In other words, even considering the evidence that cryopreservation/thawing was known to damage *some* sperm cells in a sample (Appeal Br. 10), the evidence of record is sufficient to support Examiner’s finding that a skilled artisan would reasonably expect that a fraction of the sample would survive a second cryopreservation/thawing round, just as a fraction survived the first round, and that such a fraction would be viable to produce embryos just as was the case for the fraction that remained viable following the sorting and cryopreservation/thawing steps

taught in Schenk. *See* FF1, FF2. Accordingly, Examiner’s burden to demonstrate a prima facie showing of obviousness has been met.⁹

We are not persuaded by Appellant’s unexpected results arguments. The data Appellant relies upon in Table 1 of the Specification shows that insemination with sperm that was “frozen-thawed, sorted then frozen-thawed (Froz-Sort-Froz)” resulted in more blastocysts than “frozen-thawed unsorted (Control)” sperm and roughly the same number of blastocysts as “frozen-thawed & sorted (Froz-Sort)” sperm. Spec. 17. The results showing that the two sorted samples produced more blastocysts than the Control are not unexpected because the Specification indicates that “non-viable sperm” was removed as part of the sorting process, whereas presumably that same fraction of non-viable sperm remained in the unsorted Control sample. *Id.* at 16. In addition, a comparison to the Control sample does not demonstrate unexpected results compared to Schenk, which also teaches “sorting based on viability.” Schenk, 1377; *see In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991) (“[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art.”).

We are likewise unpersuaded that a comparison of the Froz-Sort-Froz and Froz-Sort sperm in Table 1 demonstrates unexpected results sufficient to overcome Examiner’s prima facie showing. Appellant argues that the Froz-Sort-Froz sperm exhibited a “higher blastocyst development rate” than the

⁹ Appellant does not challenge Examiner’s finding that one of ordinary skill in the art would have been motivated to add a cryopreservation step prior to sorting “for the expected benefit of added time flexibility between the collection of sperm from a male animal and the sorting process.” Ans. 4.

Froz-Sort sperm. Appeal Br. 12. But the numbers reported in Table 1 for these two samples are roughly the same. *See* Spec. 17 (Table 1). Appellant has not demonstrated that one of skill in the art would consider the slightly higher percentages reported for the Froz-Sort-Froz sperm at some time points in Table 1 to be significant differences from the percentages reported for the Froz-Sort sperm.¹⁰ *Cf.* Vishwanath Decl. ¶ 8 (stating that the rate was “significantly higher” versus the “frozen-thawed, unsorted sperm,” but only “higher” as compared to the “frozen-thawed, sex-sorted sperm”). Put another way, the record before this Panel does not demonstrate that these percentages are “different in kind” and therefore probative of non-obviousness, as opposed to being “merely [differences] in degree” or experimental error. *See Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731, 739 (Fed. Cir. 2013).

In addition, Appellant has not established a sufficient nexus between the Froz-Sort-Froz data in Table 1 and claim 54. According to the Specification, the Froz-Sort-Froz sample had a lower “% motile sperm” ($66.7 \pm 7.7\%$) than the Froz-Sort sample ($85.8 \pm 2.4\%$). This result would be expected because cryopreservation was understood to reduce motility. *See* Donnelly, 892 (“The most commonly reported detrimental effect of cyropresevation on human sperm is a marked reduction in motility.”). While insemination with less motile sperm might be expected to reduce blastocyst development rate, the protocol for the experiment reported in Table 1 involved insemination “with $1 \times 10(6)$ motile sperm/ml.” Spec. 16 (emphasis added). In other words, the protocol for the experiment in Table 1

¹⁰ Table 1 reports a higher percentage for the Froz-Sort sample at 48 hours. Spec. 17.

appears to involve an additional selection step in which only the motile fraction of each sample was used for insemination. *See* Spec. 13 (describing that sperm cells may be selected based on a “desired characteristic . . . such as . . . motility”). Claim 54, however, does not recite such a selection step, nor is claim 54 limited to fertilization with “motile” sperm. Appellant has not demonstrated that the claimed method without the additional selection step would result in a comparable blastocyst development rate.

Accordingly, to the extent any of the results in Table 1 are indeed unexpected, we do not accord such evidence substantial weight. *See In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) (“For objective evidence [of nonobviousness] to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention.”).

Reweighting “the entire merits of the matter” in light of Appellant’s unexpected results evidence, we determine the preponderance of the evidence supports Examiner’s rejection. *See In re Hedges*, 783 F.2d 1038, 1039 (Fed. Cir. 1986). Accordingly, we affirm the rejection of claims 54–56, 64, 65, and 70–72 under 35 U.S.C. § 103 as obvious over Schenk and Colas.

Appellant relies on the same arguments it makes for claim 54 for each of the other three obviousness rejections. *See* Appeal Br. 19–21. As explained above, we are unpersuaded by Appellant’s arguments regarding claim 54. Since Appellant does present any additional argument for reversing Examiner’s other obviousness rejections, we affirm those rejections as well.

CONCLUSION

Examiner's rejections of claims 54–62, 64–67, and 69–72 as obvious over the cited prior art are supported by the preponderance of the evidence. Accordingly, we affirm.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
54–56, 64, 65, 70–72	103	Schenk, Colas	54–56, 64, 65, 70–72	
57	103	Schenk, Colas, Prieto	57	
58, 59, 61, 62, 67, 69	103	Schenk, Colas, DeBoer	58, 59, 61, 62, 67, 69	
60, 66	103	Schenk, Colas, DeBoer, Davidson, Massey	60, 66	
Overall Outcome			54–62, 64–67, 69–72	

AFFIRMED