UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

J KYLE BASS and ERICH SPANGENBERG,

Petitioner

v.

FRESENIUS KABI USA, LLC,

Patent Owner

Case IPR2016-00254
U.S. Pat. No. 8,476,010 B2

PATENT OWNER'S OBSERVATIONS ON CROSS-EXAMINATION OF PETITIONERS' REPLY WITNESS

1. In Ex. 2064 (316:23-317:25), Dr. Feinberg admitted that that as of 2003 (or the time of the '010 invention), "it was a well-accepted principle that sterile drugs should be manufactured using aseptic processing only when terminal sterilization is not feasible." Dr. Feinberg further admitted that U.S. regulatory guidance (Ex. 2060) also states that it was "a well-accepted principle that sterile drugs should be manufactured using aseptic processing only when terminal sterilization is not feasible." Dr. Feinberg also admitted that "it's feasible to use autoclave with the invention of the '010 patent" and that "you don't have to use a different sterilization process." (Ex. 2064 at 286:3-15.) Dr. Feinberg further admitted that Diprivan is "actually manufactured with heat sterilization" and that he "is not aware of any other manufacturer that does propofol manufacturing that uses other sterilization processes." (Ex. 2064 at 285:6-20.) This testimony is relevant because it shows that terminal sterilization is the only appropriate method of sterilizing the claimed formulations, contradicting Petitioners' argument that a POSA could use aseptic manufacture or sterile filtration with silicone oil-treated stoppers as an alternative to terminal sterilization by autoclave in the manufacturing process for formulations claimed in the '010 patent (*see* Petitioners' Reply at 21-23). This testimony also contradicts Dr. Feinberg's opinion that although references such as "Mannermaa, the '919 patent and Lehr would have discouraged a POSA from using autoclave, they would not have discouraged a

POSA from the claimed invention using other sterilization techniques." (Ex. 1044 at ¶ 24.)

2. In Ex. 2064 (344:8-15), Dr. Feinberg admitted that "filter sterilization is not suitable for Diprivan," as taught in prior art Ex. 2052. This testimony is relevant because it contradicts Petitioners' argument that a POSA would consider sterile filtration as an alternative to terminal sterilization by autoclave (*see* Petitioners' Reply at 21-23).

3. In Ex. 2064 (307:22-308:9), Dr. Feinberg admitted that "European regulatory guidance [(Ex. 2061)] says that packaging material that is incompatible with heat sterilization cannot itself be the sole reason for adopting aseptic processing," and that "European regulatory guidance directs the manufacturers to choose the best sterilization method for the formulation and select the packaging accordingly." This testimony is relevant because it shows that the prior art taught that incompatibility between the patented propofol formulations and an *autoclaved* silicone oil treated rubber stopper is not a sufficient reason to adopt aseptic processing, contradicting Petitioners' argument that a POSA would have been motivated to use aseptic manufacture or sterile filtration instead of terminal sterilization by autoclave in the manufacturing process for the claimed formulations. This testimony also contradicts Dr. Feinberg's testimony that although references such as "Mannermaa, the '919 patent and Lehr would have

discouraged a POSA from using autoclave, they would not have discouraged a POSA from the claimed invention using other sterilization techniques." (Ex. 1044 at ¶ 24.)

4. In Ex. 2064 (288:22-289:2; 290:10-16), Dr. Feinberg admitted that "the European Pharmacopoeia [(Ex. 2059)] recommends selecting a container to allow the optimum sterilization method" and that "the European Pharmacopoeia recommends terminal sterilization whenever possible." This testimony is relevant because it shows that the prior art taught that drug product containers should be selected to allow terminal sterilization since it is the preferred sterilization method, contradicting Petitioners' argument that a POSA would consider using aseptic manufacture or sterile filtration with the claimed invention after concluding that a silicone oil treated closure is incompatible with terminal sterilization.

5. In Ex. 2064 (299:19-300: 21), Dr. Feinberg admitted that that European regulatory guidance (Ex. 2060) states that "the use of alternate packaging materials should be thoroughly investigated before any decision to use non-terminal sterilization process is made" and that "terminal sterilization of the final container should be used whenever possible." This testimony is relevant because it shows that the prior art taught that drug product containers should be selected to allow terminal sterilization since it is the preferred sterilization method, contradicting Petitioners' argument that a POSA would consider using aseptic manufacture or

sterile filtration after concluding that a silicone oil treated closure is incompatible with terminal sterilization.

6. In Ex. 2064 (278:22-279:15), Dr. Feinberg admitted that Ex. 1047 discloses that "a closure for an injectable product has to fulfill the following the requirements" including that "it must be capable of sterilization at least once or twice by autoclaving." This testimony is relevant because it demonstrates that the prior art taught that compatibility with terminal sterilization is considered a requirement for a closure for an injectable product, contradicting Petitioners' argument that a POSA would consider using a closure that would require aseptic manufacture or sterile filtration with the claimed formulations.

7. In Ex. 2064 (233:4-8), Dr. Feinberg admitted that "the advantages of manufacturing efficiency are essentially economic as distinct from, for example, the efficacy of the drug and medical use." This testimony is relevant because it indicates that commercial efficiency is the principal motivation for Petitioners' proposed combinations of prior art.

8. In Ex. 2064 (308:10-24), Dr. Feinberg admitted that European regulatory guidance (Ex. 2061) "is saying commercial reasons like manufacturing efficiency [] should not be used as justification for using a sterilization method other than terminal sterilization." This testimony is relevant because it indicates that the prior art taught that commercial efficiency is not a sufficient basis to change the

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