EXHIBIT A

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United States Court of Appeals for the Federal Circuit

HOSPIRA, INC.,
Plaintiff-Appellant

v.

FRESENIUS KABI USA, LLC,
Defendant-Appellee

2019-1329, 2019-1367

Appeals from the United States District Court for the Northern District of Illinois in Nos. 1:16-cv-00651, 1:17-cv-07903, Judge Rebecca R. Pallmeyer.

Decided: January 9, 2020

ADAM G. UNIKOWSKY, Jenner & Block LLP, Washington, DC, argued for plaintiff-appellant. Also represented by BRADFORD PETER LYERLA, AARON A. BARLOW, YUSUF ESAT, REN-HOW HARN, SARA TONNIES HORTON, Chicago, IL.

IMRON T. ALY, Schiff Hardin LLP, Chicago, IL, argued for defendant-appellee. Also represented by KEVIN MICHAEL NELSON, JOEL M. WALLACE; AHMED M.T. RIAZ, New York, NY.

Before LOURIE, DYK, and MOORE, *Circuit Judges*.

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LOURIE, *Circuit Judge*.

Hospira Inc. ("Hospira") appeals from the judgment of the United States District Court for the Northern District of Illinois that claim 6 of U.S. Patent 8,648,106 ("the '106 patent") is invalid as obvious. *Hospira, Inc. v. Fresenius Kabi USA, LLC*, 343 F. Supp. 3d 823 (N.D. Ill. 2018) ("*Opinion*"). Because we find that the district court's factual findings were not clearly erroneous and that those findings support a conclusion of obviousness, we affirm.

BACKGROUND

Hospira makes and sells dexmedetomidine products under the brand name Precedex, including a ready-to-use product known as Precedex Premix. Hospira owns a number of patents that cover its Precedex Premix product. Fresenius Kabi USA LLC ("Fresenius") filed an Abbreviated New Drug Application ("ANDA") seeking approval to enter the market with a generic ready-to-use dexmedetomidine product. Hospira sued for infringement of five patents and eventually dropped all but two claims, one of which was claim 6 of the '106 patent.[1] Fresenius stipulated to infringement of claim 6, and the district court held a bench trial on its validity.

I. Prior Art Dexmedetomidine

Dexmedetomidine is a chemical compound that is effective as a sedative. '106 patent col. 1 ll. 36–37. Dexmedetomidine was first developed and patented by Farmos Yhtyma Oy ("Farmos") in the 1980s. Farmos was issued U.S. Patent 4,910,214, which disclosed the dexmedetomidine compound and its use as a sedative.

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[1] The other asserted claim was claim 8 of U.S. Patent 9,616,049, which the district court held would have been obvious and is not at issue in this appeal.

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In 1989, Farmos submitted an Investigational New Drug application ("the Farmos IND") to the U.S. Food and Drug Administration ("FDA") seeking approval to begin safety testing dexmedetomidine formulations in humans. Farmos conducted at least two human safety studies using intravenous administration of 20 μg/mL dexmedetomidine hydrochloride but subsequently abandoned its safety testing after the studies showed adverse effects.

In 1994, Farmos's successor granted Abbott Laboratories (Hospira's predecessor-in-interest) an exclusive license to make, use, and sell dexmedetomidine for human use in the United States. In 1999, Abbott Laboratories received FDA approval to market a 100 μg/mL dexmedetomidine hydrochloride formulation known as "Precedex Concentrate." Precedex Concentrate is supplied in 2 mL clear glass vials and 2 mL clear glass ampoules made from Type IA sulfur-treated glass sealed with coated rubber stoppers. The 100 μg/mL concentration of Precedex Concentrate is too strong to be directly administered to patients, and thus the label provides instructions for diluting the drug to a concentration of 4 μg/mL before intravenous administration.

Dexmedetomidine is also available as a sedative for commercial veterinary use. In 2002, the European Medicines Evaluation Agency authorized use of a product called Dexdomitor, which is a ready-to-use 500 μg/mL formulation of dexmedetomidine hydrochloride. Dexdomitor is stored in a 10 mL glass vial sealed with a coated rubber stopper and has a two-year shelf life.

II. The '106 Patent

The '106 patent is entitled "Dexmedetomidine Premix Formulation" and is directed to pharmaceutical compositions comprising dexmedetomidine (or a pharmaceutically acceptable salt of dexmedetomidine) formulated as a liquid for parenteral administration to a patient, "wherein the composition is disposed within a sealed container as a premixture." '106 patent at Abstract; *see also* '106 patent col.

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1 ll. 19–20 ("The present invention relates to patient-ready, premixed formulations of dexmedetomidine, or a pharmaceutically acceptable salt thereof . . . ."). The '106 patent describes the alleged problems associated with prior art dexmedetomidine formulations that the patented invention was intended to solve:

> To date, dexmedetomidine has been provided as a concentrate that must be diluted prior to administration to a patient. The requirement of a dilution step in the preparation of the dexmedetomidine formulation is associated with additional costs and inconvenience, as well as the risk of possible contamination or overdose due to human error. Thus, a dexmedetomidine formulation that avoids the expense, inconvenience, delay and risk of contamination or overdose would provide significant advantages over currently available concentrated formulations.

Id. col. 1 l. 61–col. 2 l. 3.

To address the perceived shortcomings of the prior art, the '106 patent states that its invention relates to "premixed pharmaceutical compositions of dexmedetomidine, or a pharmaceutically acceptable salt thereof, that are formulated for administration to a patient, without the need to reconstitute or dilute the composition prior to administration." *Id.* col. 2 ll. 7–11. The patent specifies that the invention can be formulated as a "ready to use" composition, which is a premixed dexmedetomidine composition that is "suitable for administration to a patient without dilution." *Id.* col. 3 l. 66–col. 4 l. 2.

Importantly, the '106 patent states that "[t]he present invention is based in part on the discovery that dexmedetomidine prepared in a premixed formulation that does not require reconstitution or dilution prior to administration to a patient, *remains stable and active after prolonged storage*." *Id.* col. 3 ll. 6–10 (emphasis added). The patent

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