THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

HOSPIRA, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	**Nos. 16 C 651, 17 C 7903**
	)	
FRESENIUS KABI USA, LLC,	)	**Judge Rebecca R. Pallmeyer**
	)	
Defendant.	)	

MEMORANDUM OPINION AND ORDER

Plaintiff Hospira, Inc., a Delaware corporation with its primary place of business in Illinois, manufactures pharmaceuticals and medical supplies. One of Hospira's products is a chemical compound known as dexmedetomidine, which Hospira sells to health care providers under the brand name Precedex. Between 2012 and 2014, Hospira obtained four patents covering a new product made from dexmedetomidine: U.S. Patent Nos. 8,242,158 (the "'158 Patent"), 8,338,470 (the "'470 Patent"), 8,455,527 (the "'527 Patent"), and 8,648,106 (the "'106 Patent"). (Complaint in Case No. 16 C 651 [1] ("Pl.'s First Compl."), 3.) The new product, known as Precedex Premix, is a ready-to-use, diluted version of a Hospira product that has been on the market since 1999. That product, known as Precedex Concentrate, is formulated at 100 micrograms per milliliter (μg/mL) and must be diluted with saline to a concentration of 4 μg/mL before being administered to patients. Precedex Premix has the same formulation and the same package configuration as Precedex Concentrate but is pre-diluted with saline to a 4 μg/mL concentration.

Defendant Fresenius Kabi USA, LLC is an American subsidiary of a German pharmaceutical manufacturer which is also registered in Delaware and headquartered in Illinois. In December 2015, Fresenius Kabi notified Hospira that it had filed an abbreviated new drug application ("ANDA") with the FDA, seeking approval to market its own proposed dexmedetomidine products prior to the expiry of Hospira's patents. (Answer to Complaint, Affirmative Defenses, and Counterclaims in Case No. 16 C 651 [10] ("Def.'s First Ans."), ¶ 16.)

Hospira filed suit a month later, alleging patent infringement. (Pl.'s First Compl. 8-10.) In 2017, Hospira obtained a fifth patent covering the same dexmedetomidine product—U.S. Patent No. 9,616,049 (the "'049 Patent")—and filed a second complaint of patent infringement. (Complaint in Case No. 17 C 7903 [1] ("Pl.'s Second Compl."), 3, 5-6.)

Fresenius Kabi initially denied the allegations and counterclaimed for a declaration that the patents are invalid, or, alternatively, that Fresenius Kabi's actions will not infringe. (Def.'s First Ans. 22; Answer to Complaint, Affirmative Defenses, and Counterclaims in Case No. 17 C 7903 [18] ("Def.'s Second Ans."), 7, 14-15.)[1] Following the court's claim construction order in November 2017, the parties jointly agreed to limit the number of patent claims asserted in both actions. (Joint Stipulation in Case No. 16 C 651 [93] ("Joint Stipulation"), 2.) Since then, Hospira has dropped all but claim 6 of the '106 Patent and claim 8 of the '049 Patent. Fresenius Kabi has stipulated that its proposed product would infringe those claims, but maintains its challenges to their validity. (Joint Stipulation 2-3.)

The court held a five-day bench trial on the issue of the validity of these claims on July 16, 2018 through July 20, 2018. Having reviewed the evidence presented at the trial and the parties' briefs, the court concludes that Fresenius Kabi has established by clear and convincing evidence that both claims are invalid as obvious.[2]

BACKGROUND

A. Dexmedetomidine

Dexmedetomidine is a chemical compound known as an alpha$_2$-adrenoceptor agonist. ('106 Patent, JTX 1, col. 1:34-36.) Among other things, dexmedetomidine is effective as a sedative. (*Id.* at col. 1:36-37.) A Finnish corporation, Farmos Yhtyma Oy ("Farmos"), originally

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[1] Fresenius Kabi also counterclaimed for a declaration that U.S. Patent No. 9,320,712 is invalid, or, alternatively, that Fresenius Kabi's actions will not infringe. (Def.'s Second Ans. 15-17.)

[2] In light of this conclusion, the court does not reach Fresenius Kabi's alternative argument that claim 6 of the '106 Patent is invalid for lack of enablement.

isolated dexmedetomidine in the 1980s. (Hospira's Post-Trial Responsive Brief [144] ("Hospira Resp."), 4.) In March 1990, Farmos obtained a patent that disclosed and claimed the compound: U.S. Patent No. 4,910,214 (the "'214 Patent"), JTX 134.) The '214 Patent also disclosed and claimed the use of dexmedetomidine as a sedative. (*Id.* at cols. 3-4, col. 6:15-31.) The '214 Patent expired in July 2013. (*See* Certificate Extending Patent Term Under 35 U.S.C. § 156, JTX 134 at 134.5.)

When the '214 Patent issued, the FDA had not yet approved any dexmedetomidine product. (Direct Examination of Dr. James Kipp at 254:7-10.)[3] In 1989, Farmos applied to the FDA for an investigational new drug application ("IND") to begin safety testing for dexmedetomidine formulations in humans. (*See* IND Application, JTX 35.) Farmos proposed and eventually conducted at least two safety studies of dexmedetomidine hydrochloride ("dexmedetomidine HCl") administered intravenously, meaning into a vein or veins. (IND Application at JTX 35.63, 35.69; October 1990 IND Supplement, JTX 38 at 38.3, 38.10; Hospira Resp. 4.) The concentration of dexmedetomidine in the formulation was 20 µg/mL. (IND Application at JTX 35.69; October 1990 IND Supplement at JTX 38.10.) The formulation was stored in flame-sealed glass tubes ("ampoules") made from a kind of glass known in the pharmaceutical industry as Type I glass. (IND Application at JTX 35.271, 273.) The parties agree that the studies revealed adverse safety events and that Farmos abandoned efforts to study the use of 20 µg/mL dexmedetomidine HCl in humans. (Hospira Resp. 5; Fresenius Kabi's Opening Post-Trial Brief [134] ("Fresenius Kabi Br."), 32.)

B. Precedex Concentrate

In 1994, Orion Corporation—which had by then acquired Farmos—licensed to Abbott Laboratories ("Abbott") the exclusive right to make, use, and sell dexmedetomidine for human use in the United States and certain other territories. (1994 Dexmedetomidine License and Supply

[3] Citations to direct and cross examination of witnesses refer to the transcript of the July 2018 bench trial.

Agreement, JTX 110 §§ 1.21, 1.27, 2.1.1; Hospira Resp. 5.) In 1999, Abbott obtained FDA approval for a dexmedetomidine HCl drug formulated at a concentration of 100 µg/mL. (Dexmedetomidine HCl Final Labeling ("Precedex Concentrate Label"), JTX 15 at 15.2.) Abbott marketed the drug under the trade name Precedex, and it is now known as Precedex Concentrate. (*See* Hospira Resp. 7.)

Dexmedetomidine HCl at a concentration of 100 µg/mL is too strong to administer directly to patients. (*See* Precedex Concentrate Label at JTX 15.13; Hospira Resp. 7, 8.) Accordingly, the Precedex Concentrate label directs hospital personnel to dilute the drug to a concentration of 4 µg/mL before intravenously infusing patients with the medication. (*See* Precedex Concentrate Label at JTX 15.13.) The label provides instructions on how to perform the dilution. (*See id.* (directing hospital personnel to add 2 mL of Precedex Concentrate to 48 mL of 0.9 percent sodium chloride solution, which produces a total volume of 50 mL).) The label also provides other important information about the drug, including its contents: 118 µg/mL of dexmedetomidine HCl (equivalent to 100 µg/mL of dexmedetomidine base) and 9 milligrams (mg) of sodium chloride in water. (*Id.* at JTX 15.2; *see also id.* (stating that Precedex Concentrate is "preservative-free," "contains no additives or chemical stabilizers," and has a pH of 4.5 to 7.0).) In addition, the label states that the "partition coefficient" of Precedex Concentrate "in octanol:water at pH 7.4 is 2.89." (*Id.*) Dr. James Kipp, Fresenius Kabi's expert on formulation chemistry, explained that the higher a molecule's partition coefficient, the more lipophilic—meaning likely to interact with plastic—it is. (Direct Examination of Dr. Kipp at 290:22-292:3.) A partition coefficient of 2.89 is high, according to Dr. Kipp. (*Id.* at 292:4-8.) Finally, the Precedex Concentrate label discloses that it is supplied only in 2 mL clear glass vials and 2 mL clear glass ampoules. (Precedex Concentrate Label at JTX 15.14.) It is undisputed that the vials and ampoules are made from Type IA sulfur-treated glass, and that the vials are sealed with coated rubber stoppers. (*See, e.g.*, Fresenius Kabi Br. 1; Direct Examination of Dr. Priyanka Roychowdhury at 153:6-9, 154:14-19; Direct Examination of Dr. Kipp at 310:6-9 (testifying that Precedex Concentrate "includes a sealed glass container as

its final packaging configuration, with a Teflon-coated stopper").)

Abbott transferred its rights in dexmedetomidine to Hospira in 2004 when it spun Hospira off as an independent business. (*See, e.g.*, 2004 Separation and Distribution Agreement, JTX 109 at 109.16-17, 25, 82.)

C. The Patented Invention

1. Development Process

i. Ready-to-Use Product

In 2006, Hospira decided to develop a ready-to-use dexmedetomidine drug—that is, a formulation pre-diluted to the 4 µg/mL concentration used in humans. (Hospira Resp. 8; September 2006 Hospira Precedex Line Extension Proposal ("2006 Premix Proposal"), JTX 72.) The drug, now known as Precedex Premix, is the subject of the patents-in-suit.

In a September 2006 internal document, Hospira observed that hospitals incur "added cost and inconvenience" when their pharmacy departments need to "take the 2 mL vial and convert it to patient ready." (2006 Premix Proposal at JTX 72.2.) Hospira also noted that a ready-to-use product would "have high value to the customer from both a convenience and cost standpoint." (*Id.*)

Dr. Priyanka Roychowdhury, who has a Ph.D. in pharmaceutics, and Dr. Robert Cedergen, who has a Ph.D. in biochemistry, worked on the development of Precedex Premix while they were employed at Hospira. (Direct Examination of Dr. Roychowdhury at 130:18-131:16; Direct Examination of Dr. Cedergen at 197:18-21, 199:1-20.) They are the named co-inventors of the patents-in-suit. (*See* '106 Patent, JTX 1; '049 Patent, JTX 2.) Dr. Roychowdhury testified at trial that from the perspective of a pharmaceutical formulator, a ready-to-use product has obvious advantages; any formulator would be motivated to make a ready-to-use product if there is a patient need for it; and a patient need for it existed before 2012. (Direct Examination of Dr. Roychowdhury at 141:12-15; 143:1-6; 148:23-25.) Drs. Roychowdhury and Cedergen also acknowledged that they did not come up with the idea for Precedex Premix; rather, someone at

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