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2017 Federal Circuit obviousness decisions in biopharma: 5 takeaways

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Obviousness. It is one of the most common defenses invoked in biopharma patent litigation. It is also one of the most complicated. And because Federal Circuit authority on obviousness is highly nuanced, proper presentation of evidence and related expert opinions is critical.

After reviewing the Federal Circuit's 2017 obviousness opinions for biopharma patents, we believe there are important lessons to be gleaned.

This article seeks to help patent holders and challengers alike remain current on nuanced shifts in Federal Circuit obviousness law — shifts that may mean the difference between success and failure in court.

TAKEAWAY #1 — INHERENCY AND OBVIOUSNESS

To prove that an inherent, but unknown, property is necessarily present in an obvious combination, one Federal Circuit panel expressly announced the additional requirement that the inherent property is not unexpected in the art.

In 2017, a Federal Circuit panel attempted to reconcile 25 years of precedent concerning inherency and obviousness. To prove an inherent, but unknown property is present in an obvious combination, the panel not only required proof that the property is necessarily present, but also that it was not unexpected in the art.

Background

The Federal Circuit illustrated this point in *Millennium Pharmaceuticals Inc. v. Sandoz Inc.*[1] And it formally announced it later in *Honeywell International Inc. v. Mexichem Amanco Holding S.A. DE C.V.*[2]

In *Millennium*, the patent covered a compound that combined D-mannitol and a boronate ester of bortezomib. Prior art by Adams taught esters of bortezomib, and that bortezomib rapidly degrades in liquid formulations.

Several experts testified that the general knowledge of a POSA included freeze-drying with mannitol to create non-liquid formulations. The district court thus found that freeze-drying the bortezomib of Adams with mannitol would inherently produce the claimed D-mannitol boronate ester, which made it obvious.

Rule

The Federal Circuit reversed. According to the Federal Circuit, regardless of whether freeze-drying with mannitol necessarily produces the claimed compound: "No expert testified that they foresaw, or expected, or would have intended, the reaction between bortezomib and mannitol, or that the resulting ester would have the long-sought properties and advantages."[3]

The Federal Circuit formally announced this rule in *Honeywell*.[4] There, it found the PTAB erred when it held a claimed property was obvious as inherent without addressing whether the property was unpredictable and unexpected.

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The *Honeywell* court attempted to reconcile prior Federal Circuit rulings on inherency in the obviousness context, stating "[w]hat is important regarding properties that may be inherent, but unknown, is whether they are unexpected. All properties of a composition are inherent in that composition, but unexpected properties may cause what may appear to be an obvious composition to be nonobvious."[5]

In 1993, the Federal Circuit broadly stated in *In re Rijckaert* "[t]hat which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown."[6] Before *Honeywell*, Federal Circuit cases finding inherency in the obviousness context had not reconciled *Rijckaert*.[7]

In practice

After *Millennium* and *Honeywell*, it may not be enough to simply assert that an inherent property necessarily results from an allegedly obvious combination without also addressing whether that property is unexpected and unpredictable. Patentees and challengers should pay attention to how their experts characterize prior art teachings surrounding the inherent property.

Experts for patentees should emphasize that the prior art fails to mention the inherent property and provide reasons why skilled

artisans would not expect it. Challengers should scour the prior art for teachings suggesting that the inherent property would have been predictable and expected.

TAKEAWAY #2 — TEACHING AWAY EVIDENCE

Absent express criticism of a claim limitation, the success of teaching away arguments hinges upon a prior art showing that pursuing the claimed subject matter would be "unproductive," as opposed to merely not preferred.

Background

In *Bayer Pharma AG v. Watson Laboratories Inc.,*[8] the claims covered an orally disintegrating tablet ("ODT") to treat erectile dysfunction ("ED") comprising the active vardenafil and at least two sugar alcohols, wherein the tablet disintegrates and immediately releases the active in the mouth. Prior art by Boolell and Fryburg taught formulating vardenafil as an ODT to treat ED.

Prior art by Bauer taught that two sugar alcohols could optimize the properties of a tablet. Tian and Fryburg taught that both immediate and delayed-release ODTs were known.

> Patentees seeking to avoid obviousness based on rationales for combination may wish to investigate whether a known problem or need concerning the claimed subject matter exists in the prior art.

The district court found the claims non-obvious, holding that the prior art taught away from immediate-release ODTs, because immediately releasing vardenafil in the mouth causes two problems — first, an unpleasant bitter taste and second, higher vardenafil bioavailability, which could trigger heart problems in older patients.

Rule

The Federal Circuit reversed.[9] A key to the case was the Federal Circuit's treatment of the alleged teaching away evidence. The Federal Circuit accepted the district court's findings on bitter taste and high bioavailability, but disagreed that they qualified as teaching away evidence.[10]

According to the Federal Circuit, a prior art reference teaches away when "the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the patentee."[11]

The problem for the patentee was that its expert did not use the "unproductive" buzz word, opining instead that the bitter taste and high bioavailability of vardenafil would merely lead a POSA to *prefer* a delayed-release formulation (releasing in the stomach), as opposed to the claimed immediate release ODT (releasing in the mouth).[12]

Seizing on this distinction, the Federal Circuit overturned the district court and explained "obviousness does not require that the motivation be the best option, only that it be a suitable option from which the prior art did not teach away."[13]

The Federal Circuit reached a similar result in *Meiresonne v. Google Inc.*[14] There, it affirmed a PTAB obviousness finding on claims to a computer system for searching the Internet.[15] The sole issue on appeal was whether the prior art taught away from textual descriptions, as claimed, in favor of graphical previews.[16]

Once again characterizing the prior art as merely expressing a preference for one option (graphical previews) over another (textual descriptions), the Federal Circuit refused to find a teaching away.[17]

According to the Federal Circuit "the fact that [prior art by] Finseth describes descriptive text as 'cursory, if not cryptic' does not automatically convert the reference to one that teaches away" because "Finseth does not say or imply text descriptions are 'unreliable,' 'misleading,' 'wrong' or 'inaccurate.'"[18]

In practice

Given the Federal Circuit's conclusions in these cases, patentee experts would do well to opine that pursuing the claimed combination in view of the prior art would be "unproductive" or unworkable. Patentees should avoid characterizing alternate prior art embodiments as merely preferred to the claimed subject matter.

Experts challenging validity, to the extent possible, should characterize the prior art and the opposing expert's testimony as simply expressing a preference for another option as opposed to the claimed combination.

TAKEAWAY #3 — ALTERNATE RATIONALES AND SPECIFIC MOTIVATION

Federal Circuit judges disagree as to whether the alternate rationales announced in *KSR International Co. v. Teleflex Inc.* require a separate motivation or specific reason to pursue a secondary teaching.

Recent Federal Circuit authority concerning the alternate rationales of *KSR* may have significant implications for the biopharmaceutical industry, where patent claims often recite species of particular compounds or a combination of a known active with a known formulation.

Background

In *KSR*, the Supreme Court stated "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. ... [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does."[19]

This articulation of the standard has led to ambiguity, as some Federal Circuit judges interpret *KSR*'s alternate rationales as constituting the "reason" while others interpret the "reason" as a separate requirement.

In the *en banc* case of *Apple Inc. v. Samsung Electronics Co.*[20] the claims, in relevant part, covered a portable device with a touch-screen that could be unlocked by swiping an unlock image in a particular direction. This is the general concept of "swipe to unlock" appearing on smart phones today.

Prior art by Neonode taught a mobile device with a touch-sensitive screen where the phone was unlocked by generally "sweeping right." Neonode therefore disclosed every element of the claim, except the unlock image indicating a particular direction for swiping to unlock, which was taught by Plaisant.

The specific unlock image of Plaisant is more precise than the general "sweeping" of Neonode, and therefore one is less likely to inadvertently unlock the phone. Plaisant, however, taught this feature in connection with a wall-mounted controller for entertainment, security or climate-control systems as opposed to a smartphone.[21]

One key question on appeal was whether invoking the alternate rationales of *KSR* required the challenger to show a specific reason why a POSA would combine a smart phone with features from a wall-mounted screen.

Rule

Federal Circuit judges disagree on this important issue. Writing for the majority, U.S. Circuit Judge Kimberly A. Moore affirmed the jury's non-obviousness finding, noting the absence of a specific motivation to add the missing feature.[22]

In a sharply worded dissent, U.S. Circuit Judge Timothy B. Dyk criticized the majority for misinterpreting *KSR*.

According to Judge Dyk, alternate rationales — like combining known elements and simple substitution — do not require a separate reason or motivation to combine or modify.[23] As Judge Dyk explained, "*KSR* also held, contrary to the majority, that evidence of a specific motivation to combine is not required."[24]

We have not seen much activity on Judge Dyk's dissent in 2017. In early 2017, a Federal Circuit panel deciding a small molecule patent action noted in dicta that alternate rationales do, in fact, require a separate reason or motivation. *See L.A. Biomedical Research Inst. at Harbor-UCLA Med. Ctr. v. Eli Lilly & Co.*[25]

In late 2017, a different Federal Circuit panel, including Circuit Judge Dyk, U.S. Circuit Judge Richard G. Taranto and U.S. Circuit Judge Alvin A. Schall echoed Judge Dyk's concerns and remanded a non-obviousness finding to the PTAB. *See Microsoft Corp. v. Parallel Networks Licensing LLC.*[26]

In practice

Given these disparate interpretations, patentees and challengers in the life sciences industry should take heed. Patentees may seek to rely on *Apple* and *L.A. Biomedical* to demand a reason distinct from the alternate rationales, identifying its absence as a fatal hole in a challenger's case for invalidity.

Challengers may point to *KSR*, other Federal Circuit cases and Judge Dyk's dissent. But until the Supreme Court clarifies the issue, challengers may also wish to identify a specific reason or motivation for all proposed combinations.

TAKEAWAY #4 — ROUTINE OPTIMIZATION AND ANALOGOUS ART

In the context of routine optimization, 2017 Federal Circuit case law analyzing whether prior art qualifies as analogous can be read to support opposite results.

Background

Two contrasting cases make this point.

First, the Federal Circuit held that prior art relating to vitamin B12 administration in routine medical contexts outside cancer was non-analogous and thus inapplicable to methods for treating cancer.[27]

Second, the Federal Circuit held that prior art relating to coatings used with boots, helmets and electrical tape was analogous and thus applicable to vascular drug-eluting stents.[28]

Rule

In *Lilly*, the claims covered methods for treating cancer comprising pre-administration of (1) about 350 µg to about 1000 µg folic acid and (2) about 500 µg to about 1500 µg vitamin B12, followed by administration of pemetrexed sodium.[29]

The prior art disclosed a correlation between increased pemetrexed toxicity and elevated homocysteine levels, which indicate a folic acid or vitamin B12 deficiency.

The parties disputed whether there was a motivation to select vitamin B12 for treating cancer or pemetrexed toxicity. Putting this issue to the side, the Federal Circuit analyzed whether the dose limitations of about 500 µg to about 1500 µg were subject to routine optimization.

According to the Federal Circuit, vitamin B12 doses and schedules from other "routine" medical contexts were not applicable to the field of oncology, because there was no evidence that a POSA would have applied those doses and schedules to treat cancer with pemetrexed.[30]

In *In re Ethicon Inc.*, the claims were directed to stents comprising the co-polymer VDF:HFP in a 85:15 ratio and at least one pharmaceutical agent intermixed with the co-polymer.[31]

In affirming obviousness, the Federal Circuit relied upon three prior art references. Tuch taught stents comprising a polymer and a drug. Tu taught vascular implants and heart valve leaflets

coated with various co-polymers including VDF:HFP. And Lo taught the advantages of a 85:15 ratio for VDF:HFP in coatings for boots, helmets and electrical tape.

Its uses notwithstanding, the Federal Circuit held that Lo is "reasonably pertinent to the particular problem with which the inventor is involved."[32]

U.S. Circuit Judge Pauline Newman disagreed, noting "none of these uses has any relation to a vascular stent or any biological application."[33]

In practice

Given *Lilly*, patentees may wish to take advantage of non-analogous art arguments to defeat routine optimization of result effective variables. The argument is that prior art directed to treating disease states other than those recited by the claimed subject matter is non-analogous and irrelevant.

For their part, challengers should seek out prior art teaching optimization of variables within the context of the claimed disease state. But challengers can also fall back on *Ethicon* to the extent closely analogous art is not available.

TAKEAWAY #5 — IDENTIFICATION OF A KNOWN PROBLEM OR NEED TO SUPPORT RATIONALES

In cases where identification of a known problem or need is necessary to prove a rationale for combination, the Federal Circuit has liberally interpreted the requirement, relying on prior art references concerning the general state of the art and expert testimony.

Background

In *Novartis AG v. Noven Pharmaceuticals Inc.*[34] the Federal Circuit affirmed an obviousness decision by the PTAB. The claims covered a pharmaceutical composition comprising the active rivastigmine, up to about 0.5 percent by weight of an antioxidant and a diluent or carrier.

Enz taught a transdermal patch comprising rivastigmine and an acrylic polymer. Sasaki taught that combining various active compounds with an acrylic polymer tends to reduce any therapeutic effect because the actives break down, and that adding an antioxidant to the combination prevents the drug from breaking down.

The PTAB held Enz in view of Sasaki rendered the claims obvious. Novartis' main argument on appeal was that neither Sasaki nor any other prior art reference actually reported a known oxidation problem with rivastigmine to lead a skilled formulator to add an antioxidant.

Rule

Certain Federal Circuit cases have held that in the absence of a known problem or need, there is no reason a POSA would seek to improve upon the prior art.[35] Building on this, Novartis argued that a POSA "would only have added an antioxidant when required to address a known oxidative degradation problem," which was simply not reported in the prior art for rivastigmine.[36]

To fill this gap, the PTAB and Federal Circuit relied upon generalized prior art teachings concerning rivastigmine's chemical structure, including its functional groups, to predict reactivity and degradation properties.[37]

There, the petitioner's expert relied upon prior art concerning organic chemistry, chemical kinetics and drug stability to opine that the functional groups in rivastigmine made it susceptible to oxidative degradation.[38] In finding the claims obvious, the Federal Circuit agreed with petitioner's expert and characterized oxidation as a known problem.[39]

In practice

Patentees seeking to avoid obviousness based on rationales for combination may wish to investigate whether a known problem or need concerning the claimed subject matter exists in the prior art. Absent a known problem or need, patentees may argue that the required rationale is lacking.

Parties challenging invalidity may take some comfort in *Novartis*, and look to generalized prior art teachings to assist with identification of a problem or need.

NOTES

1 862 F.3d 1356 (Fed. Cir. 2017).

2 865 F.3d 1348 (Fed. Cir. 2017).

3 *Millennium Pharm.*, 862 F.3d at 1367.

4 *Honeywell Int'l*, 865 F.3d 1348.

5 *Id.* at 1355.

6 *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993).

7 *See, e.g., PAR Pharm. Inc. v. TWI Pharm. Inc.*, 773 F.3d 1186, 1195 (Fed. Cir. 2014).

8 874 F.3d 1316 (Fed. Cir. 2017).

9 *See id.*

10 *Id.*

11 *Id.*

12 *Id.*

13 *Id.* at 1328.

14 849 F.3d 1379 (Fed. Cir. 2017).

15 *Id.* at 1380–81.

16 *Id.* at 1382.

17 *Id.* at 1383.

18 *Id.*

19 550 U.S. 398, 418 (2007).

20 839 F.3d 1034, 1048 (Fed. Cir. 2016), *cert. denied*, 138 S. Ct. 420 (2017).

21 *Id.* at 1050.

[22] *Id.* at 1051–52.

[23] *Id.* at 1077–78 (Dyk, J., dissenting).

[24] *Id.* at 1077.

[25] 849 F.3d 1049, 1064 (Fed. Cir. 2017) (quoting *KSR,* 550 U.S. at 418).

[26] No. 2016-2515, 2017 WL 5953512, at *8 (Fed. Cir. Dec. 1, 2017).

[27] *See Eli Lilly & Co. v. Teva Parenteral Meds. Inc.,* 845 F.3d 1357 (Fed. Cir. 2017).

[28] *In re Ethicon Inc.,* 844 F.3d 1344, 1351 (Fed. Cir. 2017) (Newman, J., dissenting).

[29] *Eli Lilly & Co.,* 845 F.3d at 1362.

[30] *Id.* at 1374.

[31] *In re Ethicon,* 844 F.3d at 1353.

[32] *Id.* at 1351.

[33] *Id.* at 1356 (Newman, J., dissenting).

[34] 853 F.3d 1289 (Fed. Cir. 2017).

[35] *See, e.g., Leo Pharm. Prods. Ltd. v. Rea,* 726 F.3d 1346, 1353–56 (Fed. Cir. 2013).

[36] *See Novartis,* 853 F.3d at 1295.

[37] *Id.* at 1295.

[38] *See id.*

[39] *See id.*

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