

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10X GENOMICS, INC.,
Petitioner,

v.

BIO-RAD LABORATORIES, INC.,
Patent Owner.

IPR2020-00088
Patent 9,896,722 B2

Before CHRISTOPHER M. KAISER, KIMBERLY MCGRAW, and
ELIZABETH M. ROESEL, *Administrative Patent Judges*.

Opinion for the Board filed by *Administrative Patent Judge* ROESEL.

Opinion Concurring filed by *Administrative Patent Judge* MCGRAW.

ROESEL, *Administrative Patent Judge*.

DECISION

Denying Petitioner's Request for Rehearing of Final Written Decision
37 C.F.R. § 42.71(d)

I. BACKGROUND

10X Genomics, Inc. (“Petitioner”) timely filed a request for rehearing (Paper 40, “Reh’g Req.” or “Request”) of our Final Decision (Paper 39, “Dec.”) finding some claims of U.S. Patent No. 9,896,722 B2 (“the ’722 Patent,” Ex. 1001) unpatentable.

For the reasons that follow, we deny Petitioner’s request for rehearing.

II. STANDARD OF REVIEW

As it relates to a request for rehearing of a Board decision, in pertinent part, 37 C.F.R. § 42.71(d) states:

The burden of showing a decision should be modified lies with the party challenging the decision. The request must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, or a reply.

Thus, a request for rehearing is not an opportunity to present new arguments or evidence or merely to disagree with the panel’s assessment of the arguments or weighing of the evidence.

III. ANALYSIS

Petitioner challenges our determination that Petitioner did not show by a preponderance of the evidence that dependent claims 15–17 of the ’722 Patent are unpatentable.

Claim 15 depends from claim 14 and recites: “after the separation step, further comprising placing the droplets onto a second continuous phase carrier fluid.” Ex. 1001, 89:4–6. Claim 16 depends from claim 15 and recites: “wherein the second continuous phase carrier fluid comprises a destabilizing surfactant.” *Id.* at 89:7–8. Claim 17 depends from claim 15 and recites: “after the placing step, further comprising destabilizing the droplets.” *Id.* at 89:9–10.

A. *The Petition*

The Petition's analysis of claims 15–17 is reproduced below.

Ismagilov describes reactions for creating compounds for later use, e.g., “*synthesis of macroscopic quantities* of chemical and *biological* compounds, e.g., the destruction of chemical warfare agents and *pharmaceuticals synthesis*.” *Id.*, 1:24–28; *see also id.*, 3:36–41 (“*polymerizations, crystallizations* (including small molecule and proteins), *nanoparticle synthesis*, formation of unstable intermediates, enzyme-catalyzed reactions and assays, protein binding, etc.”), 50:51–52; Ismagilov 119, ¶ 117 (reaction types not limited, listing examples). These uses would require breaking the emulsions to aggregate sufficient quantities of reaction product.

Ismagilov also discloses what Ismagilov described as “[f]luorosurfactants” with “biocompatibility in blood substitutes and other *biomedical applications*” and that were “resistant to protein adsorption.” To obtain the contents of droplets made using this preferred surfactant, The POSA would look to methods of demulsification, or breaking emulsions. To break an emulsion, it was well-known that chemical demulsifiers [*sic*], including surfactants, could be used, as described in section VI. A POSA would look to methods of demulsification. *Per* section VI, 722 Patent. A POSA also knew that perfluorooctanol could be used for droplet merging. *See* 21:16–29; 61:19–21 (using “*1H,1H,2H2H-perfluorooctanol*.”). For example, Ismagilov disclosed perfluorooctanol [*sic*] “surfactant” as 10% of the carrier fluid solution for droplet merging. Ismagilov, (“*1H,1H,2H2H-perfluorooctanol*”); Ex. 1001, 48:25–28 (“*1H,1H,2H,2H-Perfluoro-1-octanol*”). A second continuous carrier with a destabilizing surfactant was obvious, including because it was obvious to perform merging of multiple droplets (i.e., droplet breaking).

It would be obvious to add this surfactant to stable droplets in a tube or other vessel to de-emulsify and aggregate reaction product, meeting Bio-Rad's construction of continuous phase carrier fluid. Fair, ¶¶ 190–195. . . .

As above, it would have been obvious to add a second continuous phase carrier fluid with a destabilizing surfactant (perfluorooctanol) to destabilize droplets. Fair, ¶¶ 190–195.

Pet. 51–53 (heading quoting claims 16, 17 omitted; citing Ex. 1001; Ex. 1004 (“Ismagilov 091”); Ex. 1005 (“Ismagilov 119”); Ex. 1008 (Fair Declaration)). Cross-referenced section VI of the Petition included a discussion of using surfactants as demulsifiers. Pet. 11–12 (citing Exs. 1009,¹ 1057,² 1058,³ 1059⁴).

B. The Final Decision’s Analysis of Claims 15–17

The Final Decision’s analysis of claims 15–17 is reproduced below.

Petitioner’s contentions for claims 15–17 are not sufficiently supported by the teachings of Ismagilov 091. Petitioner cites the ’722 Patent’s disclosure of a 1H,1H,2H,2H-perfluoro-1-octanol as a de-stabilizing surfactant contained in a second continuous phase carrier fluid (Ex. 1001, 48:25–28) and contends that Ismagilov 091 discloses the same surfactant “for droplet merging.” Pet. 52 (Ex. 1004, 21:16–29, 61:19–21). Not true. Ismagilov 091 teaches perfluorooctanol as a surfactant to **stabilize** droplets in channels, not to destabilize or merge droplets. Ex. 1004, 21:7–35. More specifically, Ismagilov 091 teaches that “the plugs remain stable and do not leave behind any residue as they are transported through the channels” when “the surface tension at a plug fluid/channel wall interface . . . is set higher than the surface tension at a plug fluid/carrier-fluid interface . . . with a surfactant such as 10% 1H,1H,2H,2H-perfluorooctanol.” *Id.* at 21:11–22. Petitioner does not direct us to any teaching or suggestion in Ismagilov 091 that a surfactant,

¹ Excerpts of Encyclopedic Handbook of Emulsion Technology (2001).

² Excerpts of Emulsions Theory and Practice, 3rd Ed. (2001).

³ J. Wu, et al., *Effect of EO and PO positions in nonionic surfactants on surfactant properties and demulsification performance*, Colloids and Surfaces A: Physicochem. Eng. Aspects 252, 79–85 (2005).

⁴ Viovy et al., WO 2006/027757, published Mar. 16, 2006.

such as perfluorooctanol, can be used to destabilize or merge droplets.

Even if destabilizing surfactants were known in the art, Petitioner does not direct us to evidence sufficient to establish that it would have been obvious to place the droplets onto a second continuous phase carrier fluid comprising a destabilizing surfactant to destabilize the droplets, as recited in claims 15–17. Dr. Fair’s testimony (Ex. 1008 ¶¶ 190–193) is essentially the same as the Petition (Pet. 51–52) and suffers from the same deficiencies.

Dec. 62–63.

Petitioner is correct that our conclusion with respect to claims 15–17 is based on two subsidiary findings: (i) that “Ismagilov 091 teaches perfluorooctanol as a surfactant to stabilize droplets in channels, not to destabilize or merge droplets” and that “Petitioner does not direct us to any teaching or suggestion in Ismagilov 091 that a surfactant, such as perfluorooctanol, can be used to destabilize or merge droplets,” and (ii) that

Even if destabilizing surfactants were known in the art, Petitioner does not direct us to evidence sufficient to establish that it would have been obvious to place the droplets onto a second continuous phase carrier fluid comprising a destabilizing surfactant to destabilize the droplets, as recited in claims 15–17.

Reh’g Req. 3; Dec. 62–63. Each of these findings provides a sufficient independent basis for our determination as to claims 15–17.

As discussed below, Petitioner does not show that either of these findings misapprehended or overlooked the teachings of Ismagilov 091 or the arguments and evidence presented in the Petition.

C. Petitioner’s Attempt to Re-argue its Case for Unpatentability of Claims 15–17 is Not Persuasive

The Request reargues Petitioner’s case for unpatentability of claims 15–17 in a way that was not presented in the Petition. *Compare* Reh’g Req.

4–8, *with* Pet. 11–12, 51–53. For example, the Request relies on Exhibits 1009, 1057, 1058, and 1059 (Reh’g Req. 5), which were discussed in a section of the Petition addressing the state of the art, but were not specifically relied upon when addressing unpatentability of claims 15–17. Pet. 11–12 (citing Exs. 1009, 1057, 1058, 1059); *see also* Pet. 51–53 (addressing claims 15–17).

In the Request, Petitioner argues that it was known in the art to “add[] a liquid comprising a destabilizing surfactant to a test tube containing an emulsion of water droplets in oil (like that produced by Ismagilov) in order to destabilize (that is, break) the droplet emulsion.” Reh’g Req. 5 (citing Pet. 11–13; Ex. 1008 ¶ 62; Exs. 1009, 1057, 1058, 1059). That argument expands upon the argument in the Petition, which asserted that “[b]reaking, merging, and coalescing droplets with surfactants was well known” (Pet. 12) and “[i]t would be obvious to add this surfactant [1H, 1H, 2H, 2H-perfluorooctanol (“PFO”)] to stable droplets in a tube or other vessel to de-emulsify and aggregate reaction product” (Pet. 52).

Petitioner’s arguments about Exhibits 1009, 1057, 1058, and 1059 in the Request differ from Petitioner’s characterization of this evidence in the Petition. According to the Petition, Exhibit 1009 discloses “chemical ‘demulsification’ in petroleum-based emulsions” and includes “a table of chemical demulsifiers used with crude oil.” Pet. 11 (citing Ex. 1009, 541, 564, 579, 580, Table 4). According to the Petition, Exhibit 1057 discusses chemical demulsification using surface-active agents and breaking water/oil emulsions, such as “industrially important oil-field emulsions.” Pet. 11–12 (citing Ex. 1057, 289, 292). According to the Petition, Exhibit 1058 discloses “demulsifiers” as a “means of breaking water-in-oil emulsions that occur in industrial processes.” Pet. 12 (quoting Ex. 1058, Abstract).

According to the Petition, Exhibit 1059 (“Viovy”) discloses that a “side channel” can be configured to deliver a “solution containing a surfactant” and that droplet coalescence is favored when the surface tension between water droplets and the surrounding oil-based fluid is reduced by the presence of a surfactant, such as PFO. Pet. 12 (citing Ex. 1059, 10–12).

Petitioner does not direct us to teachings in Exhibits 1009, 1057, 1058, and 1059 sufficient to support its contention that it would have been obvious to add PFO as a destabilizing surfactant to a test tube containing an emulsion of water droplets in oil, like that produced by Ismagilov 091, in order to destabilize or break the droplet emulsion in order to recover the sample contained in the droplets. The cited portions of Exhibits 1009, 1057, and 1058 relate to demulsifying petroleum-based emulsions, and Petitioner does not assert that any of the chemical demulsifiers disclosed in these references would have been used to break a droplet emulsion like that produced by Ismagilov 091. Viovy discloses microfluidic devices and methods for coalescing a pair of droplets in a microchannel and discloses that a surfactant may be chosen to favor the formation of oil-in-water emulsions or to favor droplet coalescence. Ex. 1059, 5–6, 10–11. Viovy does not disclose adding PFO as a surfactant to break an emulsion of droplets in order to collect the contents of the droplets, and Petitioner did not explain sufficiently how the teachings of Viovy would have led a POSITA to use PFO in the manner asserted in the Petition. Pet. 12 (discussing Viovy); Pet. 52 (asserting that “[i]t would have been obvious to add [PFO] to stable droplets in a tube or other vessel to de-emulsify and aggregate reaction product”). Petitioner had the burden to provide an evidence-supported explanation showing that a POSITA would have understood the

prior art as suggesting the subject matter of claims 15–17, and Petitioner failed to do so, either in the Petition or in the Request.

The Request contains several inaccurate assertions about Exhibit 1009. First, contrary to the Request, Dr. Fair did not rely on Exhibit 1009’s disclosure of chemical demulsifiers. *Compare* Reh’g Req. 5 (citing “Fair [Ex. 1008] ¶ 62” as discussing Ex. 1009), *with* Ex. 1008 ¶ 62 (no mention of Exhibit 1009). Second, Petitioner asserts that Exhibit 1009 “list[s] ‘fatty alcohols’ in Table 4 as demulsifiers used at least as early as 1935.” Reh’g Req. 5–6. Petitioner’s assertion misstates Table 4 of Exhibit 1009, which discloses that “[*e*]thoxylates of . . . fatty alcohols” (not fatty alcohols themselves) were used as demulsifiers of crude oil emulsions up to 1935. Ex. 1009, 580.⁵ This is confirmed by the text of Exhibit 1009 that precedes Table 4, where *the same ethoxylates* as listed in Table 4 are disclosed as examples of nonionic surfactants useful as chemical demulsifiers.⁶ Third, the Request asserts that “[f]atty alcohol ethers (that is, chemicals like PFO that have a hydrocarbon tail and an alcohol head group) have been used by those in the art as destabilizing surfactants to break water-

⁵ To be consistent with the Petition, we cite the original pagination of Exhibit 1009. The Request cites the exhibit-stamped pagination, which in this instance is pages 127–128.

⁶ Exhibit 1009 discloses: “Chemicals used as demulsifiers may be simple surfactants. These may be cationic . . . ; anionic . . . ; nonionic . . . ; and zwitterionic” Ex. 1009, 579. Examples of each type of surfactant are disclosed. *Id.* The first three examples of “nonionic” surfactants are: “fatty alcohol ethers [CH₃(CH₂)₁₀CH₂O(C₂H₄O)_nH], fatty esters [(CH₃(CH₂)₁₀COO (C₂H₄O)_nH], [and] alkyl phenol ethers [R-Ph-O-(C₂H₄O)_nH].” *Id.* These are the same three chemicals that Table 4 lists as having been used as demulsifiers of crude oil emulsions up to 1935: “Ethoxylates of fatty acids, fatty alcohols, and alkylphenols.” *Id.* at 580.

in-oil emulsions since at least 1935.” Reh’g Req. 5 (citing Pet. 11; Ex. 1008 ¶ 62; Ex. 1009, 579–580). That assertion is mere attorney argument, supported neither by Dr. Fair’s testimony nor by Exhibit 1009.

As already mentioned, Dr. Fair did not rely on Exhibit 1009’s disclosure of chemical demulsifiers. Exhibit 1009 discloses that fatty alcohol ethers such as $\text{CH}_3(\text{CH}_2)_{10}\text{CH}_2\text{O}(\text{C}_2\text{H}_4\text{O})_n\text{H}$ (an ethoxylated fatty alcohol) were used as chemical demulsifiers of crude oil emulsions up to 1935. Ex. 1009, 579–580. But there is no support in Petitioner’s citations for its assertion that PFO is “like” the fatty alcohol ethers that Exhibit 1009 discloses were used as chemical demulsifiers of crude oil emulsions. On the contrary, Dr. Fair characterizes PFO as “a fluorinated carbon chain with an alcohol” and a “fatty alcohol,” *not* a fatty alcohol ether or fatty alcohol ethoxylate. Ex. 1008 ¶ 62. Even if PFO and fatty alcohol ethoxylates both have a hydrocarbon tail and an alcohol head group, that is not enough to prove that PFO was known in the art as a destabilizing surfactant to break water-in-oil emulsions, as argued by Petitioner. Reh’g Req. 5. Petitioner’s case against claims 15–17 hinged on its assertion that it would have been obvious to use PFO to break an emulsion of droplets, but Petitioner did not bring forward evidence to sufficient to meets its burden to show that PFO was known for this use prior to the effective date of the ’722 Patent.⁷

Next, the Request argues that “PFO was known by those of ordinary skill in the art to be a destabilizing surfactant (a fatty alcohol) useful for breaking water-in-oil emulsions when a fluorinated oil is used (e.g., as taught by Ismagilov).” Reh’g Req. 6 (citing Pet. 11, 52; Ex. 1008 ¶¶ 62,

⁷ As discussed below, we are not persuaded that Ismagilov 091 supports Petitioner’s contention that PFO was known for emulsion-breaking.

192, 193; Ex. 1004, 61:19–21, 64:8–65:15; Ex. 1059, 11–12). As support for that argument, Petitioner relies on portions of Ismagilov 091 and Viovy that were not discussed in the Petition or the Fair Declaration. Although Petitioner and Dr. Fair cited Viovy’s disclosure of PFO (Pet. 12 (citing Ex. 1059, 12); Ex. 1008 ¶ 62 (same)), they did not rely on Viovy to support an argument that PFO was useful for breaking water-in-oil emulsions when a fluorinated oil is used.

In any event, we are not persuaded that Viovy supports Petitioner’s assertion. Like Ismagilov 091, Viovy is concerned with “reducing the risk of interaction of the packets [droplets] with the wall of the microchannel in the presence of the embedding fluid [carrier fluid].” *Compare* Ex. 1059, 11:19–21, *with* Ex. 1004, 21:7–35 (disclosing that a fluorinated surfactant is used to “allow[] the formation of plugs that do not stick to the channel walls”). Viovy teaches to reduce the risk of droplets interacting with the microchannel walls in the same way as Ismagilov 091: by making the surface tension between the droplets and the microchannel wall higher than the surface tension between the droplets and the carrier fluid. Ex. 1004, 21:16–35 (“the surface tension at a plug fluid/channel wall interface . . . is set higher than the surface tension at a plug fluid/carrier-fluid interface . . . with a surfactant”); Ex. 1059, 11:23–32 (“the interfacial tension between the droplet and the microchannel wall is made larger than the interfacial tension between the droplet and the surrounding fluid, by treating the microchannel wall and/or by including in the droplet and/or in the fluid additives. . . . The surface tension between water and hydrogenated oil-based fluids can be decreased by the presence of surface-active molecules.”). Like Ismagilov 091, Viovy teaches that PFO can be used as a surfactant with a fluorinated carrier fluid to reduce the surface tension at the droplet-carrier

fluid interface. Ex. 1004, 21:7–35; Ex. 1059, 11:31–12:6. Contrary to Petitioner’s assertion, Viovy does not teach PFO for breaking a droplet emulsion, and Petitioner does explain sufficiently how the teachings of Viovy would have led a POSITA to use PFO in the manner asserted in the Petition.

The Request also relies on Example 4 of Ismagilov 091, asserting that the droplet merging experiments were performed using a 10:1 mixture of perfluorodecaline (“PFD”) and PFO. Reh’g Req. 6 (citing (Ex. 1004, 64:8–65:15)). Neither the Petition nor the Fair Declaration relied on Example 4 of Ismagilov 091. Although the Petition and Dr. Fair asserted that a “POSA also knew that perfluorooctanol could be used for droplet merging” (Pet. 52 (citing Ex. 1004, 21:16–29, 61:19–21); Ex. 1008 ¶ 192 (same)), that assertion is not supported by Ismagilov 091, which provides no teaching or suggestion that PFO can be used to destabilize or merge droplets. Ismagilov 091 teaches forming droplets using a mixture of PFD and PFO as the carrier fluid and further teaches that PFO prevents the droplets from sticking to the channel walls. Ex. 1004, 21:16–29, 62:9–20, Fig. 26. As further discussed below, Petitioner does not provide evidence or explanation sufficient to show that it would have been obvious to add more PFO to the droplets to break the emulsion.

Contrary to Petitioner’s argument, Example 4 of Ismagilov 091 does not teach that PFO promotes droplet merging. PFO is not even mentioned in the example. According to Petitioner, the examples in Ismagilov 091 were “typically performed” using a mixture of PFD and PFO. Reh’g Req. 6. Petitioner does not explain what would have led a POSA to conclude that PFO promotes droplet merging, when it is used as surfactant in all or most of

the examples, most of which do not involve droplet merging. Example 5, for instance, illustrates splitting plugs. Ex. 1004, 65:17–57.

Ismagilov 091 illustrates the role of PFO in Example 13C, not Example 4, which does not even mention PFO. In Example 13C, aqueous plugs were formed in a carrier fluid flowing through a microchannel, where the carrier fluid is a mixture of fluorinated oil and PFO. Ex. 1004, 72:37–41, 72:54–56. A microphotograph shows “water plugs attached to the PDMS wall.” *Id.* at 72:48–51, Fig. 39. According to Ismagilov 091, “[t]his attachment occurs when low concentrations of surfactant, or less-effective surfactants are used” and “[i]n this case, [PFO] is less effective than 1H,1H,2H,2H-perfluorodecanol.” *Id.* at 72:51–54. The explicit discussion of the role of PFO in Example 13C reinforces our finding that Ismagilov 091 teaches PFO for preventing droplets from sticking to the channel walls, but does not teach or suggest that PFO promotes droplet merging.

Next, Petitioner argues that “in order to perform the synthesis of biological compounds, pharmaceuticals, or nanoparticles and the protein crystallizations that Ismagilov teaches as uses for its system, a POSA would know that it would be necessary (and desirable) to break the emulsion to collect the contents of the droplets for further use.” Reh’g Req. 7 (citing Pet. 51; Ex. 1008 ¶¶ 190, 191). That argument differs from the Petition to the extent it relies on desirability rather than necessity. The Petition argued that the uses disclosed in Ismagilov 091 “would **require** breaking the emulsions to aggregate sufficient quantities of reaction product.” Pet. 51 (emphasis added); *see* Ex. 1008 ¶ 191 (same).

Regardless of whether Petitioner’s argument now that emulsion-breaking would have been necessary and desirable differs from Petitioner’s original argument that emulsion-breaking would have been necessary,

Petitioner did not provide evidence or explanation sufficient to show that emulsion-breaking would have been either necessary or desirable when synthesizing biological compounds, pharmaceuticals, or nanoparticles, as disclosed in Ismagilov 091. Dr. Fair's testimony that Ismagilov 091's uses "would require breaking the emulsions" is conclusory and unexplained. Ex. 1008 ¶ 191 (testifying without explanation that Ismagilov's "uses would require breaking the emulsions to aggregate sufficient quantities of reaction product"). In addition, Petitioner did not cite even this conclusory testimony in its argument that emulsion-breaking was necessary. Pet. 51. Meanwhile, Ismagilov 091 provides numerous examples of uses of its methods and devices, but no suggestion that emulsion-breaking would be necessary or desirable. Accordingly, we determined that Petitioner did not "direct us to evidence sufficient to establish that it would have been obvious to place the droplets onto a second continuous phase carrier fluid comprising a destabilizing surfactant to destabilize the droplets, as recited in claims 15–17." Dec. 63. As discussed more fully below, none of Petitioner's arguments for rehearing persuades us that we erred in determining that the evidence of record failed to show a reason why a person of ordinary skill in the art would have used PFO to break the emulsions in Ismagilov 091.

Dr. Fair's testimony might have been persuasive if he had provided an example of a synthesis or reaction from Ismagilov 091 where a POSA would have found it necessary or desirable to add PFO to demulsify the droplets after they had been separated. For example, Ismagilov Example 12 titled "Nanoparticle Experiments with and without Plugs" compares two methods of forming nanoparticles, one using microfluidics and droplet formation, and the other without microfluidics or droplets. Ex. 1004, 70:49–71:19. A

“UV-VIS spectrum” was used to evaluate whether the nanoparticles were monodisperse or polydisperse. *Id.* at 71:5–7, 71:17–19. There is no mention of how the samples were prepared for spectroscopy or of any need for different steps, such as demulsification, that were necessary to prepare the microfluidics sample, as compared with the non-microfluidics sample.

The closest Dr. Fair came to providing an example to illustrate his testimony is droplets that have been stabilized with a biocompatible fluorosurfactant. Ex. 1008 ¶ 192 (quoting Ex. 1004, 37:23–25). But nothing in Ismagilov 091’s discussion of biocompatible fluorosurfactants suggests anything about emulsion-breaking or the addition of another surfactant, such as PFO, to break the emulsion.

In our view, Petitioner’s argument about emulsion-breaking is based on impermissible hindsight. The ’722 Patent teaches a method of sample recovery whereby the creamed emulsion is placed onto a second continuous phase carrier fluid containing a de-stabilizing surfactant such as PFO. Ex. 1001, 48:6–38. Petitioner incorrectly interprets Ismagilov 091 with the benefit of this teaching.

The Request departs even more fundamentally from the Petition’s theory of obviousness. The Petition and the Fair Declaration were based on the theory that it would have been obvious to add a destabilizing surfactant—PFO—to de-emulsify droplets that have been stabilized by a first surfactant—“[f]luorosurfactants” with “biocompatibility in blood substitutes and other biomedical applications.” Pet. 52 (emphasis omitted; quoting Ex. 1004, 37:23–25); Ex. 1008 ¶¶ 192, 193. According to the Petition and the Fair Declaration, “[t]o obtain the contents of droplets made using *this preferred surfactant*, [t]he POSA would look to methods of demulsification, or breaking emulsions.” Pet. 52; Ex. 1008 ¶ 192 (emphasis

added). “This preferred surfactant” referred to what Ismagilov describes as “[f]luorosurfactants” with “biocompatibility in blood substitutes and other biomedical applications,” i.e., “[f]luorosurfactants terminated with OEG[oligoethylene glycol]-groups.” Pet. 52; Ex. 1008 ¶ 192; Ex. 1004, 37:23–25.

The Petition explained that “the Ismagilov droplets were stabilized by the long-fluorinated-tail surfactant.” Pet. 10 (citing Ex. 1017, 222:18–223:9, Dr. Ismagilov’s testimony from a prior litigation); *see also* Ex. 1008 ¶ 60 (“Dr. Ismagilov testified that the droplets disclosed by Ismagilov were stable because of the surfactant used.”). According to the Petition and the Fair Declaration, the cited testimony discusses the OEG-terminated surfactants disclosed in Ismagilov 091. Pet. 10 n.1; Ex. 1008 ¶ 60 n.1 (citing Ex. 1004, 37:23–45, Fig. 24). Dr. Fair explained that “[s]table droplets will cream or sediment without, for example, coalescing with other droplets they are close to.” Ex. 1006 ¶ 60. Thus, the obviousness case advanced in the Petition and the Fair Declaration was premised on the theory that “it would have been obvious to add this surfactant,” i.e., PFO, “to *stable* droplets,” i.e. droplets that had been stabilized with fluorosurfactant, “in a tube or other vessel to de-emulsify and aggregate reaction product.” Pet. 52 (emphasis added); Ex. 1008 ¶¶ 192, 193; Ex. 1004, 37:23–25.

Petitioner’s Request abandons the theory of obviousness advanced in the Petition and the Fair Declaration, making no mention of droplets stabilized by a fluorosurfactant. Contrary to the arguments advanced in the Request, Dr. Fair’s testimony does not support obviousness of adding a destabilizing surfactant unless the droplets are stable. Ex. 1004 ¶ 193. The only example Dr. Fair provided of stable droplets were those “made using this preferred surfactant,” i.e., “[f]luorosurfactants” with “biocompatibility

in blood substitutes and other biomedical applications.” *Id.* ¶ 193.

Dr. Fair’s testimony does not support the new arguments presented in the Request, which rely on Example 4 of Ismagilov 091 as teaching PFO for droplet merging. Reh’g Req. 6, 10–11. In that example, the droplets were not stabilized by a fluorosurfactant.

For all of these reasons, Petitioner’s attempt to re-argue its case for unpatentability of claims 15–17 is not persuasive.

D. The Panel Did Not Misapprehend or Overlook The Teachings of Ismagilov 091

Petitioner argues that we misread Ismagilov 091 when finding that it “teaches perfluorooctanol as a surfactant to stabilize droplets in channels, not to destabilize or merge droplets.” Reh’g Req. 8; Dec. 63 (citing Ex. 1004, 21:7–35). After considering Petitioner’s rehearing arguments, we are not persuaded that we misapprehended or overlooked the teachings of Ismagilov 091. Our finding is fully supported by the passage from Ismagilov 091 quoted in the Final Decision. Dec. 63. There, we stated:

Ismagilov 091 teaches that “the plugs remain stable and do not leave behind any residue as they are transported through the channels” when “the surface tension at a plug fluid/channel wall interface . . . is set higher than the surface tension at a plug fluid/carrier-fluid interface . . . with a surfactant such as 10% 1H,1H,2H,2H-perfluorooctanol.”

Id. (quoting Ex. 1004, 21:11–22).

For the first time in the Request, Petitioner attempts to distinguish two types of droplet stability: (1) stability against sticking to the channel walls and (2) stability against coalescence or merger. Reh’g Req. 9–10. The Petition drew no such distinction. Even if Petitioner is correct that the term “destabilizing” in claims 16 and 17 refers to surfactants that promote droplet

coalescence (*id.*), that does not show error in our finding about Ismagilov 091, which teaches PFO to stabilize droplets in channels and does not teach PFO to destabilize or merge droplets.

The Request repeats the unsupported assertion from the Petition that Ismagilov 091 discloses PFO “for droplet merging.” Reh’g Req. 10; Pet. 52 (Ex. 1004, 21:16–29, 61:19–21). Neither the Petition nor the Request points to sufficient support for that assertion. The Request relies on Example 4 of Ismagilov 091, which was neither cited nor discussed in the Petition. Reh’g Req. 10–11. For the reasons discussed above, even if it is assumed that Example 4 uses the same carrier fluid/surfactant mixture as disclosed in Example 1, there is no suggestion in Ismagilov 091 that the surfactant (PFO) plays any role in promoting the merging of droplets.

Petitioner does not show that the Final Decision misapprehended or overlooked any teaching in Ismagilov 091 about the use of PFO for destabilizing or merging droplets.

E. The Panel Did Not Misapprehend or Overlook Petitioner’s Arguments or Evidence Relating to a Second Continuous Phase Carrier Fluid

Petitioner asserts that the Final Decision overlooked Petitioner’s discussion of Patent Owner’s claim construction and Petitioner’s argument that “a POSA would know that it would be necessary and desirable to break the Ismagilov droplet emulsion to collect the contents of the droplets for further use after performing Ismagilov’s synthesis or crystallization reactions” and “the addition of a destabilizing surfactant such as PFO was a routine, known way to do that.” Reh’g Req. 15 (citing Pet. 11–13, 18–19, 51–53; Ex. 1008 ¶¶ 62, 78, 79, 190–193). We did not overlook these arguments. They are addressed by our finding that “[e]ven if destabilizing surfactants were known in the art, Petitioner does not direct us to evidence

sufficient to establish that it would have been obvious to place the droplets onto a second continuous phase carrier fluid comprising a destabilizing surfactant to destabilize the droplets, as recited in claims 15–17.” Dec. 63. Although our finding does not expressly refer to the construction for “continuous phase carrier fluid” relied upon by Petitioner (Pet. 19), that construction does not change the fact that Petitioner did not direct us to evidence sufficient to support its argument that Ismagilov 091’s disclosed reactions “would require breaking emulsions to aggregate sufficient quantities of reaction product.” Pet. 51. As discussed above, Petitioner did not provide evidence or explanation sufficient to show that emulsion-breaking would be necessary or even desirable when synthesizing biological compounds, pharmaceuticals, or nanoparticles, as disclosed in Ismagilov 091.

F. Petitioner Does Not Show Good Cause For Admitting New Evidence

Petitioner filed Exhibits 1088 and 1089 with its Request. These exhibits were not of record at the time the Final Decision was entered. Petitioner argues that good cause exists for admitting Exhibits 1088 and 1089 because it “was never given an opportunity to respond to the FWD’s novel, erroneous theory that PFO is a stabilizing surfactant.” Reh’g Req. 15. We disagree.

Petitioner had the burden of proving that the challenged claims are unpatentable. There is no requirement for the Board to provide notice to Petitioner and an opportunity to fill gaps in its case before issuing a final decision that Petitioner did not meet its burden of proof. Allowing Petitioner to submit new evidence under the circumstances presented here would be inconsistent with the standard applicable to a request for rehearing, which

requires Petitioner to show that the Board overlooked or misapprehended Petitioner's arguments or evidence. 37 C.F.R. § 42.71(d) (2020).

Moreover, our finding that Ismagilov 091 teaches PFO as a surfactant to stabilize droplets in channels (Ex. 1004, 21:7–35) is neither novel nor erroneous. The finding is based on a portion of Ismagilov 091 relied upon in the Petition, including for claims 15–17. Pet. 52 (citing Ex. 1004, 21:16–29 to show unpatentability of claims 15–17); *see also* Pet. 14 (summarizing Ismagilov 091 and citing Ex. 1004, 21:7–35); Pet. 29–30 (quoting Ismagilov 091's disclosure that “the plugs remain stable and do not leave behind any residue as they are transported through the channels,” citing Ex. 1004, 21:7–35). Furthermore, Ismagilov 091's teaching that PFO surfactant stabilizes droplets in channels by reducing the surface tension at the droplet/carrier fluid interface, as compared with the surface tension at the droplet/channel wall interface (Ex. 1004, 21:7–35) is consistent with and bolstered by Viovy's teaching that adding PFO surfactant is one way to make interfacial tension between the droplet and the microchannel wall larger than the interfacial tension between the droplet and the surrounding fluid. Ex. 1059, 11:23–12:6.

Thus, Petitioner has not established good cause for admitting Exhibits 1088 and 1089. Consequently, although we do not exercise our authority under 37 C.F.R. § 42.7(a) to expunge Exhibits 1088 and 1089, we do not admit them. *See Huawei Device Co. v. Optis Cellular Tech., LLC*, IPR2018-00816, Paper 19 at 3–4 (PTAB Jan. 8, 2019) (precedential) (expunging exhibits filed with a request for rehearing when the petitioner failed to establish good cause for admitting the exhibits); *see also* Consolidated Trial

Practice Guide 90 (Nov. 2019)⁸ (“Absent a showing of ‘good cause’ prior to filing the request for rehearing or in the request for rehearing itself, new evidence will not be admitted.”).

Even if we were to consider Exhibits 1088 and 1089, they do not change our views. Exhibit 1088 is an excerpt from an expert rebuttal report of Dr. Bruce Gale served by Patent Owner in an unrelated district court litigation, and Exhibit 1089 is an excerpt from Dr. Gale’s deposition testimony. Petitioner directs us to Dr. Gale’s opinion that Ismagilov 091 teaches that droplets merge when they contact each other. Reh’g Req. 12–13 (citing Ex. 1088 ¶¶ 68, 70 (citing Ismagilov 091 [Ex. 1004], 9:5–7, 28:4–6, 28:67–29:1 and Ex. 1089, 91:11–16). None of the cited evidence mentions PFO or any role it plays in promoting droplet merging. Moreover, Dr. Gale opines that Ismagilov 091 does not disclose “pooling droplets at all” (Ex. 1088 ¶ 63) and “does not provide any description of any well or reservoir in which plugs are pooled so that they contact each other without fusing” (*id.* ¶ 69), a position directly at odds with our findings about Ismagilov 091 and Petitioner’s and Dr. Fair’s positions in this proceeding. Dec. 27–28; Pet. 35–37; Ex. 1008 ¶¶ 127–129 (asserting that Ismagilov 091 discloses collection wells or reservoirs from which droplets can be collected by micropipette).

Petitioner also directs us to Dr. Gale’s testimony that PFO “can be used . . . in a variety of ways” and that using it as a destabilizing surfactant to promote droplet merging “has been done before.” Req. Reh’g 13 (quoting Ex. 1089, 126:16–23). Dr. Gale’s testimony does not provide persuasive support for Petitioner’s argument because it fails to identify *when* PFO had

⁸ Available at <https://www.uspto.gov/TrialPracticeGuideConsolidated>.

been used as a destabilizing surfactant to promote droplet merging, and it fails to support Petitioner's position that Ismagilov 091 discloses PFO for droplet merging.

IV. CONCLUSION

We deny Petitioner's Request for Rehearing because we determine that Petitioner has not met its burden to show that, in the Final Decision, we misapprehended or overlooked any matter.

V. ORDER

For the foregoing reasons, it is hereby:

ORDERED that Petitioner's request for rehearing is *denied*; and

FURTHER ORDERED that Exhibits 1088 and 1089 are not admitted.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10X GENOMICS, INC.,
Petitioner,

v.

BIO-RAD LABORATORIES, INC.,
Patent Owner.

IPR2020-00088
Patent 9,896,722 B2

Before CHRISTOPHER M. KAISER, KIMBERLY MCGRAW, and
ELIZABETH M. ROESEL, *Administrative Patent Judges*.

MCGRAW, *Administrative Patent Judge*, concurring.

I join the majority’s decision denying Petitioner’s Request for Rehearing.

I write separately to highlight that the panel need not determine whether the evidence of record establishes that perfluorooctanol (“PFO”), or other fluorinated surfactants, can be used as a destabilizing agent to merge droplets in order to deny Petitioner’s Request for Rehearing of our determination that Petitioner did not show by a preponderance the evidence that claims 15–17 are unpatentable over US 7,129,091 B2 (Ex. 1004, “Ismagilov 091” or “Ismagilov”) and US Pub. No. 2002/0058332 A1 (Ex. 1006).

Petitioner’s arguments to show the unpatentability of independent claim 14—e.g., that fluorosurfactants of Ismagilov 091 are used to stabilize droplets so that the droplets will not merge together but rather, will separate from the immiscible fluid based on density when in a separation chamber—are inconsistent with Petitioner’s arguments to show the unpatentability of dependent claims 15 through 17—e.g., that a fluorosurfactant disclosed in Ismagilov 091 (i.e., PFO) is used to destabilize aqueous droplets so that the droplets will merge together.

For example, the Petition asserts that “the Ismagilov droplets were stabilized by the *long-fluorinated-tail surfactant*” and that the Ismagilov emulsions “would pool stably and would float.” Pet. 10 (citing Ex. 1017, 222:18–223:9); *see also* Pet. 45–46 (asserting that Ismagilov discloses separating droplets from immiscible fluid in a separation chamber as required by claim 14 because “providing droplets of different density from the immiscible fluid into an output well or reservoir and allowing those droplets to float or sink relative to the oil” discloses the separating step); *see also* Pet. 14 (stating that the plugs in Ismagilov 091 “are droplets that are surrounded by an immiscible fluid” and “Ismagilov testifying regarding creating stable ‘droplets’”).

In contrast, Petitioner argues with respect to claims 15–17 that a person skilled in art would know that “PFO [a fluorosurfactant disclosed in Ismagilov 091], could be used for droplet merging. Pet. 52 (citing Ex. 1004, 21:16–29, 48:25–28, 61:19–21). In its Request for Rehearing, Petitioner asserts that each of the 17 examples disclosed in Ismagilov 091 use a 10:1 mixture of the fluorinated oil perfluorodecaline to PFO. *See* Req. Reh’g 10 (citing Ex. 1004, 61:19–21; Pet. 52; Ex. 1008 ¶ 192). Petitioner further asserts that Example 4 of Ismagilov describes experiments where plugs were

merged (coalesced) using that 10:1 mixture of perfluorodecaline and PFO. *Id.* at 11 (citing Ex. 1004, 64:8–67, Figs. 33b–33c). Petitioner asserts that these and other teachings of Ismagilov 091, together with other identified disclosures “confirm that a POSA [person of ordinary skill in the art] was familiar with PFO’s use as a destabilizing surfactant that can be added to the continuous phase to promote merger/coalescence of droplets to destabilize droplet emulsions.” *Id.* at 11 (citing, *inter alia*, Pet. 11–13, 51–53; Ex. 1008 ¶ 62, 190–193).

Thus, Petitioner’s argument that the fluorosurfactants used in Ismagilov (i.e., PFO) are used to stabilize droplets, made to support its unpatentability argument of claim 14, is inconsistent with Petitioner’s argument that a POSA would have known to add PFO to destabilize Ismagilov’s stable droplets, made to support its unpatentability argument of claims 15–17. Stated another way, Petitioner is arguing that fluorinated surfactants, such as PFO, are used to create highly stable droplets in an immiscible fluid of fluorinated oil that will not coalesce in the separation chamber, while also arguing that the addition of PFO to stable droplets in an immiscible fluid of fluorinated oil will destabilize the droplets. These inconsistencies are not explained. As such, regardless of whether Ismagilov discloses or suggests, or a person skilled in the art would have understood, that PFO could be used to destabilize droplets, Petitioner has not sufficiently explained its inconsistent positions that a PFO can also be used to stabilize droplets.

Given these inconsistent arguments regarding independent claim 14 and its dependent claims 15–17, Petitioner’s arguments fail to show that the panel’s decision that Petitioner has not shown by a preponderance of the evidence that claims 15–17 are unpatentable should be modified.

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Patent 9,896,722 B2

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