

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TRANS OVA GENETICS, LC.
Petitioner,

v.

XY, LLC
Patent Owner.

Case IPR2018-00248
Patent 7,723,116 B2

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

COTTA, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.64

I. INTRODUCTION

Trans Ova Genetics, LC. (“Petitioner” or “Trans Ova”) filed a Petition requesting an *inter partes* review of claims 42–59, 65–67, and 69 of U.S. Patent No. 7,723,116 B2 (Ex. 1001, “the ’116 patent”).¹ Paper 2 (“Pet.”). XY, LLC (“Patent Owner” or “XY”) filed a Preliminary Response to the Petition. Paper 6.² We determined, based on the information presented in the Petition and Preliminary Response, that there was a reasonable likelihood that Petitioner would prevail in showing that at least one of the challenged claims was unpatentable under 35 U.S.C. § 103(a) as obvious over the cited art. Pursuant to 35 U.S.C. § 314, the Board instituted trial on June 7, 2018. Paper 7 (“Institution Decision” or “Inst. Dec.”).

Patent Owners filed a Response to the Petition (Paper 17, “PO Resp.”) and Petitioner filed a Reply to Patent Owners’ Response (Paper 21, “Reply”). Petitioner filed a Motion to Exclude Evidence (Paper 24, “Mtn.”), to which Patent Owner filed an Opposition (Paper 25, “Mtn. Opp.”), and Petitioner filed a Reply (Paper 26, “Mtn. Reply”). On March 21, 2019, the parties presented arguments at an oral hearing. The transcript of the hearing has been entered into the record. Paper 28 (“Tr.”).

We have jurisdiction under 35 U.S.C. § 6. We issue this Final Written Decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. Based on the record before us, we conclude that Petitioner has demonstrated by a preponderance of the evidence that claims 42–59, 65, and 69 of the ’116

¹ Petitioner identifies Trans Ova Genetics, LC and Intrexon Corporation as real parties in interest. Pet. 2.

² Patent Owner identifies XY, LLC, and Inguran, LLC as real parties in interest. Paper 4, 2.

patent are unpatentable. We dismiss as moot Petitioner's Motion to Exclude.

A. Related Proceedings

Petitioner and Patent Owner identify *XY, LLC et al. v. Trans Ova Genetics, LC*, Case No. 1:17-cv-00944 (D. Col.) as relating to the '116 patent. Pet. 3; Paper 4, 2. Petitioner also identifies IPR2018-00247 as relating to the '116 patent. In IPR2018-00247, Petitioner challenged different claims of the '116 patent than are challenged in this proceeding. Pet. 3. On June 7, 2018, we issued a decision declining to institute review of the claims challenged in IPR2018-00247.

B. The '240 Patent (Ex. 1001)

The '116 patent issued May 25, 2010, identifying Kenneth M. Evans and Thomas B. Gilligan as co-inventors. Ex. 1001. The patent discloses "the use of a pulsed laser on a flow system for particle analysis" that can be used for "separating live X-chromosome bearing and Y-chromosome bearing sperm of all mammals at higher speeds, better purities and with equal or better sperm health outcomes, meaning less damage to sperm." *Id.* at 1:14–27.

The '116 patent teaches that laser light may be used to analyze biological particles by using a detector to "measure the change in intensity of the source light after incidence upon a particle(s) being analyzed." *Id.* at 2:17–21. According to the '116 patent, "it can be useful to accurately determine very small differences in the illumination light or emission light from two very similar biological particles (for example an X-chromosome bearing sperm cell versus a Y-chromosome bearing sperm cell)." *Id.* at 2:30–34.

The '116 patent discloses that, traditionally, a continuous wave (CW) laser is used for the analysis of particles in flow cytometry. *Id.* at 2:41–42. However, using CW lasers on sperm cells “can result in lower fertility of the sperm cells.” *Id.* at 2:47–48. The '116 patent discloses, “[s]urprisingly, even though sperm sorted on a high speed flow cytometer may be damaged by UV light between about 300-500 mW, it is now shown in this invention that powers between about 100-500 mW may not be damaging to sperm if they are delivered in pulses.” *Id.* at 5:39–44. “As a result, by the use of special forms of pulsed laser light, further improvements in the speed and sample purity can be seen. These types of lasers may be essential in the design and development of new flow cytometers perhaps having multiple sorting streams as well.” *Id.* at 6:4–9.

C. Challenged Claims

Petitioner challenges claims 42–59, 65–67, and 69 of the '116 patent. Claim 42, the only independent claim among the claims challenged in this proceeding, is reproduced below:

42. A flow cytometry system for sperm comprising:
a sheath fluid port to introduce a sheath fluid;
a sample injection element having an injection point
through which irradiatable sperm cells may be introduced into
said sheath fluid, said irradiatable sperm cells comprise[]
stained sperm cells having a percentage of stain as compared to
a standard control, said percentage of stain selected from a
group consisting of about 90%, about 80%, about 70%, and
about 60% of maximum stain;
a nozzle located in part below said injection point;
an oscillator to which said [] sheath fluid is responsive;
a pulsed laser;
a beam splitter;

a sperm cell fluorescence detector to detect fluorescence from said irradiatable sperm cells located in a stream flowing out of said nozzle;

said sperm cell fluorescence detector located near said stream of irradiatable sperm cells;

a processing unit connected to said sperm cell fluorescence detector to evaluate detected fluorescence from said irradiatable sperm cells;

a drop charge circuit located near said stream of irradiatable sperm cells flowing out of said nozzle to apply an electrical condition to a stream of said irradiatable sperm cells and sheath fluid, said drop charge circuit is responsive to said processing unit and applies said electrical condition based on said evaluated detected fluorescence;

a first and second deflection plate responsive to said processing unit, each plate disposed on opposite sides of a free fall area in which a drop forms, wherein said first and second deflection plates are oppositely charged; and

a sperm cell collector located below said first and second deflection plates.

Ex. 1001, 59:5–38.

D. Instituted Grounds of Unpatentability

We instituted trial based on each challenge to the patentability of the '116 patent presented in the Petition. The Petition challenged the patentability of claims 42–59, 65–67, and 69 of the '116 patent on the following grounds (Pet. 6):

Ground	References	Basis	Claim(s) Challenged
1	Evans ³ and Piper ⁴	§ 103(a)	42

³ Evans et al., WO 01/85913 A2, published Nov. 15, 2001 (Ex. 1005, “Evans”).

⁴ Piper et al., WO 92/08120, published May, 14, 1992 (Ex. 1009, “Piper”).

Ground	References	Basis	Claim(s) Challenged
2	Evans, Piper, and Tardif ⁵	§ 103(a)	42–59, 65, and 69
3	Evans, Piper, Tardif, and Lakowicz ⁶	§ 103(a)	51
4	Evans, Piper, Tardif, and Fukuda ⁷	§ 103(a)	66 and 67

Petitioner submitted the Declaration of Dr. J. Paul Robinson (Ex. 1003) in support of the Petition. Patent Owner submits the Declaration of Dr. Giacomo Vacca (Ex. 2002) in support of the Response to the Petition.

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. 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 “is someone with at least a Bachelor’s of Science degree in the biological sciences or closely related discipline and at least 5 years’ experience in one or more of the

⁵ Tardif et al., *Use of Hoechst 33342 Stain to Evaluate Live Fresh and Frozen Bull Sperm by Computer-Assisted Analysis*, 19(2) *Journal of Andrology* 201–206 (1998) (Ex. 1006, “Tardif”).

⁶ Lakowicz et al., US Patent No. 5,504,337, issued April 2, 1996 (Ex. 1008, “Lakowicz”).

⁷ Fukuda et al., US Patent No. 5,173,740, issued Dec. 22, 1992 (Ex. 1010, “Fukuda”).

following areas: flow cytometry, sperm sorting, and/or biomedical engineering.” Pet. 5–6. Patent Owner contends that Petitioner’s identification of the person of ordinary skill in the art “neglect[s] a key aspect of the relevant field, namely, lasers.” PO Resp. 22. Patent Owner’s expert, Dr. Vacca, contends that one of ordinary skill in the art “would possess a Bachelor’s degree in physics, optics, electrical engineering, or a biological science; at least 3 years’ experience with lasers; and at least 5 years’ experience in flow cytometry or sperm sorting.” Ex. 2002 ¶ 21.

Although Patent Owner’s proposed skill level specifies 3 years of experience with lasers, while Petitioner’s proposed skill level does not, we do not perceive any meaningful difference between the proposals that would impact our patentability analysis. Based on our review of the ’116 patent and the prior art, it appears that flow cytometry commonly involves the use of a laser. *See e.g.*, Ex. 1001, 3:29–32 (“Flow cytometry, using a high-speed cell analysis, or highspeed cell analysis and sorting instrument, often relies on a laser light source to illuminate a stream of fluid in which particles are entrained.”); Ex. 2002 ¶ 48 (“In the system design common to a large majority of all flow cytometers, . . . [a] narrow sample stream . . . is passed through an optical interrogation section, where light from one or more sources (typically lasers) is focused onto the cells”). Accordingly, 5 years of experience with flow cytometry, as specified on both parties’ constructions, would likely encompass significant laser-related experience.

Nonetheless, given the focus of the ’116 patent on the use of a pulsed laser, we adopt Patent Owner’s proposed skill level to make clear that the skilled artisan would have experience working with lasers. This determination is consistent with the level of skill in the art that is reflected in

the prior art of record. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001). We find that Dr. Robertson and Dr. Vacca are both qualified to provide opinions as to the perspective and knowledge of a person of ordinary skill in the art POSA. *See* Ex. 1003 ¶¶ 5–16; Ex. 1004; Ex. 2002 ¶¶ 6–15; Ex. 2003. Neither witness indicates that his opinion would change under a different definition of the level of ordinary skill in the art.

B. Claim Construction

We interpret claims of an unexpired patent using the “broadest reasonable construction in light of the specification of the patent in which [they] appear[.]” 37 C.F.R. § 42.100(b) (2017).⁸ Under that standard, we interpret claim terms using “the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant’s specification.” *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997). “Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaim[s] the broader definition.” *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004).

In our Institution Decision, we construed the following claim language, “having a percentage of stain as compared to a standard control,” so that we could determine whether the cited art disclosed the claimed

⁸ A recent amendment to this rule does not apply here, because the Petition was filed before November 13, 2018. *See* “Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board,” 83 Fed. Reg. 51,340 (Oct. 11, 2018) (amending 37 C.F.R. § 42.100(b) effective November 13, 2018).

percentage of stain. Inst. Dec. 8–11. At oral argument, Patent Owner represented that there was no need for us to construe this limitation because Patent Owner “concede[d] that there is no separate independent patentability based on outstanding limitation.” Tr. 26. Patent Owner further represented that “all the claims in this proceeding stand or fall with the pulsed laser limitation.” *Id.* at 25; *see also id.* at 26 (Conceding unpatentability if the panel finds in favor of Petitioner on the pulsed laser limitation: “JUDGE OBERMANN: Okay. So in other words, if we rule against you and we find that the pulsed laser would have been obvious to incorporate here, you will concede that there is no other -- you’re not pursuing any other ground of -- MR. SAFIULLAH: Your Honor, for this proceeding we are not pursuing any other ground other than the pulsed laser limitation.”).

Although the parties offer briefing regarding several additional claim terms (Pet. 15–21; PO Resp. 23–29), in view of Patent Owner’s representations at oral argument, we determine that no explicit construction of these claim terms is necessary to decide this case. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (“[W]e need only construe terms ‘that are in controversy, and only to the extent necessary to resolve the controversy’” (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))); *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) (“[C]laim terms need only be construed ‘to the extent necessary to resolve the controversy’”).

C. Principles of Law

To prevail in this *inter partes* review of the challenged claims, Petitioner must prove unpatentability by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d).

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations, including (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

We analyze the instituted grounds of unpatentability in accordance with the above-stated principles.

C. Ground 1

Petitioner asserts that claim 42 is rendered obvious by the combination of Evans and Piper. *See* Pet. 27–37. We have considered the question of patentability in view of all the evidence and arguments presented in this proceeding. Based on the record developed during this proceeding, we determine that Petitioner has shown by a preponderance of the evidence that claim 42 would have been obvious over the combination of Evans and Piper.

i. *Disclosures of the Asserted Prior Art*

Evans

Evans discloses the use of flow cytometry to isolate X-chromosome bearing and Y-chromosome bearing populations of spermatozoa. Ex. 1005, 14:5–18:12. Figure 1 of Evans is reproduced below.

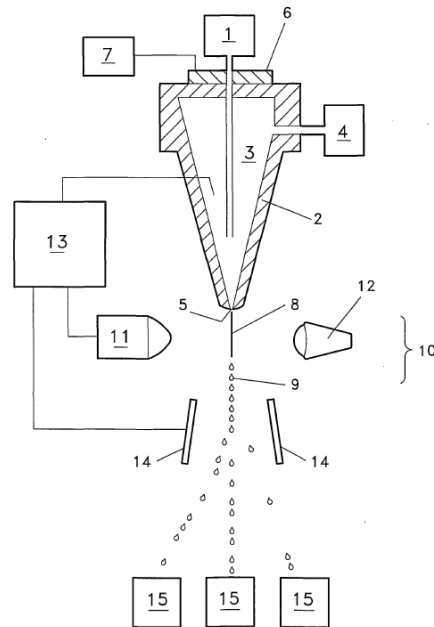


Figure 1 shows “a flow cytometer embodiment of [Evans’] invention.” *Id.* at 16:6. As shown in Figure 1, Evans’ flow cytometer includes a “cell source (1)” from which cells are deposited in a “fluid stream or sheath fluid (3)” within “nozzle (2).” *Id.* at 16:6–10. The sheath fluid (3) is supplied by “sheath fluid source (4).” *Id.* at 16:10–11. “[An] oscillator (6) acts upon the sheath fluid (3)” causing the “sheath fluid . . . exiting the nozzle orifice (5)” to “eventually and regularly form[] drops (9)” which “may entrain . . . sperm cells.” *Id.* at 16:16–22.

Evans’ flow cytometer may be used to separate sperm cells using a “particle or cell sensing system (10)” and a “detector or sensor (11)” that respond to the “relative presence or relative absence of a characteristic, such as fluorochrome bound to the particle or cell or the DNA within the cell that

may be excited by an irradiation source such as a laser exciter (12).” *Id.* at 16:24–17:3. “Because X-chromosome bearing spermatozoa contain more DNA than Y-chromosome bearing spermatozoa, the X-chromosome bearing spermatozoa can bind a greater amount of fluorochrome than Y - chromosome bearing spermatozoa. Thus, by measuring the fluorescence emitted by the bound fluorochrome upon excitation, it is possible to differentiate between X-bearing spermatozoa and Y-bearing spermatozoa.” *Id.* at 17:9–14.

To separate sperm cells, “emitted light can be received by sensor (11) and fed to some type of separation discrimination system or analyzer (13) coupled to a droplet charger which differentially charges each droplet (9) based upon the characteristics of the particle or cell contained within that droplet (9).” *Id.* at 17:15–19. Because the droplets are differentially charged “electrostatic deflection plates (14)” are able to “deflect drops (9) based on whether or not they contain the appropriate particle or cell.” *Id.* at 17:19–21.

Piper

Piper discloses the use of “a pulsed laser light source in a flow cytometer,” which Piper teaches is a “technique for rapid measurement of biological and physical properties of cells and particles.” Ex. 1009, 1:3–7. Piper discloses that using pulsed lasers in flow cytometry has advantages over conventional CW radiation sources, including that they are low cost and compact, and that they provide long-term reliability, high instantaneous illumination intensities, relaxed beam focusing requirements, good beam uniformity, and wavelength versatility. Ex. 1009, 1:33–2:20, 3:15–33.

ii. *Pulsed Lasers v. Continuous-wave Lasers*

Continuous-wave lasers are “a type of laser where the output is constant over time; in other words, it is always ‘ON.’” Ex. 2002 ¶ 31. Pulsed lasers are “a type of laser where the output is not constant over time, but occurs in discrete flashes, or short bursts of photons (pulses).” *Id.* ¶ 32. Because pulsed lasers flash on and off, they can be characterized as having both a “peak” and an “average” power.⁹ *Id.* ¶ 33. “Peak power is the maximum instantaneous power reached by the laser over the course of any one of its pulses. Average power is the power averaged over both the ON and OFF times.” *Id.*

The purpose of a laser in a flow cytometry system is to “deliver photons to passing cells so they can be interrogated.” *Id.* ¶ 39. According to Dr. Vacca “[o]ne of the most important parameters of this interaction is how many photons are delivered to the cell over the time that the cell spends transiting the laser beam.” *Id.* ¶ 39. Dr. Vacca explains how the amount of energy delivered to a cell can be calculated for CW and pulsed lasers:

For a CW laser, the energy per transit can be found simply with $E_{trans} = P * t_{trans}$.¹⁰ Care is needed, however, with pulsed lasers. Mode-locked pulsed lasers have relatively high repetition rates of ~ 80 MHz, leading to interpulse spacings of 12.5 ns; these are much shorter than typical cell transit times, which generally are around 2 μ s. Therefore, for mode-locked lasers, the energy per transit can be calculated as

⁹ “Power is defined in physics as the amount of energy or work (expended, transferred, delivered, etc.) in a unit of time. Power P is measured in watts (W) and is equal to energy E (measured in Joules, J) divided by the time t over which such energy is expended (measured in seconds, s): $P = E / t$.” Ex. 2002 ¶ 29.

¹⁰ “ E_{trans} ” is defined as the total energy carried by the laser beam, over its entire cross section, in the typical time (“ t_{trans} ”) it takes a cell to cross transit the laser beam. *Id.* ¶ 39. “ P ” is defined as power. *Id.* ¶ 36.

for CW lasers, simply using the laser's average power in the calculation. On the other hand, Q-switched lasers have relatively low repetition rates of ~ 1 to 100 kHz, leading to interpulse spacings of 10 to 1,000 μs ; these are much longer than typical cell transit times. Therefore, with Q-switched lasers, if a cell is hit by a pulse at all, it will be hit by only one pulse. In this case, the energy per transit is simply equal to the energy per pulse.

Id. ¶ 40. “Of course only a fraction of this energy actually interacts with the cell under analysis, since in flow cytometry the beam is focused to a spot considerably larger than the particles to be analyzed.” *Id.* ¶ 170. Further, “of the fraction that does impinge upon the cell, only a percentage of that actually gets absorbed by the cell.” *Id.*

iii. Analysis

Petitioner directs us to substantial evidence that all of the limitations of claim 42, with the exception of limitation requiring “a pulsed laser,” are disclosed by Evans. Pet. 27–37. Patent Owner does not contest that Evans discloses these limitations. See PO Resp. 29–38; Tr. 25 (“[A]ll the claims in this proceeding stand or fall with the pulsed laser limitation.”). Based on the arguments and evidence presented during this review, we determine that Petitioner has shown by a preponderance of the evidence that Evans discloses all of the limitations of claim 42, with the exception of the limitation requiring “a pulsed laser,” for the reasons set forth in the Petition. The remainder of our analysis focuses on the disputed limitation of claim 42, i.e., the requirement for “a pulsed laser.”

With respect to the requirement of claim 42 for “a pulsed laser,” Petitioner relies upon Piper. Pet. 31–34. Piper discloses the use of a “pulsed laser light source in a flow cytometer.” Ex. 1009, 1:3–4. Based on the

disclosure of Piper, Petitioner contends that “it would have been obvious for a POSA to modify Evans’ flow cytometry system with Piper’s pulsed laser . . . given the many advantages of pulsed lasers taught by Piper.” Pet. 33. For support, Petitioner directs us to Piper’s disclosure, which identifies “disadvantages of continuous lasers in flow cytometry, including that they are more expensive to purchase, install, and operate, have a relatively short laser tube lifetime, and are difficult to align.” *Id.* at 32 (citations omitted). Petitioner also directs us to Piper’s teaching that pulsed lasers “have particular advantages in application as flow cytometry sources”—including improved signal levels, relaxed beam focusing, good beam uniformity, and wavelength versatility. *Id.*

Patent Owner contends that a POSA would not have found it obvious to incorporate a pulsed laser in Evans’ flow cytometry system because “the massive amounts of energy delivered in even a single pulse[] by Piper’s pulsed laser would have killed each exposed sperm cell.” PO Resp. 29. According to Patent Owner, “[a] POSA would not have had a reason to use a pulsed laser to sort sperm cells, would not have had a reasonable expectation of success in using a pulsed laser to sort sperm cells, and would been led away from using pulsed lasers based on Piper’s disclosures.” *Id.*

Based on the arguments and evidence presented during this review, we find that Petitioner has shown by a preponderance of the evidence that it would have been obvious to incorporate a pulsed laser in a system of flow cytometry, like that disclosed in Evans, to sort sperm.

Evans discloses a system of flow cytometry for sorting stained sperm cells. Ex. 1005, 16:6–18:12 (detailing system for flow-sorting sperm), 8:22–9:2. Evans’ flow cytometry system may include “an irradiation source such

as a laser exciter (12) generating an irradiation beam to which the particle can be responsive.” *Id.* at 17:3–4, 31:5–11 (disclosing an electromagnetic radiation source “which can be laser light”). Evans, however, does not teach that the “laser exciter” can be pulsed.

Piper discloses the use of a pulsed laser in flow cytometry. Ex. 1003 ¶ 90; Ex. 1009, 1:3–4 (“The invention pertains to flow cytometry and more particularly to a pulsed laser light source in a flow cytometer.”). Piper describes disadvantages of using continuous lasers in flow cytometry, including that they are expensive to purchase, install, and operate (Ex. 1009, 1:33–2:3), have a relatively short laser tube lifetime (*id.* at 2:3–10), and are difficult to align (*id.* at 2:11–20). In contrast, Piper discloses that “high repetition rate pulse lasers, have particular advantages in application[s] such as flow cytometry.” *Id.* at 3:27–29. These advantages include “long term reliability in the low-power regime,” “compact size,” “low cost,” “relaxed beam focussing [sic] requirements,” “good beam uniformity,” “wavelength versatility,” and “high instantaneous illumination intensities.” *Id.* at 3:23–32.

Dr. Robinson testifies that in view of Piper, “[t]he POSA would have been motivated to” “modify the basic flow cytometry system, such as that disclosed in Evans, by using a pulsed laser, such as that taught by Piper” “given the many advantages of pulsed lasers taught by Piper.” Ex. 1003 ¶ 93. We credit this testimony, which is consistent with the disclosure of Piper and is not persuasively refuted by Patent Owner. Accordingly, we find that the skilled artisan would have been motivated to incorporate a pulsed laser in Evans’ flow cytometry system. Dr. Robinson further testifies that “the POSA would have reasonably expected Piper’s pulsed laser to work for

flow cytometry applications because Piper specifically taught that its pulsed laser was particularly useful and effective in flow cytometry systems like the one specifically disclosed in Evans.” *Id.* The testimony is also consistent with the prior art and persuasive. Accordingly, we find that the skilled artisan would reasonably have expected that a pulsed laser could be successfully incorporated in Evans’ flow cytometry system.

We acknowledge the evidence presented by Patent Owner that copper vapor lasers (“CVLs”) and certain neodymium-doped yttrium aluminum garnet (“Nd:YAG”) lasers, which are mentioned by Piper as examples of pulsed lasers that are “immediately available” or “becoming available” (Ex. 1009, 3:17–23), operate at powers that would likely destroy cells. Ex. 2002 ¶¶ 166–183. In particular, Dr. Vacca testifies that CVLs are “mainly used for micromachining applications” and “would make a fine choice for . . . drilling holes in metal plates,” but not for sorting cells. *Id.* ¶¶ 167–168. According to Dr. Vacca, CVLs typically have peak powers between 50 and 5000 kW, and therefore the energy per transit they impart would “totally obliterate the cells [they are] meant to interrogate.” *Id.* ¶¶ 168, 173. Similarly, Dr. Vacca testifies that a Q-switched Nd:YAG laser¹¹ is

¹¹ Dr. Vacca acknowledged that the genus of Nd:YAG lasers is broad and that Piper does not identify a specific species of Nd:YAG laser. Ex. 2002 ¶ 179. According to Dr. Vacca, there are two main categories of pulsed laser, Q-switched and mode-locked, with Q-switched lasers generally having “high average power (on the order of watts) and . . . very high peak power, on the order of kilowatts,” while mode-locked lasers generally have “lower power (milliwatts) and produce much smaller (on the order of watts) output pulses.” *Id.* ¶ 35. Dr. Vacca relied upon Q-switched Nd:YAG lasers as an exemplary species based on his conclusion that Piper suggests they were equivalent to CLVs. Ex. 2002 ¶¶ 179–180. We do not agree with Dr. Vacca that Piper suggests a specific species of Nd:YAG lasers. See Ex. 1009 at 3.

a “‘sleghammer-type’ tool” with “very similar characteristics to CVLs.” *Id.* ¶¶ 182, 183. In view of the characteristics of CVLs and Q-switched Nd:YAG lasers, Dr. Vacca testifies that “[a] practitioner seeking to improve the sperm sorting process would . . . not be motivated to use Piper’s disclosure of either a CVL or a Q-switched Nd:YAG laser instead of Evans’s CW laser, since the effect of doing so, as explained above, would be lethally destructive to the sperm cells.” *Id.* ¶ 184.

We do not find Patent Owner’s arguments or Dr. Vacca’s testimony persuasive to rebut Petitioner’s showing of the obviousness of incorporating a pulsed laser in Evans’ flow cytometry system because Piper is not limited to CVLs and Q-switched Nd:YAG lasers. Ex. 1009, 3:15–33. Patent Owner concedes that Piper is not “solely limited to the CVL or Nd YAG specifically” but suggests “the entire disclosure of Piper when read from front to back is disclosing these very high powered lasers.” Tr. 38. We do not read Piper so narrowly. Moreover, the POSA is also person of ordinary creativity, not an automaton, and it would have been well within the grasp of the POSA to select an appropriately powered laser to minimize damage to sperm cells. *KSR*, 550 U.S. at 421.

Piper’s disclosure of lasers that may be used in connection with its invention is quite broad. As Dr. Vacca explains, Piper’s identification of Nd:YAG lasers as exemplary is, itself, broad because it encompasses more than just Q-switched lasers. Ex. 2002 ¶ 179 (“Pulsed Nd:YAG lasers can be, e.g., Q-switched, cavity-dumped, mode-locked, flash-pumped, diode-pumped, fundamental or frequency-doubled, -tripled, or even -quadrupled, and with many variations within each of those categories.”). Moreover, Piper broadly describes its invention as involving “pulsed lasers” or, more

specifically, “high repetition rate pulsed lasers.” Ex. 1009, 3:27–28 (teaching that “high repetition rate pulsed lasers have particular advantages in application as flow cytometry”), 1:3–4 (“The invention pertains to flow cytometry and more particularly to a pulsed laser light source in a flow cytometer.”), 2:24–28 (“[A] flow cytometer having a flow system is provided characterized by a pulsed laser light source”). These disclosures are not limited to CVLs or Q-switched Nd:YAG lasers or even to “very high powered lasers.” To the contrary, Piper expressly contemplates that solid state lasers, of which Nd:YAG lasers are an example, will dominate in applications requiring “long-term reliability in the low-power regime” and states that such lasers are “especially appropriate to applications requiring multiple sources such as flow cytometry.” *Id.* at 3:20–27. Accordingly, we find that the ordinary artisan would not have considered Piper’s teachings to be limited to high powered lasers, and instead would have understood them to encompass any high repetition rate pulsed laser available at the time.

The record reflects that pulsed lasers operating at peak and average powers lower than what Dr. Vacca describes for CVL and C-switched Nd:YAG lasers were available prior to the filing of the application that resulted in the ’116 patent. For example, the ’116 patent describes two Vanguard lasers—one having an average power output of 0.15 watts and a peak power of 234.375 watts, the other having an average power output of 0.35 watts and a peak power of 546.875 watts—as “typical pulsed lasers.” Ex. 1001, 23:25–53. The ’116 patent also indicates that a 80 MHz Vanguard laser was available in 2001. *Id.* at 17:36–40 (explaining that the Vanguard Laser was “manufactured by Spectra-Physics” and was described in

“LaserForefront, Spectra-Physics, No. 30 (2001)”); *see also* Tr. 35 (“Your Honor, and I -- it’s not our contention that these lasers didn’t exist. Pulsed lasers that could be brought to lower powers existed at the time.”); Ex. 1024, 99:6–22 (Dr. Vacca deposition testimony acknowledging existence of differently powered pulsed lasers). The peak and average powers of these “typical pulsed lasers” are orders of magnitude lower than those of the CVLs and Nd:YAG lasers that Dr. Vacca describes as “obliterate[ing] the cells [they are] meant to interrogate.” *See* Ex. 2002 ¶¶ 168, 173, 182 (describing CVLs as having peak powers of 50–5000 kW and Nd:YAG lasers as having an average power of 50 W and a peak power of approximately 33 kW).

As discussed above, the POSA has a relatively high degree of skill. *See supra* pp. 6–8. We find that it would have been well within the grasp of the POSA to select an appropriately powered laser to minimize damage to sperm cells. *See* Ex. 2004, 19:19–20:5 (Dr. Robinson testimony that it would not have been difficult to adjust laser power and “change the experimental setup to test in different powers” explaining: “If you don’t have enough power to excite the dye, you would turn it up. If you have too much power, you would turn it down.”); Ex. 1005, 21:21–26, 25:12–16 (Evans reference describing operating flow cytometer with differently powered lasers).

Patent Owner also argues, more generally, that a POSA “would not have been motivated to [use] pulsed lasers to sort sperm cells – even if the average power were lower,” because pulsed lasers “were thought to be more damaging than CW lasers because of the pulsed laser’s high peak power (high energy per pulse).” PO Resp. 30–31. We acknowledge Dr. Vacca’s

testimony that pulsed lasers deliver peak powers and peak intensities¹² that are orders of magnitude larger than their average power, and thus, orders of magnitude larger than the average power of a conventional CW laser.

Ex. 2002 ¶ 38.¹³ We also acknowledge Dr. Vacca’s opinion that in view of the larger peak powers of pulsed lasers, a POSA would have had a “disincentive to move to pulsed lasers with higher peak powers than the maximum advisable CW laser power.” *Id.* ¶ 67.

We are not persuaded by Dr. Vacca’s testimony that the relatively high peak pulse power of pulsed lasers would have discouraged a POSA from using pulsed lasers because Piper clearly suggests to use pulsed lasers in flow cytometry for cell sorting. Ex. 1009, 1:3–4 (“The invention pertains to flow cytometry and more particularly to a pulsed laser light source in a flow cytometer.”); *id.* at 8:23–25 (“The device of the present invention is ideally suited to cell counting, cell sorting and cell identification in hospitals, research facilities and clinical laboratories.”). We find that, to the extent peak pulse power would have caused a POSA concern, Piper’s suggestion to use pulsed lasers in flow cytometry to sort cells would have assuaged such concerns. This is particularly so given the relatively high degree of skill in the art including years of experience with both lasers and flow cytometry and cell sorting (*see supra* pp. 6–8), and the fact that the POSA is presumed

¹² In this context, intensity is defined as the number of photons (of a certain wavelength) per unit time (i.e., the power P) going through a unit area A : $I = P / A$. Ex. 2002 ¶ 36.

¹³ Although the peak pulse power is higher than the average power of a comparable CW laser, the total energy delivered to the each cell using a pulsed laser like the Vanguard laser is “comparable or, in fact, significant smaller than the equivalent energy carried by a CW laser in the same span.” Ex. 2002 ¶ 176.

not to be an automaton but a person of ordinary creativity. *KSR*, 550 U.S. at 421.

Piper’s teaching to use a pulsed laser to sort cells in flow cytometry is consistent with Evans’ teaching that “[a] reduced amount of irradiation time within the excitation laser beam may result in less stress or damage to the spermatozoa.” Ex. 1005, 24:28–25:1. Piper’s teaching to use a pulsed laser is also consistent with Evans’ stated objective to “decrease the total lumens an object is exposed to,” and, more specifically, to “increase the power of the light source without increasing the total lumens the object is exposed to.” *Id.* at 9:14–18. Whereas Evans achieves this objective not by pulsing its beam but by changing the shape of its beam pattern, reducing the height but increasing the width of its beam (*id.* at 25:2–18, Fig 13a and 13b), using a pulsed laser in place of a CW laser with a comparable average power would similarly reduce the time sperm is exposed to laser light and potentially reduce the total lumens sperm are exposed to. *See* Ex. 2002 ¶ 176 (Dr. Vacca testimony explaining that, compared to a CW laser having similar average power, the total energy delivered to the each cell using a pulsed laser is “comparable or, in fact, significant[ly] smaller than the equivalent energy carried by a CW laser in the same span”). We find that this would have supported the teaching in Piper to use a pulsed laser in flow cytometry to sort cells and would have supported the reasonable expectation of a POSA that they would be successful in doing so.

We acknowledge that the peak pulse power of a pulsed laser may be higher than the average power of a CW laser, but we are not persuaded that this consideration outweighs the potential benefits a pulsed laser would provide in reduced time of exposure and reduced total energy delivered in

considering a POSA's motivation and expectation of success. *See* Ex. 1005, 9:14–18, 24:28–25:1; Ex. 2002 ¶ 39 (Dr. Vacca testimony that “beyond average (and peak) power, beyond average (and instantaneous) intensity (all of which are characteristics of the laser and the beam), it is important to define the *interaction* of such beam with a cell. One of the most important parameters of this interaction is how many photons are delivered to the cell over the time that the cell spends transiting the laser beam. This can be referred to as the **energy per cell**.”); *see also* Ex. 2002 ¶ 171 (wherein Dr. Vacca used the “total amount of energy carried by the beam during a cell's entire transit time through the laser beam” as “the analogue” to compare CVLs and CW lasers).

In the portion of its Response discussing the “Background of the Technology,” Patent Owner provides evidence that “[s]perm cells are fragile and susceptible to damage during the flow cytometric sorting process.” PO Resp. 5–7. For example, Patent Owner cites evidence that it was known that irradiation could damage sperm cells. *Id.* (citing Ex. 2007, 266 (“[E]xposure of these stained [sperm] cells to laser illumination results in a significant increase in the proportion of sperm nuclei showing chromosomal damage as well as an increase in the degree of damage per sperm nucleus.”); Ex. 1005, 5:2–3 (“Irradiation of cells, such as spermatozoa, with laser light may result in damage to the cells or the DNA contained within them.”); Ex. 1001, 2:46–48 (“For example, with respect to sperm cells, irradiation can result in lower fertility of the sperm cells.”)).¹⁴ Patent Owner also cites evidence that it was

¹⁴ Patent Owner also cites a more recent study discussing the impact of laser power on sorted-sperm recover which finds that although the authors expected that “the lower the laser output power the less effect upon the fertilization and embryo development,” in fact, exposure of sperm to “125

known that flow cytometry could be damaging to sperm cells. *See e.g.*, Ex. 2006, 1178 (1993 article by Petitioner’s expert, Dr. Robinson, suggesting that using flow cytometry to sort sperm “may be damaging to mammalian chromosomes, mak[ing] flow cytometry unlikely to become a commercially practical method”) (cited at PO Resp. 5); Ex. 2002 ¶¶ 57–59 (Dr. Vacca opining that given some of the unique characteristics of sperm, it is “even more important to avoid imparting any unnecessary stress on [sperm] during the sorting process, and there are several risks of doing so: relatively high fluid pressures, relatively high velocity gradients leading to strong shear forces, impact forces upon collection of a cell-containing sorted droplet, and even the amount of UV light that the cells are subjected to during interrogation”).

At oral argument, Patent Owner argued that “even if the pulsed lasers were available, no one would think to use them for sperm sorting because they believed that the upper limit of powers that the sperm cell could take was 300 milliwatts.” Tr. 40. Petitioner contends that this is a new argument that was not presented in Patent Owner’s Response, depriving Petitioner of the opportunity to respond. Tr. 52. We agree with Petitioner that Patent Owner did not specifically argue that the unique fragility of sperm provides a reason for distinguishing the claimed flow cytometry system over the cited art. *See* PO Resp. 29–38. We nonetheless address the Patent Owner’s argument because the “fragility” of sperm was discussed in the Response as “background.” PO Resp. 5–7.

mW did not affect fertilization rate or embryonic development, but 25 mW increased the percentage of unfertilized eggs and underdeveloped embryos.” Ex. 2013, 1335 (cited at Resp. 7).

We are not persuaded that Patent Owner's evidence regarding the "fragility" of sperm renders the use of a pulsed laser in a sperm sorting flow cytometry application non-obvious. Evans' disclosure of sorting sperm in a flow cytometry system addresses Patent Owner's evidence suggesting that a POSA would have had concerns about using flow cytometry to sort sperm (Ex. 2006, 1178; Ex. 2002 ¶¶ 57–59) and Evans' use of a CW laser would have suggested to a POSA that illuminating sperm with some degree of laser light was acceptable, particularly given that the POSA has a relatively high degree of skill. *See supra* pp. 6–8.

We acknowledge that the peak pulse power of a pulsed laser may be considerably higher than the average power of a comparable CW laser. However, we are not persuaded that this would have given a POSA reason to doubt that Piper's teaching to sort cells in a flow cytometer using pulsed lasers could be applied with a reasonable expectation of success to sperm cells because Piper's teaching is not limited to any particular type of cells. Ex. 1009, 1:3–4; *id.* at 8:23–25. We recognize that sperm may be more difficult to work with than some other types of cells, but Piper does not specify that pulsed lasers may be used only in sorting more robust cell types and the evidence does not reflect that sperm cells are so far outside the norm as not to be encompassed by Piper's teaching of "cell sorting." *See* Ex. 2004, 43:23–53:25 (Dr. Robinson opining on the relative difficulties of sorting different types of cells, characterizing cell cultures, lymphocytes and yeast cells as comparatively easier to work with than sperm, platelets, and neutrophils); Ex. 2002 ¶¶ 57–58 (Dr. Vacca opining that sorting sperm cells for gender selection presents "some particular difficulties" as compared to sorting cells in general). Moreover, as discussed above, using a pulsed laser

in place of a CW laser with a comparable average power would reduce the time sperm is exposed to laser light and reduce the total lumens sperm are exposed to. Accordingly, we find that a POSA would reasonably have expected Piper's teachings regarding the use of a pulsed laser to be applicable to Evans' flow cytometry system for sorting sperm cells. See Ex. 1003 ¶¶ 78, 93.

Patent Owner argues that Piper's solution to the problem of ensuring each cell is illuminated teaches away from using pulsed lasers to sort sperm cells. PO Resp. 36–37. Piper teaches that the relatively short pulse duration and relatively long duty cycle for pulsed lasers “ha[d] previously been taken to rule out the use of pulsed lasers for flow cytometry” because it was difficult to “ensur[e] each cell is illuminated as it passes through the interaction region.” Ex. 1009, 3:33–4:11. However, Piper's “inventors . . . demonstrated that pulsed lasers operating at high pulse rates (~ 10 kHz) can be quite simply matched to the droplet flow rates (also $\sim 10^4$ per second) usually employed, given appropriate adjustments in focal spot size of the illuminating beam at the interaction region.” *Id.* at 4:4–7. Piper further teaches that “only approximate synchronisation of the laser pulse rate and droplet flow rate is necessary if an extended focal spot size is used so that the transit-time across the interaction region is of the order of the interpulse period.” *Id.* at 4:8–11. Patent Owner argues that “[a]t the time of the invention, a POSA would have recognized that Piper's solution would be unworkable for sorting sperm cells for multiple reasons.” PO Resp. 37. Patent Owner explains:

First, because cells in a sample stream do not arrive at the interrogation laser at equally spaced (*i.e.*, predetermined) times, adopting Piper's pulsed laser would cause a drastic reduction in

the purity of the sort, an increase in aborted sorts, and a reduction in effective sorting rate. Ex. 2002, Vacca Decl., ¶ 191. Second, spreading out the beam's focal spot size over a larger area than is typically used for sperm sorting applications would cause extremely high rate of coincidences, which would degrade the sort purity, increase aborted sorts, and ultimately reduce the effective sort rate. *Id.* at ¶ 192. Third, there would be greater uncertainty in longitudinal position of a detected cell because of the number of additional cells within the beam spot (*i.e.*, because of its larger size). That would result in having to deflect a large number of droplets for each detected cell, which would cause the sort rate to plummet. *See id.* at ¶ 196.

Id.

We are not persuaded that these arguments rebut Petitioner's showing because we find that Piper's solution was specific to lasers having pulse rates that are approximately the same as the droplet flow rate of a flow cytometer. By the time the '116 patent was filed, pulsed lasers having significantly higher pulse rates were available. For example, a Vanguard lasers discussed in the '116 specification is disclosed to have a pulse rate of "80 million pulses per second (80 MHz)." Ex. 1001, 17:37–39. We find that the availability of such lasers would have obviated the need to synchronize the pulse rate with the droplet flow rate, and thus, obviated Patent Owner's argument that Piper's solution was unworkable. Selecting such a laser would have been well within the relatively high level of ordinary skill in this particular field of endeavor. *See supra* pp. 6–8.

Patent Owner argues that the advantages of pulsed lasers taught by Piper are "completely divorced from the issue of whether any of these advantages would have motivated a POSA to *sort sperm cells*" and that there is no evidence that the advantages identified in Piper would allow Piper's laser "to be used successfully in flow cytometry to sort sperm cells." PO

Resp. 35. Patent Owner then cites testimony from Dr. Vacca rebutting the advantages taught by Piper.¹⁵ *Id.* We are not persuaded that this evidence rebuts Petitioner’s showing.

For the reasons discussed above, particularly given the relatively high degree of skill in the art, we find that a POSA would reasonably have expected that Piper’s laser could be used successfully in Evans’ flow cytometry system to sort sperm cells. Further, the POSA would have been looking for ways to improve sperm cell sorting, and the POSA would have been well-informed of the parameters for selecting a pulsed laser less likely to damage those relatively delicate cells. As to Dr. Vacca’s testimony rebutting the advantages of pulsed lasers, Dr. Vacca concedes that one of the benefits of pulsed lasers identified in Piper – “high illumination intensities” – is an advantage, but contends that it would have been recognized as an advantage “*only in retrospect* due to the disclosure of the ’116 Patent.” Ex. 2002 ¶ 186. This is not persuasive to rebut Petitioner’s showing because Piper unequivocally teaches that high instantaneous illumination is an advantage. Ex. 1009, 3:28–30 (“[H]igh repetition rate pulsed lasers have particular advantages in application as flow cytometry sources including high instantaneous illumination intensities (giving high signal levels).”). Dr. Vacca does not explain why a POSA would have failed to appreciate this expressly taught benefit until the disclosure of the ’116 patent. See Ex. 2002 ¶ 186.

¹⁵ Patent Owner cites to paragraphs 191–197 of the Vacca Declaration. PO Resp. 35. However, these paragraphs do not address the advantages of pulsed lasers. We understand Patent Owner to have intended to cite paragraphs 186–189 of the Vacca declaration and direct our analysis to those paragraphs.

Dr. Vacca's testimony dismissing Piper's teaching that pulsed lasers have the advantage of "good beam uniformity" is similarly unpersuasive. Dr. Vacca opines that CVL and Nd:YAG lasers do not provide good beam uniformity. *Id.* ¶ 188. However, as discussed above, we do not find Piper's disclosure to be so limited.

Although Dr. Vacca's testimony rebutting the advantages of "relaxed beam focusing requirements" and "wavelength versatility" is more persuasive, we do not agree that either of these properties would have been considered a drawback to using pulsed lasers. Moreover, we find that even excluding "relaxed beam focusing requirements" and "wavelength versatility," as advantages of pulsed lasers, the other advantages disclosed by Piper—i.e., high instantaneous illumination intensity, good beam uniformity, long-term reliability, compact size, and low cost—provide sufficient reason for a POSA to have incorporated a pulsed laser in Evans' flow cytometry system. Ex. 1009, 3:23–32; Ex. 1003, ¶ 93; Ex. 2002 ¶¶ 186–189.

Patent Owner argues that the existence of a long-felt need demonstrates the non-obviousness of the claimed flow cytometry system. According to Patent Owner, the use of pulsed lasers and the sorting of sperm by flow cytometry were both separately known "at least as early as 1992," but "the need to lessen the damage to sperm cells caused by constant UV radiation (through CW lasers) went unresolved until the invention of the '116 patent." PO Resp. 56. Patent Owner argues that the 10-year gap between this knowledge and the filing of the application that resulted in the '116 patent, "directly counters Petitioner's argument that combining the pulsed laser with a flow cytometry system for sexing sperm would have

been obvious.” *Id.* at 57. We are not persuaded that Patent Owner has shown long-felt need.

Prior to the filing of the application for the ’116 patent, it was known that CW lasers could be used in flow cytometry to sort sperm. *See generally* Ex. 1005. Patent Owner has not identified persuasive evidence that the ’116 patent provided a solution to a problem recognized at the time the application for the ’116 patent was filed. PO Resp. 56–60 (citing Ex. 2002, ¶¶ 165–167); *In re Gershon*, 372 F.2d 535, 538 (CCPA 1967) (“Since the alleged problem in this case was first recognized by appellants, and others apparently have not yet become aware of its existence, it goes without saying that there could not possibly be any evidence of either a long-felt need in the . . . art for a solution to a problem of dubious existence or failure of others skilled in the art who unsuccessfully attempted to solve a problem of which they were not aware.”); *In re Kahn*, 441 F.3d 977, 990–91 (2006) (“Absent a showing of long-felt need or the failure of others, the mere passage of time without the claimed invention is not evidence of nonobviousness.”).

For the reasons set forth above, we find that Petitioner has established by a preponderance of the evidence that claim 42 would have been obvious over the combination of Evans and Piper.

D. Ground 2, claim 42

Petitioner asserts that claims 42–59, 65, and 69 would have been obvious over the combination of Evans, Piper, and Tardif. *See* Pet. 38–52. We have considered the question of patentability in view of all the evidence and arguments presented in this proceeding. For the reasons discussed in section E, below, we begin with a detailed analysis of independent claim 42.

Based on the record developed during this proceeding, we determine that Petitioner has shown by a preponderance of the evidence that claim 42 would have been obvious over the combination of Evans, Piper, and Tardif.

i. Disclosures of the Asserted Prior Art

Evans and Piper

The disclosures of Evans and Piper are discussed *supra* pp. 11–12.

Tardif

Tardif discloses research performed “to investigate possible procedures for evaluating living bull sperm stained with Hoechst 33342.” Ex. 1006, Abstract. Tardif studied how factors including the concentration of Hoechst 33342 stain affect sperm. *Id.* In one experiment, Tardif studied sperm stained with 0, 2.5, 5, 10 and 20 µg/ml of Hoechst 33342. *Id.* at 202. In a second experiment, Tardif studied sperm stained with 0, 10, 20, 40 and 60 µg/ml of Hoechst 33342. *Id.* at 202–203. In the second experiment, “it was determined that 40 to 60 µg/ml of dye in EYGT [egg yolk-glycerol-Tris] or WMG [whole milk-glycerol], with UV illumination for 20 minutes, was optimal.” *Id.* at Abstract. In a third experiment, Tardif replicated the “most useful treatments” from the prior experiments, and stained sperm at concentrations of 40, 50, and 60 µg/ml of Hoechst 33342. *Id.* at 204.

Tardif concluded, “[a]s a result of these experiments, concentrations of dye and convenient operational exposure times were established that did not appreciably alter the proportion of motile sperm or other motion characteristics.” *Id.* at 205. In addition, Tardif found that while a stain concentration of 2.5 µg/ml may be sufficient for computer assisted sperm analysis in a simple medium, sperm entrained in complex media, such as

EYGT or WMG, may require “considerably higher concentrations” of Hoechst 33342 for “proper staining.” *Id.*

Tardif also discloses exposing the fluorescently stained cells to a strobe light. “The exposure to the strobe light is about 10 to 15 microseconds, with a frequency of 60 cycles/second, so sperm are exposed very briefly.” *Id.* at 205.

ii. Analysis

In Ground 2, Petitioner applies Evans and Piper as discussed in connection with Ground 1. As explained above in our analysis of Ground 1, we agree with Petitioner that the combination of Evans and Piper teaches the limitations of claim 42. In Ground 2, Petitioner additionally relies upon Tardif, asserting that Tardif provides “additional motivation . . . to use a pulsed laser . . . in Evans’ system” by teaching “the advantage of using a pulsed radiation source on stained sperm instead of a conventional continuous light source.” Pet. 41. According to Petitioner, Tardif teaches that pulsed light sources are advantageous because they “minimize[] the time sperm are subjected to potentially harmful UV exposure.” *Id.* In view of this teaching, Petitioner, supported by the testimony of Dr. Robinson, argues that “a POSA would have sought to minimize the harm to sperm known to be caused by the UV light of a laser beam . . . [by] replac[ing] Evans’ CW laser with a pulsed laser.” *Id.* at 42.

Patent Owner contends that Tardif does not supply additional motivation to use a pulsed laser and, in fact, “directly teaches away from replacing a CW laser with Piper’s high-energy, high-powered laser to sort *sperm cells*.” PO Resp. 38–40.

We have already found that it would have been obvious to a POSA to use a pulsed laser in Evans' system for sorting sperm in view of the disclosures of Evans and Piper. We agree with Petitioner that Tardif provides additional motivation to use a pulsed laser. Tardif discloses:

Although continuous exposure of fluorescently stained cells to UV illumination is often harmful, the illumination in the Hamilton Thorn IVOS unit is not continuous. The exposure to the strobe light is about 10 to 15 microseconds, with a frequency of 60 cycles/second, so sperm are exposed very briefly.

Ex. 1006, 205. We find that this teaching supports a POSA's motivation to minimize exposure of sperm to UV light by using a pulsed light source. See Ex. 1003 ¶ 108.

Patent Owner argues that Tardif does not provide motivation to "modify Evans . . . with a very high pulsed-energy laser" because "cells would not be expected to survive the high energies" of Piper's pulsed lasers. PO Resp. 38. This argument is not persuasive because, as discussed above, we find that Piper's disclosure is not limited to the use of "very high pulsed-energy laser."

Patent Owner argues that "[a] POSA would not have been motivated to use a pulsed laser unless minimizing the exposure time—in the form of pulses—actually reduced the amount of energy of the harmful UV radiation that the cell was exposed to." *Id.* This argument is not persuasive because, as discussed above, as compared to a CW laser with similar average power, the total energy delivered to each cell using a pulsed laser is "comparable or, in fact, significantly smaller than the equivalent energy carried by a CW laser in the same span." Ex. 2002 ¶ 176. For the same reason, we are not persuaded by Patent Owner's argument that Tardif's teaching to minimize

the amount of UV light that the cells are exposed to “teaches away from replacing a CW laser with Piper’s high-energy, high-power laser to sort *sperm cells*.” PO Resp. 39.

Moreover, a reference teaches away from a claimed invention if it “criticizes, discredits, or otherwise discourages” modifying the reference to arrive at the claimed invention. *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004). Here, Patent Owner does not identify clear evidence of a “teaching away” in the prior art. *See e.g., Galderma Labs., LP v. Tolmar, Inc.* 737 F.3d 731, 738–39 (Fed. Cir. 2013) (finding that “[a] teaching that a composition may be optimal or standard does not criticize, discredit, or otherwise discourage investigation into other compositions” and thus the prior art “do[es] not teach away from the claimed invention”). We will not “read into a reference a teaching away from a process where no such language exists.” *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1364 (Fed. Cir. 2006). Given the evidence, discussed above, of a suggestion to combine the references, this is not a case where the combined teachings of the applied prior art, fairly read in their entirety, establish a teaching away. *Cf. Ecolochem, Inc. v. Southern California Edison Co.*, 227 F.3d 1361, 1373–74 (Fed. Cir. 2000) (finding clear evidence of teaching away based on lack of suggestion to combine two processes).

Patent Owner argues that Tardif’s teachings are inapplicable for sorting sperm cells because Tardif used its pulsed strobe light to image cells rather than to sort them. *Id.* Based on Dr. Vacca’s testimony, Patent Owner argues that the intensity of Tardif’s strobe light is 147,000 times lower than that of the pulsed laser disclosed in the ’116 patent and that this low

intensity light would “not be sufficient to sort sperm cells, and would therefore, not provide a motivation to use a pulsed laser for sperm sorting.” *Id.* at 39–40 (citing Ex. 2002 ¶¶ 201–203, 206).

Tardif studied the effect of fluorescent dye on sperm subjected to UV light and is, thus, reasonably pertinent to the use of flow cytometry to sort sperm. Ex. 1006, 201. That the intensity of Tardif’s strobe light may be insufficient for flow cytometry does not preclude the use of Tardif’s teachings in our obviousness analysis because “[t]he test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference Rather, the test is what the combined teachings of those references would have suggested to those of ordinary skill in the art.” *In re Keller*, 642 F.2d 413, 425 (CCPA 1981).

Here, Petitioner does not propose to incorporate Tardif’s strobe light into Evans’ flow cytometry system. Rather, Petitioner relies upon Tardif for its general teaching to minimize UV exposure by using a pulsed light. See Pet. 42 (arguing that “a POSA would have been further prompted by Tardif to use a pulsed radiation source, such as a pulsed laser”); Reply 17 (arguing that Tardif teaches that “pulsed light helps limit UV damage to fluorescently-stained sperm cells”); Ex. 1003, ¶ 108 (Dr. Robinson testimony that Tardif would have provided a POSA with “additional encouragement to use a pulsed radiation source”). We agree with Petitioner this teaching provides additional motivation to use a pulsed radiation source. We are not persuaded that Tardif, or any other applied reference, contains clear language that would have discouraged an ordinarily skilled artisan in this particular field of endeavor from employing a pulsed radiation source.

E. Dependent Claims and Additional Grounds

In addition to challenging claim 42, Petitioner also asserts that dependent claims 43–59, 65, and 69 would have been obvious over the combination of Evans, Piper, and Tardif, that dependent claim 51 would have been obvious over the combination of Evans, Piper, Tardif, and Lakowicz, and that dependent claims 66 and 67 would have been obvious over the combination of Evans, Piper, Tardif, and Fukuda. Pet. 42–55. Despite challenging Petitioner’s proof with respect to several dependent claims in its Response (*see* PO Resp. 40–56), at the hearing in this case Patent Owner clearly and unequivocally waived its arguments with respect to these claims and took the position that all of the claims stood or fell based upon the “pulsed laser” limitation in claim 42. Counsel for Patent Owner stated:

[I]n our estimation, the [P]etitioner’s evidence was so weak on the [inaudible] laser limitation alone we chose to attack that issue alone. And so in other words, this case, all the claims in this proceeding stand or fall with the pulsed laser limitation.

Tr. 25. Counsel for Patent Owner repeated this position in colloquy with Judge Obermann:

JUDGE OBERMANN: Okay. So in other words, if we rule against you and we find that the pulsed laser would have been obvious to incorporate here, you will concede that there is no other -- you’re not pursuing any other ground of –

MR. SAFIULLAH: Your Honor, for this proceeding we are not pursuing any other ground other than the pulsed laser limitation.

Id. at 26; *see also id.* (counsel for Patent Owner, conceding in the context of the pulsed laser limitation, “that there is no separate independent

patentability based on [sic] outstanding limitation”); *see also id.* at 51 (counsel for Petitioner summarizing “I would just like to note at the outset that counsel conceded that the stained percentage limitation is not a material issue and that this case boils down to the pulsed laser issue which is as I said at the beginning of my presentation”). Consistent with this waiver, the entire focus of Patent Owner’s oral argument was on the pulsed laser limitation and neither party devoted any of their argument time to addressing any of the dependent claims. Tr. 3–60.¹⁶

We accept Patent Owner’s representation that “all of the claims in this proceeding stand or fall with the pulsed laser limitation” as evidence that the dependent claims at issue in this proceeding are not independently patentable and as a waiver of any argument to the contrary. Thus, given our determination that independent claim 42 would have been obvious, we determine that the subject matter of dependent claims 43–59, 65–67, and 69 would also have been obvious. More specifically, we determine that claims 43–59, 65, and 69 would have been obvious over the combination of Evans, Piper, and Tardif, that claim 51 would have been obvious over the combination of Evans, Piper, Tardif, and Lakowicz, and that claims 66 and 67 would have been obvious over the combination of Evans, Piper, Tardif, and Fukuda.

¹⁶ Prior to Patent Owner’s representation that “all the claims in this proceeding stand or fall with the pulsed laser limitation,” counsel for Petitioner also addressed the “percentage of stain” limitation of claim 42. Tr. 5–19. Petitioner’s discussion of the “percentage of stain” limitation at oral argument was consistent with the panel’s email in advance of the hearing, indicating that “the panel [was] particularly interested in discussing construction of the terms ‘standard control’ and ‘maximum stain.’” Ex. 3001.

III. MOTION TO EXCLUDE

On January 14, 2019, Petitioner filed a Motion to Exclude, seeking to exclude Exhibit 2001 as hearsay under Federal Rule of Evidence 801 and as irrelevant. Paper 24, 2–3. In addition, Petitioner moved to exclude certain graphic material appearing at pages 12 and 14 of Exhibit 2002 and at pages 11–12 of Patent Owner’s Response as lacking authentication under Federal Rule of Evidence 901 and as irrelevant. *Id.* at 3–5. On February 11, 2019, Patent Owner filed an Opposition to Petitioner’s Motion to Exclude. Paper 25. Petitioner submitted a Reply in support of its Motion to Exclude on February 19, 2019. Because we do not rely the material at issue to reach our final decision, we dismiss as moot Petitioner’s Motion to Exclude.

IV. CONCLUSION

Upon consideration of the Petition, Response, Reply, the briefing on Patent Owner’s Motion to Exclude, and the evidence before us, including that adduced at oral argument, we determine that Petitioner has proven by a preponderance of the evidence that claim 42 would have been obvious over the combination of Evans and Piper. We determine that Petitioner has also proven by a preponderance of the evidence that claims 42–59, 65, and 69 would have been obvious over the combination of Evans, Piper, and Tardif. We determine that Petitioner has also proven that claim 51 would have been obvious over the combination of Evans, Piper, Tardif, and Lakowicz. We determine that Petitioner has also proven by a preponderance of the evidence that claims 66 and 67 would have been obvious over the combination of Evans, Piper, Tardif, and Fukuda. We dismiss as moot Petitioner’s motion to exclude.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has proven by a preponderance of the evidence that claims 42–59, 65, and 69 of U.S. Patent No. 7,723,116 are unpatentable;

ORDERED that Petitioner’s motion to exclude is dismissed;

ORDERED that, pursuant to 35 U.S.C. § 318(b), upon expiration of the time for appeal of this decision, or the termination of any such appeal, a certificate shall issue canceling claims 42–59, 65, and 69 of U.S. Patent No. 7,723,116; and

FURTHER ORDERED that, because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

IPR2018-00248
Patent 7,723,116 B2

PETITIONER:

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