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Lessons on inherency challenges after *Hospira v. Fresenius Kabi USA*

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MARCH 11, 2020

Did the U.S. Court of Appeals for the Federal Circuit create a new burden-shifting framework for patent litigation challenges that are based on allegations of inherency?

While the answer is unclear, a recent ruling provides important lessons for patent litigants involved in inherency challenges.

LITIGATION BACKGROUND

In *Hospira Inc. v. Fresenius Kabi USA LLC*, 946 F.3d 1322 (Fed. Cir. 2020), the Federal Circuit affirmed the U.S. District Court for the Northern District of Illinois' decision to invalidate a patent claim based on inherent obviousness.

The litigation arose when Hospira filed suit against Fresenius based on the latter's filing of an Abbreviated New Drug Application seeking to market a generic version of Hospira's ready-to-use dexmedetomidine product.

The asserted claim, which covers Hospira's Precedex (dexmedetomidine HCl) Premix product,[1] is directed to a ready-to-use liquid composition of dexmedetomidine at a concentration of about 4 µg/mL disposed within a sealed glass container, where the composition exhibits no more than about a 2% decrease in the concentration of dexmedetomidine over a period of at least five months.[2]

The District Court found the patent was obvious over a combination of prior art. *Hospira Inc. v. Fresenius Kabi USA LLC*, 343 F. Supp. 3d 823 (N.D. Ill. 2018).

The judge found a person of ordinary skill in the art would have been motivated to prepare a composition of dexmedetomidine within a sealed glass container at the recited concentration with a reasonable expectation of success, but that the 2% stability limitation was nowhere taught or suggested by the prior art.

Nonetheless, both the lower court and the Federal Circuit agreed that the asserted claim was invalid for inherent obviousness — the principle that, in some circumstances, a missing claim limitation may be supplied by inherency in an obviousness analysis.[3]

LAW OF INHERENT OBVIOUSNESS

Proving inherent obviousness in patent litigation is a notoriously stringent endeavor.

The Federal Circuit has repeatedly stated what it said in *Par Pharmaceutical Inc. v. TWI Pharmaceutical Inc.*, 773 F.3d 1186 (Fed. Cir. 2014): that the concept of inherency "must be carefully circumscribed" in the obviousness context, and that a party must "meet a high standard in order to rely on inherency to establish the existence of a claim limitation in the prior art in an obviousness analysis."[4]

The Federal Circuit also said that high standard requires that the party advancing a theory of inherent obviousness must show that "the limitation at issue *necessarily must* be present, or *the natural result* of the combination of elements explicitly disclosed by the prior art" (emphasis added).

Such a showing is particularly challenging in view of the court's warnings that "[i]nherency ... may not be established by probabilities or possibilities," and "[t]he mere fact that a certain thing *may* result from a given set of circumstances is not sufficient."[5]

The Federal Circuit in *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342 (Fed. Cir. 1999), clearly laid out the policy rationale for these requirements: "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer."

Importantly, because in litigation the ultimate burden to show obviousness (by clear and convincing evidence) rests with the patent challenger, it is the proponent of the inherent obviousness argument that retains the burden to make the required showing that the prior art necessarily includes the missing limitation, or that the missing limitation is the natural result of the asserted prior art combination.

In contrast, when prosecuting a patent application, the U.S. Patent and Trademark Office "can require *an applicant* to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product."[6]

The rationale for the burden-shifting framework before the PTO has been couched as fair, but it is also eminently practical — "the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith."[7]

These rationales do not apply to patent litigants advancing a theory of inherency, as such parties (at least in theory) have the resources to prepare and test compositions disclosed or suggested by the prior art to prove whether a missing claim limitation is inherent to the composition.

Moreover, because a party advancing an inherency argument bears the ultimate burden to prove invalidity by clear and convincing evidence, the case for burden-shifting in the litigation context is weaker.

EVIDENCE OF INHERENCY IN *HOSPIRA*

A cursory reading of the Federal Circuit's opinion in *Hospira* suggests a divergence from the traditional framework applied for assertions of inherent obviousness in the litigation context.

But understanding whether the panel actually implemented such a change requires a detailed review of evidence of inherency presented by the litigants, as well as the legal and factual conclusions drawn by both the lower and appellate courts.

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In the first instance, the District Court premised its finding of inherent obviousness on two prior art combinations:

(1) a more concentrated 100 µg/mL solution of dexmedetomidine known as Precedex (dexmedetomidine HCl) Concentrate in combination with the knowledge of a person with ordinary skill in the art.

(2) Precedex Concentrate in combination with Dexdomitor, a ready-to-use 500 µg/mL dexmedetomidine formulation indicated for veterinary use.

The Precedex Concentrate product required dilution prior to administration to a patient, resulting in additional costs and inconvenience, in addition to risks of contamination and overdose due to human error.

As a result, the District Court found that these prior art combinations would have led an ordinarily skilled person to a "preferred embodiment" — a ready-to-use, sealed glass container containing a 4 µg/mL solution of dexmedetomidine HCl that did not require dilution prior to administration.

The court then stated that Fresenius need only prove that this preferred embodiment was invalid, and "thus need only prove inherency for that embodiment."

In its effort to meet that burden, Fresenius presented fact and expert testimony regarding stability data for more than 20 tested samples of the preferred embodiment, including 18 batches from Hospira's Precedex Premix New Drug Application, and three batches from Fresenius' own ANDA for its proposed generic product.

In response, Hospira argued that Fresenius had failed to meet its burden because it had not *excluded the possibility* that the asserted preferred embodiment could be prepared in a way that would fail the 2% stability limitation.

Hospira asserted that, because of the stringent requirements for proving inherency, Fresenius was required to show that no matter how the preferred embodiment was prepared, it would *never* fail the 2% limitation.

On its face, this is a sensible argument — inherency requires that the limitation at issue is shown to be *necessarily* present or *the natural result* of the asserted combination, and not just *likely* to be present.

However, the District Court interpreted Hospira's argument to be that Fresenius had to prove that *every possible embodiment of the asserted claim* necessarily met the stability limitation, which it rejected as an incorrect statement of the law.[8]

Hospira attempted to correct this misunderstanding on appeal, arguing that all of the batches tested by Fresenius were prepared using "special manufacturing techniques designed to ensure stability," techniques developed by the inventors and disclosed in the patent-in-suit.

In other words, it was no surprise that Fresenius established that batches made according to the process disclosed in the patent-in-suit possessed the claimed stability limitation — as that was exactly what the inventors invented and disclosed.

But Hospira contended that this showing was insufficient to prove inherency because it failed to establish that batches of the preferred embodiment made *without* using the "special manufacturing techniques" developed by the inventors would also necessarily possess the claimed stability.

Nonetheless, the Federal Circuit appeared to dismiss this argument, stating that the challenged claim "is not a method claim, it is not a product-by-process claim, and there are no limitations in claim 6 regarding the manufacturing process by which the recited ... composition must be prepared. ... Importing such limitations from Example 5 into the claim, as Hospira seeks to do, would be improper."

At first blush, this appears to be a non sequitur — Hospira's argument was not that the *scope of the asserted claim* was limited by these manufacturing processes, but rather that Fresenius' evidence of inherency for the preferred embodiment was limited to compositions made by that process, leaving open the possibility that other methods might result in a

composition that failed the stability limitation, and thus defeating inherency.

Did the Federal Circuit modify the framework for proving inherency?

Taking Hospira's arguments at face value suggests that the Federal Circuit either (1) effectively reduced Fresenius' burden to show inherency (finding sufficient the showing that *at least some* instances of the asserted prior art embodiment demonstrated the missing claim limitation), or (2) shifted the burden to Hospira to disprove inherency based on Fresenius' evidence, and found that Hospira failed to provide evidence sufficient to shift the burden back to Fresenius.

But whether this accurately represents the Federal Circuit's reasoning requires a more detailed review of what the court actually considered to be the asserted prior art combination.

Both the lower and appellate courts made clear that there were two such prior art combinations:

(1) Precedex Concentrate in combination with the knowledge of a person of ordinary skill.

(2) Precedex Concentrate in combination with Dexdomitor.

In addition, both courts premised their analysis on the finding that these combinations would have led a person of ordinary skill to the 4 µg/mL dexmedetomidine HCl preferred embodiment.

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From here, the open question is: What course of action would the hypothetical person of ordinary skill have been motivated to take to reach this preferred embodiment based on the cited art?

One possibility is that the identification of the Precedex Concentrate as prior art means that a person of ordinary skill would have knowledge of that product, its composition and the contents of its label, and would have been motivated to prepare a composition of dexmedetomidine at a concentration of 4 µg/mL by whatever means they saw fit.

Because the special manufacturing techniques designed to ensure stability did not form a part of the prior art, the ordinarily skilled artisan might, as Hospira suggested, pursue a different path that might have produced a composition of the preferred embodiment that did not meet the key 2% stability limitation.

This prospect gives much greater weight to Hospira's argument that Fresenius failed to meet the burden of showing that the missing 2% stability limitation was necessarily present or the natural result of the preferred embodiment.

The other possibility is that a person of ordinary skill would have simply taken the commercially available 100 µg/mL Precedex Concentrate product itself, diluted it to 4 µg/mL as the label instructed, and placed it in a sealed glass container.

If the latter possibility is accepted, the courts' analysis is much more easily understood, as testimony from one of the inventors of the patents-in-suit and Hospira's corporate representative established that there was "no difference" between the Precedex Premix product and Precedex Concentrate when diluted to 4 µg/mL as the label instructed and that these compositions would be identical.

Inherency must therefore have been established, as the composition made by the hypothetical person of ordinary skill would be identical to the commercial Precedex Premix product, which Hospira acknowledged was an embodiment of the asserted claim.

Indeed, the Federal Circuit noted that the patent itself states that the invention was based on "the *discovery* that dexmedetomidine prepared in a premixed formulation ... *remains stable and active after prolonged storage*" (emphasis in original).

The similarity of this language to the Federal Circuit's policy rationale for inherent obviousness — that newly discovered properties of prior art compositions do not render the composition newly patentable — is striking.[9]

LESSONS LEARNED

Regardless of the exact rationale underlying the Federal Circuit's decision, parties on both sides of inherent obviousness (and anticipation) allegations are sure to attempt to leverage the language of the *Hospira* opinion and the underlying facts to their advantage.

But beyond creating fodder for legal argument, there are practical lessons that patent litigants can take away from this case.

First, patentees facing an allegation of inherency in litigation should continue to underscore the "high standard" required by a patent challenger attempting to establish that a missing limitation "necessarily must be present" or "the natural result" of the asserted prior art combination, particularly in the obviousness context, where the concept of inherency "must be carefully circumscribed."[10]

But these parties would also be wise to affirmatively attack evidence offered to show inherency in order to weaken the proponent's case and potentially meet any responsive burden that a court might impose.

Furthermore, attacks against arguments of inherency should be bolstered by expert testimony, and potentially by additional test data.

The *Hospira* opinion suggests that attorney argument alone (which was what the patentee was left with after the lower

court discounted the expert testimony and data it offered) may not be sufficient to defeat a prima facie case of inherency.

While parties are often loath to conduct their own experimental testing, that course should at least be considered. In addition, lesser measures, such as searching the public record and the patentee's own records for potentially relevant data, could also be fruitful and should be explored.

Second, challengers to patent claims should not read *Hospira* to lessen the burden to show inherency.

A court might limit the impact of *Hospira* on future cases because the particular facts of that case (such as the statement in the asserted patent suggesting that the missing stability limitation was inherent in the claimed compositions, and testimony by patentee's own witnesses that the claimed compositions were identical to a prior art product when diluted as instructed in its label) are unlikely to apply in all circumstances.

Moreover, it is unclear whether a court would actually adopt a burden-shifting framework for future inherency cases based on the language in the panel's opinion.

Nonetheless, a proponent of inherency that has set forth its prima facie case should point out where the patentee has unsuccessfully rebutted that case, either by the failure to provide evidence apart from attorney argument or by the submission of evidence that is not germane to the asserted prior art embodiment.

Care should also be taken to ward against arguments from the patentee that cross the line from attacking evidence of inherency to arguing limitations not present in the claims.

Notes

[1] Hospira asserted claim 6 of U.S. Patent No. 8,648,106, which depends from claim 1. Claim 1 recites "1. A ready to use liquid pharmaceutical composition for parenteral administration to a subject, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof disposed within a sealed glass container, wherein the liquid pharmaceutical composition when stored in the glass container for at least five months exhibits no more than about 2% decrease in the concentration of dexmedetomidine," and claim 6 recites "the ready to use liquid pharmaceutical composition of claim 1, wherein the dexmedetomidine or pharmaceutically acceptable salt thereof is at a concentration of about 4 mg/mL."

[2] The Precedex Premix product includes dexmedetomidine in the form of a hydrochloride salt (i.e., dexmedetomidine HCl).

[3] *Par Pharm. v. TWI Pharm. Inc.*, 773 F.3d 1186 (Fed. Cir. 2014).

[4] *See Millennium Pharm. Inc. v. Sandoz Inc.*, 862 F.3d 1356 (Fed. Cir. 2017).

[5] *Hansgirg v. Kemmer,* 102 F.2d 212 (C.C.P.A. 1939) (emphasis added). The same standards apply to establishing inherent anticipation. *See Monsanto Tech. LLC v. E.I. DuPont De Nemours & Co.*, 878 F.3d 1336 (Fed. Cir. 2018); *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342 (Fed. Cir. 1999); *Verdegaal Bros. Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628 (Fed. Cir. 1987).

[6] *In re Best*, 562 F.2d 1252 (C.C.P.A. 1977), citing *In re Ludtke*, 441 F.2d 660 (C.C.P.A. 1971) (emphasis added).

[7] *In re Brown*, 459 F.2d 531 (C.C.P.A. 1972).

[8] While Hospira presented data and expert testimony it claimed showed that the missing limitation was not always present in the asserted preferred embodiment, the District Court dismissed this evidence, finding it less reliable than evidence presented by Fresenius.

[9] *See Atlas,* 190 F.3d at 1347.

[10] *PAR Pharm.*, 773 F.3d at 1195-96; *Millennium Pharm.*, 862 F.3d at 1367.

This article first appeared in the March 11, 2020, edition of Westlaw Journal Intellectual Property.

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