

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

J KYLE BASS and ERICH SPANGENBERG
Petitioners

v.

FRESENIUS KABI USA, LLC
Patent Owner

U.S. Patent No. 8,476,010
Issue Date: July 2, 2013

Title: PROPOFOL FORMULATIONS WITH
NON-REACTIVE CONTAINER CLOSURES

Inter Partes Review No. IPR2016-00254

**EXHIBIT 1044 – SUPPLEMENTAL DECLARATION OF THOMAS N.
FEINBERG, PH.D.**

I, THOMAS N. FEINBERG, PH.D., hereby declare and state as follows:

1. I have been retained by the Gonsalves Law Firm ("the firm") as an expert in connection with the above-captioned matter. I am being compensated for my time. My compensation in this matter is neither dependent nor related to the outcome of this matter. I have never before been retained by the firm in any capacity. I have been retained by counsel in connection with the above-captioned *inter partes* review ("IPR") Petition. Specifically, I have been asked to prepare this Supplemental Declaration to address the Patent Owner's Response as well as their exhibits including the expert declaration.

2. I have reviewed the Patent Owner's Response and its exhibits including the expert declaration.

3. I have a substantial amount of experience and knowledge about the manufacturing and packaging of drug compositions like Diprivan[®]. I have over 20 years of experience with the analytical requirements of drug packaging (Ex. 1002, Dr. Feinberg's Declaration, ¶¶ 4-5; Ex. 1003, Dr. Feinberg's Curriculum Vitae, pp. 1-4).

4. It is my opinion that a person of ordinary skill in the art (POSA) would have been motivated to combine the teachings of propofol from the Diprivan PDR and Farinotti with the teachings of a silonized bromobutyl stopper from the '864

patent or the '043 patent, and reasonably expect success. No non-obvious differences exist between the combination and the claimed subject matter.

5. I understand that the Patent Owner (PO) argued that the purported manufacturing benefit of siliconization would not have “motivate[d] a POSA to replace the commercially successful stoppers used with Diprivan® with the closures disclosed in the '864 and WO '043 patents” (Petition, p. 28).

6. It is my opinion that the PO’s argument is wrong. First, there is substantial evidence that a POSA would have been motivated to use a siliconized bromobutyl rubber stopper in a container of a propofol composition to address machinability problems with rubber stoppers (*e.g.*, friction between the rubber closure and metallic machinery, clumping of parts, excessively high required insertion force). Smith et al. discusses the advantages (page S4) of siliconization: “[m]achinability is greatly improved through the use of lubricated packaging components. Siliconization of rubber products reduces the friction present between the rubber closure and the metallic machinery. Lubrication helps eliminate clumping of parts as they are smoothly fed from hoppers to machine paths. These lubricated components then easily transverse down machine guides, reducing any possible problems, which are ultimately very costly in terms of lost production time.” Smith also outlines two other important characteristics of siliconized rubbers — reduction of insertion force (page S4, Section III. B.) and sealability (Section III. C.)

7. Another reference (Pharmaceutical Packaging Technology) similarly indicates that a POSA would have been motivated to use a siliconized bromobutyl rubber stopper in a container of a propofol composition to address machinability problems with rubber stoppers (e.g., friction between the rubber closure and metallic machinery, clumping of parts, excessively high required insertion force):

Most closures are lightly coated with silicone oil, such as a polydimethyl siloxane, as a means of reducing particulate formation as it acts as a lubricant between closures. It also reduces considerably the inherent tackiness in many rubber formulations. The main advantage of a silicone oil coat is that it facilitates the stoppering operation by lubricating the passage of the closures through assembly machines and insertion into the barrel or vial opening.

(Ex. 1045, Pharmaceutical Packaging Technology, November 30, 2000 Chapter 12 pg 361). As indicated by a study in another prior art reference (Sudo), the lubricated stopper was demonstrated to have the lowest sliding value of all tested examples (Ex. 2042, the Sudo '794 patent, col. 22, line 56).

8. It is my opinion that the PO did not demonstrate that the prior art teaches away from the claimed invention.

9. PO argued that “measurements of actual silicone oil contamination from siliconized stoppers exceed both pharmacopeial limits and the particle

distributions associated with Diprivan[®]” (Petition, p. 37). PO cites to several references (e.g., Smith, Vernon, 1968 Bulletin of the Parenteral Drug Association, the May 2003 edition of the Pharmaceutical & Medical Packaging publication, FDA correspondence, Sudo, the ‘504 patent, the ‘919 patent, and Mannermaa) in an attempt to support its argument (*id.* at pp. 37-43). Indeed, one of these prior art references, Sudo ‘794 patent, is another example of siliconization available to a POSA that would have been obvious to use to improve manufacturing ease.

10. But none of the references cited by Petitioner would have taught away from the claimed invention of using a siliconized bromobutyl stopper in a container of a propofol composition for many reasons. First, many of the references cited by Petitioner do not mention that the particulate contamination exceeds either the pharmacopeial limits or levels in Diprivan[®]. For example, Smith does not disclose that any particulates from siliconized stoppers would exceed pharmacopeial limits or the levels associated with Diprivan[®] (*see e.g.*, Exhibit 2035, Smith, col. 58). Rather, Smith indicates only that testing would need to be performed to determine whether any contamination would be meaningful as I have previously stated in my deposition transcript:

speaking from the expertise that I have in extractibles [sic] and leachables, is that there are lots of measurable differences, and you will always find leachables. Whether that's meaningful, it really depends

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