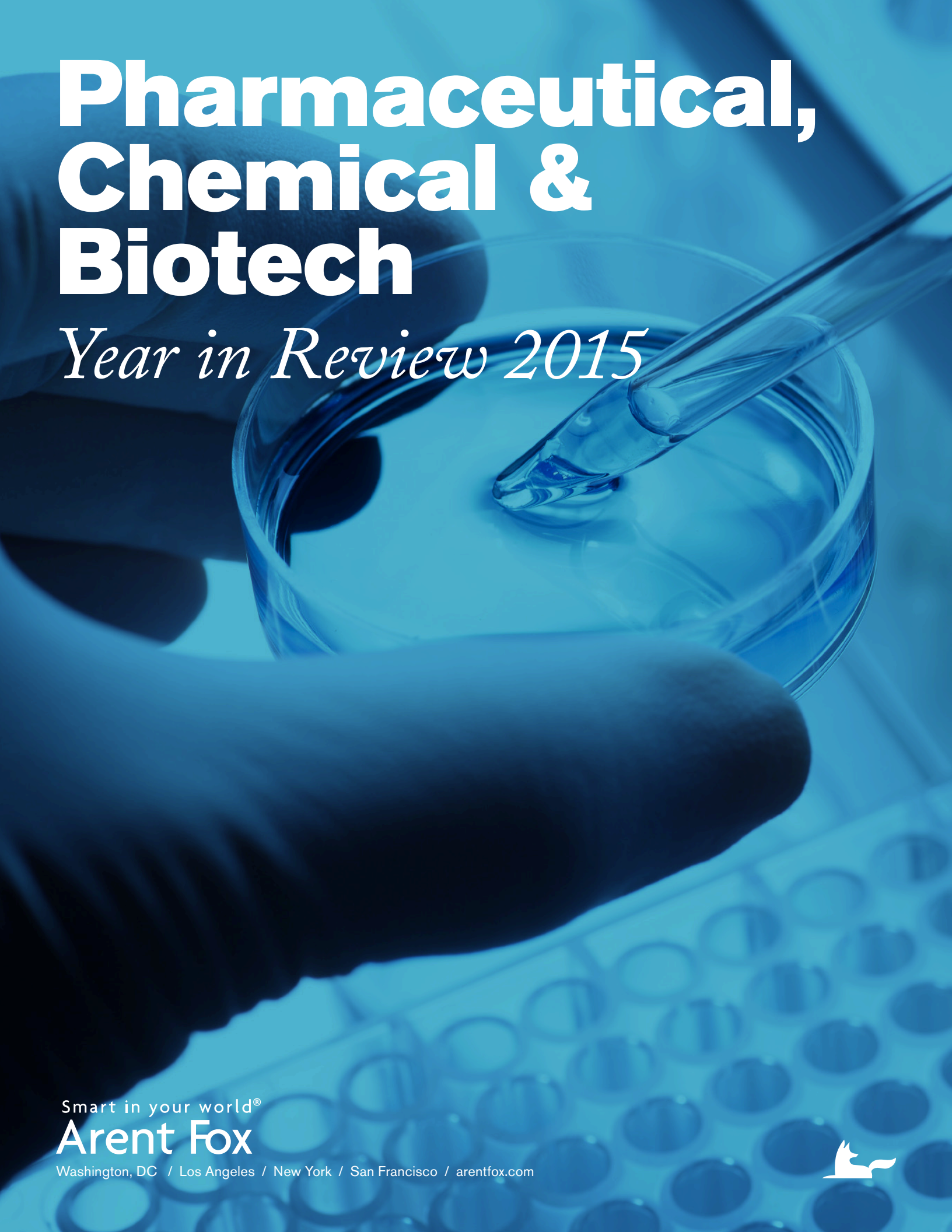
Pharmaceutical, Chemical & Biotech

Year in Review 2015



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Introduction

As in previous years, 2015 brought us a combination of both expected and unexpected holdings by the Supreme Court and the Federal Circuit.

On the expected side of the ledger, the Supreme Court continued its pattern of reversing the Federal Circuit, this year regarding claim construction and induced infringement. Also, true to past history, the Federal Circuit on remand took the Supreme Court's holdings setting forth new tests on both indefiniteness and claim construction, and reached the same result. In particular, in *Teva,* the Federal Circuit once again found Teva's claims to be indefinite, even giving deference to the testimony of Teva's expert, based on the prosecution history. In *Nautilus*, the Federal Circuit on remand continued to find the claims definite, even under the Supreme Court's newly minted test for indefiniteness.

Also on the expected side, the Federal Circuit found against Sequenom, even after *en banc* review, in what many in the life science community believe to be an over-reading of *Mayo v. Prometheus*.

On the unexpected side, the court continues to be all over the map on anticipation and has injected a lot of uncertainty in an area that most would have regarded as fairly settled and stable a few years ago. There are two aspects to this confusion. First, the court continues to interject a "criticality" element into anticipation reviews, whereas previously such showings were limited to obviousness. This is leading to some bizarre outcomes and one can only hope that the court will come to terms with this. Second, the court has been all over the map in its review of whether generic prior art anticipates a claimed species, finding in some instances that a relatively small group is not anticipatory, but in other instances that a vast group is anticipatory.

Also on the unexpected side, the court has largely become a rubber stamp for IPR's, with a nearly 90% affirmance rate. While certainly one would have expected a substantial majority of IPRs to have been affirmed given standards of deference owed to the Patent Office, the lengths to which the court has gone in some instances to uphold the PTO has been surprising, such as in *Gnosis I* and *II*.

Table of Contents

Supreme Court Cases

Even though claim construction is a question of law, the Federal Circuit must apply the "clearly erroneous" standard when reviewing subsidiary factual matters in a district court's claim construction determination.

In *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831 (2015), the Supreme Court considered what standard the Federal Circuit should use when reviewing a trial judge's resolution of an underlying factual dispute during claim construction. The claim term at issue was the meaning of "molecular weight of about 5 to 9 kilodaltons." *Id.* at 842. The district court, after resolving conflicting expert testimony regarding how to interpret Teva's specification, determined that "molecular weight" referred to peak molecular weight ("Mp") and held that the claims were definite. On appeal, the Federal Circuit reviewed all aspects of the district court's claim construction decision *de novo*, and concluded that the term "molecular weight" was indefinite, primarily in view of conflicting constructions proffered by Teva's counsel during prosecution of two related applications, wherein Teva argued that molecular weight was Mp in one application and weight average molecular weight ("Mw") in the other one.

On review, the Supreme Court rejected the Federal Circuit's standard of review, holding that under the federal rules of civil procedure, a court of appeals "must not ... set aside" a district court's "[f]indings of fact" unless they are "clearly erroneous." *Id.* at 833. The Supreme Court explained that, in view of the Rule's "clear command," the Federal Circuit must apply the "clearly erroneous" standard when reviewing subsidiary factual matters made in the course of its construction of a patent claim. The Court elaborated that "when the district court reviews only evidence intrinsic to the patent (the patent claims and specifications, along with the patent's prosecution history), the judge's determination will amount solely to a determination of law, and the Court of Appeals will review that construction *de novo*." *Id.* at 841. The Court acknowledged that

> In some cases, however, the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period. . . . In cases where those subsidiary facts are in dispute, courts will need to make subsidiary factual findings about that extrinsic evidence. These are the 'evidentiary underpinnings' of claim construction that we discussed in *Markman*[1], and this subsidiary factfinding must be reviewed for clear error on appeal.

Id.

Testimony of each party's expert regarding the meaning of the term "molecular weight" is a "subsidiary fact" that goes beyond the patent's intrinsic evidence, which must be reviewed under the "clearly erroneous" standard.

Here, the district court indeed had to look beyond the intrinsic record and consider conflicting expert testimony between Sandoz's expert and Teva's expert regarding the meaning of "molecular weight." In particular, Teva's expert argued that "molecular weight" means Mp but Sandoz's expert disagreed based on certain discrepancies in Figure 1 of the patent. The district court accepted Teva's expert's explanation regarding these so-called "discrepancies" and concluded that "molecular weight" referred to Mp. Because the Federal Circuit rejected Teva's expert's explanation without finding that the district court's determination was "clearly erroneous," the Supreme Court concluded that the Federal Circuit used the wrong standard of review. The Court vacated the decision and remanded the case for further proceedings, as discussed *infra*.

Because intent to bring about infringement is the focus of the scienter element for induced infringement; a good faith belief of invalidity is not a defense to induced infringement, even though good faith belief of non-infringement is.

In *Commil USA, LLC v. Cisco Sys., Inc.*, 135 S. Ct 1920 (2015), the Court reviewed whether a good-faith belief of patent invalidity suffices as a defense to induced infringement for a patent to a method of implementing short-range wireless networks. Commil alleged that Cisco induced infringement by selling infringing equipment to its customers for use. Because it is "axiomatic that one cannot infringe an invalid patent," the Federal Circuit held that "an accused inducer's good-faith belief of invalidity may negate the requisite intent for induced infringement." *Id.* at 1925. Citing *Global Tech's*[2] holding that induced infringement under § 271(b) requires knowledge that the induced acts constitute patent infringement, the court saw "no principled distinction between a good-faith belief of invalidity and a good-faith belief of non-infringement for the purpose of whether a defendant possessed the specific intent to induce infringement of a patent." *Id.*

The Supreme Court disagreed, holding that

> The scienter element for induced infringement concerns infringement; that is a different issue than validity. Section 271(b) requires that the defendant "actively induce[d] infringement." That language requires intent to "bring about the desired result," which is infringement. . . . And because infringement and validity are separate issues

1 *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996).

2 *Global–Tech Appliances Inc. v. SEB S.A.*, 563 U.S. 754 (2011).

> under the Act, belief regarding validity cannot negate the scienter required under § 271(b).

Id. at 1928.

The Court also cited the presumption of validity as negating reliance on a good-faith belief of invalidity as a defense to induced infringement, finding that "if belief in invalidity were a defense to induced infringement, the force of that presumption would be lessened to a drastic degree, for a defendant could prevail if he proved he reasonably believed the patent was invalid." *Id.* at 1929. Finally, the Court cited "practical reasons not to create a defense based on a good-faith belief in invalidity,"[3] including the fact that "accused inducers who believe a patent is invalid have various proper ways to obtain a ruling to that effect"[4] such as a declaratory judgment action asking a federal court to declare the patent invalid, *inter partes* review at the Patent Trial and Appeal Board, or *ex parte* reexamination.

The obvious day-to-day takeaway from this case paired with *Global Tech* is that a good-faith non-infringement opinion is far more valuable than an invalidity opinion as a defense to induced infringement.

Eligibility Under § 101

Because the presence of cell-free fetal DNA in maternal plasma or serum is a natural phenomenon, even though unknown before the invention, further inclusion of conventional PCR and detection steps is not sufficient to "transform the nature of the claim" into a patent-eligible application.

In *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015), the Federal Circuit gave us one of its first glimpses of how it will approach eligibility requirements under Section 101 in view of the new paradigms following *Myriad*,[5] *Alice*,[6] and *Mayo*.[7] The inventors discovered the presence of cell-free fetal DNA ("cffDNA") in maternal plasma and serum, the portion of maternal blood samples that other researchers had previously discarded as medical waste. The patent claims recite amplifying the cffDNA contained in a sample of a plasma or serum from a pregnant female and detecting the paternally inherited cffDNA. The patent also provides for making a diagnosis of certain fetal characteristics based on the detection of paternally inherited cffDNA.

The district court held that the claims recite the natural phenomenon of paternally inherited cffDNA, and that the claims did not add enough to the natural phenomenon to make the claims patent eligible under § 101 because the steps of amplifying and detecting were well-understood, routine, or conventional activity when the application was filed. The district court also found that the claimed processes posed a risk of preempting a natural phenomenon.

The Federal Circuit began its review by restating the two-step framework set forth in *Mayo* for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts:

1. Determine whether the claims at issue are directed to a patent-ineligible concept;

2. If the answer is yes, consider the elements of each claim both individually and "as an ordered combination" to determine whether additional elements "transform the nature of the claim" into a patent-eligible application, i.e., whether "an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'"[8]

Applying the first step, the court found that the method "starts with cffDNA taken from a sample of maternal plasma or serum—a naturally occurring non-cellular fetal DNA that circulates freely in the blood stream of a pregnant woman" and "ends with paternally inherited cffDNA, which is also a natural phenomenon." *Id.* at 1376. Because the method "begins and ends with a natural *phenomenon*," "the claims are directed to matter that is naturally occurring." *Id.* (emphasis added). Turning to the second step, the court found "that the practice of the method claims does not result in an inventive concept that transforms the natural phenomenon of cffDNA into a patentable invention." *Id.* at 1376.

In so finding, the court drew parallels with *Mayo* in an effort to justify its holding. The court noted that Prometheus's "[m]ethods for determining metabolite levels … were already 'well known in the art'" and that "the process at issue amounted to 'nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients.'" *Id.* at 1377. Accordingly, quoting the Supreme Court, the Federal Circuit noted that "'[s]imply appending conventional steps, specified at a high level of generality,' was not enough to supply an inventive concept." *Id.* The Federal Circuit thus found ineligibility given that the steps of PCR amplification and detection of the amplified cffDNA were clearly routine.

3 135 S. Ct at 1929.

4 *Id.*

5 *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013).

6 *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct 2347 (2014).

7 *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct 1289 (2012).

8 788 F.3d at 1375.

Although pre-emption of all uses of a natural phenomenon may signal patent ineligibility, the absence of complete pre-emption does not demonstrate patent eligibility.

Finally, the court addressed Sequenom's argument that its method did not pre-empt all uses of cffDNA, arguing that there are numerous other uses of cffDNA aside from those claimed. The court noted that

> While preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility. In this case, Sequenom's attempt to limit the breadth of the claims by showing alternative uses of cffDNA outside of the scope of the claims does not change the conclusion that the claims are directed to patent ineligible subject matter. Where a patent's claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework, as they are in this case, preemption concerns are fully addressed and made moot.

788 F.3d at 1379.

This is a case that could have just as easily gone the other way, based on whether the word term "conventional" is construed broadly or narrowly. When the Supreme Court was referring to the "conventional" steps in *Mayo*, it was referring to steps that were literally carried out in the prior art, i.e., administration of the specifically claimed drug to a patient and determining the metabolite level of that drug in the patient's blood. (("[T]he steps in the claimed processes (apart from the natural laws themselves) ***involve well-understood, routine, conventional activity previously engaged in by researchers in the field***"). 132 S. Ct. 1289, 1294 (emphasis added). By contrast, while the general technique of PCR amplification is certainly "conventional," the claim at issue recited not only performing PCR, but doing it specifically on cffDNA in the maternal plasma or serum. This is not a step that was previously engaged in by researchers in the field. Thus, one could argue confusion on the part of the Federal Circuit in its construction of the term "conventional," based on whether the actual steps are conventional (as was the case in *Mayo)* or whether only the techniques, but not the actual steps, were conventional (as is the case here).

Finally, Supreme Court precedent recognizes that the definition of "conventional" does not include use of conventional steps where it would not have been obvious to use those conventional steps. For example, in *Eibel Process Co. v. Minn. & Ontario Paper Co.*, 261 U.S. 45 (1923), the court reviewed Eibel's papermaking machine and process, where Eibel took the prior art process and merely raised the height of the pitch of the machine to make paper stock flow faster by gravity. The appellate court, like the Federal Circuit here, found that Eibel merely took a conventional process in combination with an unpatentable principle of nature, gravity ("[T]he prior art and the obvious application of the principle that water will run down hill in their opinion robbed it of novelty or discovery.") *Id.* at 52. Eibel argued that his invention using a higher pitch "cause[d] the stock to travel by gravity at a velocity approximately equal to the speed of the making wire, which I believe to be a new principle of operation." *Id.* at 57. The Supreme Court framed the issue as "whether Eibel's discovery was invention rather than the mere obvious and simple application of known natural forces." *Id.* at 62. The Court noted that even though Eibel relied on a natural phenomena such as gravity, there was invention in discovering the problem ("The invention was not the mere use of a high or substantial pitch to remedy a known source of trouble. ***It was the discovery of the source not before known, and the application of the remedy, for which Eibel was entitled to be rewarded in his patent***.") *Id.* at 68 (emphasis added). Similarly here, the invention was not merely application of conventional steps to a natural phenomenon, but "the discovery of the source not before known." *Id.* at 68.

Accordingly, to the extent the court urged that the Supreme Court tied its hands in this matter, one could make the counterargument that not only did the court have a perfectly reasonable way to distinguish *Mayo*[9], but the court actually defied earlier Supreme Court precedent in reaching its conclusion.

Anticipation/ Obviousness

Even though no actual "sale" occurred when batches of a drug made by a patented process passed from a third party supplier to the inventor, the on-sale bar applies because the inventor nonetheless received a "commercial benefit" more than one year before filing.

In *Meds. Co. v. Hospira, Inc.*, 791 F.3d 1368 (Fed. Cir. 2015), the court reviewed whether The Medicine Company's ("TMC's") patent directed to the drug bivalirudin (sold commercially as Angiomax®), a synthetic peptide used as an anti-coagulant, was invalid under the on-sale bar. TMC obtained pharmaceutical batches of the drug from a supplier, Ben Venue Laboratories ("BVL"). After receiving two batches of the drug from BVL with levels of Asp[9]-bivalirudin impurity that exceeded the FDA's approved maximum of 1.5%, TMC developed methods to minimize the impurity and obtained patents directed to such methods. However, more than one year before filing its patent applications, TMC hired BVL to prepare three batches of bivalirudin using an embodiment of the patented method, for which BVL invoiced TMC and released the batch for commercial and clinical packaging.

9 *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct 1289 (2012).

Applying the two-part test of *Pfaff v. Wells Elecs., Inc.,* 525 U.S. 55, 67-68 (1998), the district court found that although the claimed invention was "ready for patenting," it was not "the subject of a commercial offer for sale" because (1) BVL only sold manufacturing services, not pharmaceutical batches; and (2) the batches fall under the experimental use exception.

On review, the Federal Circuit agreed that "title to the pharmaceutical batches did not change hands," i.e., there was no sale. 791 F.3d at 1370. However, the court noted that "we have found the on-sale bar to apply where … the inventor commercially exploited the invention before the critical date, even if the inventor did not transfer title to the commercial embodiment of the invention." *Id.* at 1370-71. Citing *D.L. Auld Co. v. Chroma Graphics Corp.*, 714 F.2d 1144, 1147 (Fed. Cir. 1983), the court noted that the on-sale bar can apply, even without a title transfer, where an inventor sells products made by a patented method. The court found "no principled distinction between the commercial sale of products prepared by the patented method at issue . . . and the commercial sale of services that result in the patented product-by-process here." 791 F.3d at 1371. Here, TMC paid BVL for performing services that resulted in the patented product-by-process and thus a "sale" of services occurred which "provided a commercial benefit to the inventor more than one year before a patent application was filed." *Id.* There is no indication in the case that TMC ever sold the subject batches to customers.

Because the product transferred from a supplier to the inventor was made by a process meeting all the limitations of the claim, it was irrelevant under the on-sale bar whether the inventor knew that the process reliably produced a product meeting those limitations.

The court found that "it is irrelevant whether [TMC] knew that the process limitations of the asserted claims reliably and consistently produced levels of Asp^9-bivalirudin below 0.6%" because "[t]here is no dispute that the batches had the levels of Asp^9-bivalirudin required by the claims." *Id.* at 1371-72. Citing *Abbott Labs. v. Geneva Pharm.,* 182 F.3d 1315, 1319 (Fed. Cir. 1999), the court noted that "[i]f a product that is offered for sale inherently possesses each of the limitations of the claims, then the invention is on sale, whether or not the parties to the transaction recognize that the product possesses the claimed characteristics." 781 F.3d at 1371. Similarly, the court rejected TMC's reliance on the experimental use exception, finding that even if TMC did not appreciate the maximum impurity level limitation until after 25 batches of the drug were manufactured, the sale of the invention negates any need to establish conception or reduction to practice. The court found that "[t]his is not a situation in which the inventor was unaware that the invention had been reduced to practice, and was experimenting to determine whether that was the case" because "[t]he batches sold satisfied the claim limitations." *Id.* at 1372.

There are two problems with this case. First, the statute states that the bar applies when the invention is "on-sale," and not merely when the inventor received "a commercial benefit." One could argue that *Auld* is consistent with this, because when one sells a product made by a patented process, there still is an actual ***sale*** occurring of the product of that process. Second, in disregarding the experimental use exception, the panel did not appear to recognize that there is a huge distinction between selling a product deemed commercially suitable more than a year before the filing date versus obtaining a product from a supplier where further experimentation is necessary before selling to the public. It's the difference between giving a draft to a coworker to check for errors versus publishing.

Court vacates panel decision and grants en banc *review to reconsider whether application of the on-sale bar requires a transfer of title and whether there should be a "supplier exception."*

In apparent recognition of the panel's error, the full court vacated the above decision and granted TMC's request for an en banc review.[10] The court requested briefing on the following questions:

1. Do the circumstances presented here constitute a commercial sale under the on-sale bar of 35 U.S.C. § 102(b)?
    a. Was there a sale for the purposes of § 102(b) despite the absence of a transfer of title?
    b. Was the sale commercial in nature for the purposes of § 102(b) or an experimental use?
2. Should this court overrule or revise the principle in *Special Devices, Inc. v. OEA, Inc.*, 270 F.3d 1353 (Fed. Cir. 2001), that there is no "supplier exception" to the on-sale bar of 35 U.S.C. § 102(b)?

Although transfer of an invention from an inventor to a third party "without limitation or restriction or injunction of secrecy" is a public use, unauthorized transfers of plant material from the inventor's agent to a farmer and then from the farmer to his cousin was not a public use because both recipients treated their possession of the plants as confidential.

In *Delano Farms Co. v. Cal. Table Grape Comm'n*, 778 F.3d 1243 (Fed. Cir. 2015), the court reviewed the question of whether the actions of two individuals who obtained samples of two patented plant varieties in an unauthorized manner and planted them in their own fields constituted an invalidating public use of the plant varieties. The district court found that the actions of those

10 *Meds. Co. v. Hospira, Inc.*, 805 F.3d 1357 (Fed. Cir. 2015).

individuals did not constitute a public use of the two plant varieties and therefore rejected appellants' challenge to the patents.

The USDA displayed the fruit of two different table grape varieties during an open house. A grape grower who attended, Jim Ludy, convinced a USDA representative to give him plant material for the two varieties despite the representative's lack of authority to do so, with the "understanding" that the plant material was to be kept a secret. After receipt of the plant material, Jim Ludy provided buds of both varieties to his cousin Larry Ludy, again with the understanding that their possession of the varieties "was supposed to be a secret." The cousins subsequently grew the varieties but neither sold any grapes nor provided plant material to anyone else until after the critical date. Although visible from publicly accessible roads, none of the vines was marked or labeled in any way nor could the particular variety of the grapes be readily ascertained from simply viewing the vines. One other person, a table grape marketer named Mr. Sandrini who worked with the cousins, saw the vines of the varieties prior to the patents' critical date.

Appellants argued that Jim Ludy's provision of plant material to his cousin resulted in public use, citing *Egbert v. Lippmann*, 104 U.S. 333 (1881) for the proposition that

> If an inventor, having made his device, gives or sells it to another, to be used by the donee or vendee, without limitation or restriction, or injunction of secrecy, and it is so used, such use is public, even though the use and knowledge of the use may be confined to one person.

Id. at 336. Although here it was not the actual inventor who gave the varieties to another, appellants argued that "Jim Ludy obtained control over the unreleased varieties" and "for purposes of the public use doctrine . . . stands in place of the inventor" for giving his cousin the unreleased plant material "without limitation or restriction, or injunction of secrecy." 778 F.3d at 1248. The court disagreed, because "appellants' argument . . . is squarely contrary to the district court's findings of fact" that "both Ludys knew that they were not authorized to have the plants and that they needed to conceal their possession of the plants." *Id.* Thus, in contrast to *Egbert,* "[t]he facts of this case . . . show that Jim Ludy sought to maintain control of the plants he obtained" and although he shared the plants with his cousin, "the evidence showed that Larry Ludy was aware of the need to keep the plants secret, and at Jim Ludy's urging, Larry Ludy continued to treat his possession of the unreleased varieties as confidential and non-public." *Id.* at 1249.

Fact that third party saw patented grape vines is not a "public use" where (1) it was not possible to practice the invention without possession of the vines; and (2) the third party was a confidant of a party obliged to keep the invention secret.

The court likewise rejected the appellants' second argument that the cousins' disclosure of the unreleased plants to the marketer, Mr. Sandrini, constituted a public use, finding that "[u]nlike the Ludys . . . Mr. Sandrini could not practice the inventions because he did not possess plant material until after the critical date." *Id.* Further, the court found that the disclosure of the plants' existence to Mr. Sandrini did not demonstrate a lack of confidentiality by the cousins because "Mr. Sandrini was a friend, business partner, and mentor of the Ludys" and all involved "had incentives to keep the Ludys' possession secret, creating an environment of confidentiality." *Id.*

Cultivation of patented grape vines in public view is not an invalidating "public use" where (1) the vines could not be reliably identified simply by viewing alone; (2) the vines were not labeled; and (3) only the two growers and one confidant recognized the otherwise unreleased varieties.

Finally, the court disagreed with appellants' argument that the lack of secrecy with which the cousins cultivated the unreleased varieties mandates a finding of public use, concluding that although both cousins grafted the plants and grew them in locations that were visible from public roads, "the appellants ignore the district court's finding that grape varieties cannot be reliably identified simply by viewing the growing vines alone." *Id.* Here, "[t]he plantings of the unreleased varieties were extremely limited," "were not labeled in any way, and the appellants introduced no evidence that any person other than the Ludys and Mr. Sandrini had ever recognized the unreleased varieties." *Id.* The court noted that under its precedent, if members of the public are not informed of, and cannot readily discern, the claimed features of the invention in the allegedly invalidating prior art, the public has not been put in possession of those features.

Although a claim to a range is anticipated by prior art showing a specific point in the range, prior art's teaching of a polyethylene composition including "at least" 0.1, 0.2, and 0.4 parts by weight of the fatty acid amide does not disclose such specific points so as to anticipate the claimed range of 0.05 to 0.5%.

In *Ineos USA LLC v. Berry Plastics Corp.*, *783 F.3d 865* (Fed. Cir. 2015), the court reviewed the summary judgment holding of anticipation by the district court of Ineos' claims directed to polyethylene-based compositions which can be used to form shaped products, such as screw caps for bottles. The composition comprises a polyethylene, 0.05 to 0.5% by weight of at least one saturated fatty acid amide represented by $CH_3(CH_2)_nCONH_2$ in which n ranges from 6 to 28 and 0 to 0.15% by weight of a subsidiary lubricant.

The prior art disclosed the polyethylene component, a stearamide meeting the saturated fatty acid amide limitation, and a subsidiary lubricant. Ineos argued that the prior art "discloses no single

species within the genus of [the claim]" nor does it disclose that stearamide or any other primary lubricant "should be included . . . in an amount between 0.05 and 0.5% by weight." *Id.* at 868. On review, the court noted that "[w]hen a patent claims a range, as in this case, that range is anticipated by a prior art reference if the reference discloses a point within the range" or "if it describes the claimed range with sufficient specificity such that a reasonable fact finder could conclude that there is no reasonable difference in how the invention operates over the ranges." *Id.* at 869. The court agreed with Ineos that the prior art's disclosure of at least 0.1, at least 0.2, or at least 0.4 parts by weight of the lubricant did not disclose a point within the range, citing *Atofina's*[11] holding that "the disclosure of a range . . . does not constitute a specific disclosure of the endpoints of that range." 783 F.3d at 869.

In the absence of a showing of a critical difference between the claimed range of 0.05 to 0.5% by weight of fatty acid amide lubricant in a polyethylene packaging composition and prior art ranges of at least 0.1, 0.2, and 0.4 parts by weight of the amide, the claim is anticipated.

However, the court agreed with Berry that "Ineos failed to raise a genuine question of fact about whether the range claimed is critical to the operability of the invention." *Id.* Citing *Atofina* and *ClearValue*,[12] the court noted that to distinguish a prior art range, the patentee must show criticality, i.e., that the claimed range and the prior art range work differently. Here, the 0.05 to 0.5% by weight range for the primary lubricant was met by the prior art because Ineos failed to show the criticality of the recited range to the invention, noting that whereas the specification "describes the novelty of the invention as eliminating the odor and taste problems associated with prior art bottle caps while still maintaining good slip properties," "Ineos has not established that any of these properties would differ if the range from the prior art . . . is substituted for the [claimed range]." 783 F.3d at 870. The court rejected Ineos' reliance on testimony that the claimed range is critical to avoid unnecessary manufacturing costs and the appearance of undesirable blemishes on the bottle caps, holding that "even if true, this has nothing to do with the operability or functionality of the claimed invention"[13] which relates to the claimed invention's slip properties or improved odor and taste properties. Finally, the court concluded that while testimony concerning reduced manufacturing costs could be relevant where a method of manufacture claim is at issue, this is not the case before us.

Prior art disclosing a saturated fatty acid amide having 12 to 35 carbon atoms anticipates the 22 carbon saturated fatty acid amide behenamide because behenamide is a common fatty acid amide lubricating agent in the packaging industry, the genus is small, and patentee provided no information regarding large size of genus.

Lastly, the court reviewed Ineos' dependent claim 3, which specifies that the primary lubricant is the saturated fatty acid amide behenamide. Although the prior art does not explicitly disclose behenamide, it does fall within the narrower genus of saturated fatty acid amides having 12 to 35 carbon atoms defined in the prior art because it is a saturated fatty acid amide with 22 carbon atoms. The court accepted Berry Plastics' assertion, supported by expert declaration, that behenamide is a common fatty acid amide lubricating agent used in the packaging industry and that "[f]rom this evidence we cannot conclude that the [district] court erred in finding that the [prior art] discloses behenamide." *Id.* at 872. The court noted that "[v]erbatim disclosure of a particular species is not required in every case for anticipation because disclosure of a small genus can be a disclosure of each species within the genus." *Id.* The court found that "Ineos provided no detailed information on how large this genus is to support its contention that this genus does not disclose behenamide," nor does it "state that behenamide is not a common lubricant within this species." *Id.*

This case to some extent continues the can of worms that the Federal Circuit created by radically changing the law of anticipation in *ClearValue*. In particular, for some inexplicable reason, the court now assesses issues of criticality of results in an anticipation analysis whereas earlier case law, such as *Atofina,* simply looked at the size of the prior art generic teaching in relation to the species claimed. Anticipation should simply ask–does the prior art disclose the invention or doesn't it? Criticality should go to obviousness. The court is also all over the map regarding the size of the genus necessary to disclose the invention, both in terms of ranges and selection of species. For example, to select behenamide required not only selection from 24 different chain lengths (12-35), but also among unbranched and branched fatty acid amides, which actually makes the number much, much larger. Yet in *Shire*[14] , discussed below, selection from 36 members was considered too vast.

Also, having interjected criticality into anticipation analyses, what led the court to decide that the criticality has to be specifically disclosed in the specification? This is not a requirement for unexpected results to rebut obviousness rejections! Further, although the court dismissed reduced manufacturing costs as not being relevant to Ineos' product claims, why did it likewise dismiss evidence of reduced blemishes, which clearly does relate to the product? The court does not tell us. For some inexplicable reason, the court also seems to be reading the claim as requiring the reduction in improved slip properties and reduction malodor, which while certainly recited as benefits in the specification, is not

11 *Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991 (Fed. Cir. 2006).

12 *ClearValue, Inc. v. Pearl River Polymers, Inc.*, 668 F.3d 1340 (Fed. Cir. 2012).

13 783 F.3d at 871.

14 *Shire LLC v. Amneal Pharm., LLC*, 802 F.3d 1301 (Fed. Cir. 2015).

required by the claim. Regrettably, until the court comes to terms with its recent detour on the doctrine of anticipation, we are going to continue to have cases that contort the law, such as this one.

Because one of ordinary skill could immediately envisage the combination of a ruthenium binder with PVD deposition, the claims are anticipated by a reference disclosing ruthenium as one of five optional binder metals and PVD as one of three deposition techniques.

In *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376 (Fed. Cir. 2015), the court addressed whether prior art disclosing a genus of optional binders and deposition techniques was anticipatory, i.e., sufficiently narrow, such that one of ordinary skill could "immediately envisage,"[15] Kennametal's claimed combination of a binder comprising ruthenium and coating by a physical vapor deposition ("PVD") process.

The cited reference, Grab, discloses a carbide substrate and a cobalt-chromium binder which may ***optionally*** include one of five additional metals including tungsten, iron, nickel, ruthenium, and rhenium. Grab also disclosed three different coating techniques, two of which were chemical vapor deposition methods ("CVD"s) and one of which was a physical deposition method ("PVD"). On appeal, Kennametal argued that Grab does not disclose the combination of ruthenium as a binder and a PVD coating noting that "Grab discloses five potential metals to use in the binder." *Id.* at 1382. Furthermore, because the example in Grab uses one of two CVD deposition methods, and not a PVD, Kennametal contended that the use of ruthenium as a binder and the contemplation of the use of PVD as a coating were among a multiplicity of options "so that a person of skill in the art would not immediately envisage the claimed combination." *Id.* Ingersoll responded that Grab discusses a coating, which allows for three coating techniques, including PVD, along with any one of five metal binders, including ruthenium. Thus, according to Ingersoll, Grab effectively discloses the combination of PVD coating with ruthenium.

On review, the court found that "with the exception of combining ruthenium binders with PVD coatings, claim 5 of Grab expressly recites all the elements" of the claim, i.e., it recites "a binder consisting of one of five metals, one of which is ruthenium, together with a coating." *Id.* Further, "Grab only discloses three coating methods, one of which is PVD. While CVD and MTCVD coatings are the coatings on which Grab focuses, it 'also contemplate[d] that one or more layers of a coating scheme may be applied by [PVD].'"

> Because all the limitations of Kennametal's claim are specifically disclosed in Grab, the question for the purposes of anticipation is "whether the number of categories and components" disclosed in Grab is so large that the combination of ruthenium and PVD coatings "would not be immediately apparent to one of ordinary skill in the art."

Id. The court found that Grab's express contemplation of PVD coatings is sufficient evidence that a person of skill in the art, reading Grab's claim 5, would immediately envisage applying a PVD coating. The court thus held that "substantial evidence supports the Board's conclusion that Grab effectively teaches 15 combinations, of which one anticipates [Kennametal's claims]." *Id.* at 1383. In response to Kennametal's argument that "there is no evidence in Grab of 'actual performance' of combining the ruthenium binder and PVD coatings," the court found that "this is not required" because anticipation only requires that those suggestions be enabled to one of skill in the art. *Id.*

This is a case that was problematic for both the court and the patentee. For example, the court and the Board seem to have disregarded the fact that the five binder metals from which ruthenium was selected were disclosed as being optional. So in fact, the combination of ruthenium and PPD was one in 18, not one in 15 possibilities. That's a 20% difference in the size of the selection. It also seems that Kennametal could have done more to help its own cause. For example, Grab required the inclusion of both cobalt and chromium as binders, and only employed ruthenium as one of five additional optional binders. However, Grab provided no disclosure at all as to how much ruthenium to include. Accordingly, Kennametal might have argued that even if one of ordinary skill in the art were to select ruthenium as an additional binder, there was no disclosure to include the ruthenium in amounts sufficient to provide a binding effect. The problem for Kennametal was twofold, however. First, Kennametal's independent claim simply said the binder comprises ruthenium, so that the claim itself did not require enough ruthenium to provide a binding effect. Second, Kennametal did not argue separate patentability for its claims that did specify quantities of ruthenium. This is one of those cases where the law probably dictated differently, but Kennametal just did not do enough to warrant reversal.

One last point of note is the court's conclusion that anticipation only requires enablement, not actual exemplification of the PVD method. The problem with looking at this in terms of enablement is that that the answer will almost invariably be yes, for the simple reason that if it weren't enabled, then how could the claimed invention itself work? For this reason, the court's finding of anticipation based on mere enablement for proposed embodiments representing just one of many choices is one that will doom a patentee in most instances. An approach truer to the C.C.P.A. and earlier Federal Circuit precedent that requires more precision for a finding of anticipation would avoid this problem.

15 *Id.* at 1382.

Claim directed to mesylate salts of L-lysine-d-amphetamine ("LDX") not disclosed by prior art disclosing list of 18 amino acids, including lysine, in the L- or D-configuration, even in view of preference for L-configuration, because a person of ordinary skill would not "immediately envisage" LDX.

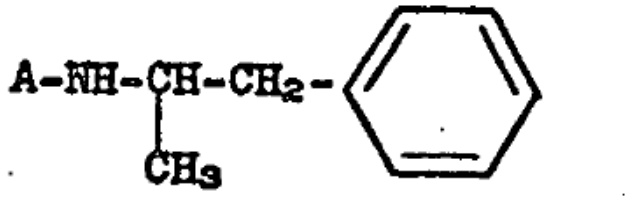
In Shire LLC v. Amneal Pharm., LLC, 802 F.3d 1301 (Fed. Cir. 2015), the court reviewed the validity of Shire's patent directed to amphetamines for treating attention deficit hyperactivity disorder ("ADHD"), which were covalently modified to decrease their activity when administered in abusively high doses but retain the activity of the unmodified amphetamine when administered at prescribed doses. The claims under review recite (1) methods of using amphetamine derivatives, in particular a mesylate salt of an L-lysine-d-amphetamine to treat ADHD; and (2) the mesylate salts of LDX and crystalline forms thereof.

On summary judgment, the district court concluded that (1) the prior art did not disclose LDX or make it obvious; (2) the prior art did not disclose that LDX was known as an active drug substance; (3) the prior art provided no motivation to pick LDX as a starting compound; and (4) the prior art provided no motivation to make mesylate salts of LDX.

Defendants argued that there was a factual issue as to whether Australian Patent Application No. 54,168/65 ("AU '168"), actually discloses LDX based on (1) its identification of 18 amino acids by name, including lysine, with a stated preference for L-amino acids and d-amphetamine such that "a person of skill in the art would immediately envisage LDX;"[16] and (2) disclosure of LDX in Formula IV and Example 24. The court disagreed, noting that AU '168 discloses combining amphetamine "in any of its stereochemical forms, with numerous amino acids, in various stereochemistries and with many potential protecting groups," and therefore does not "specifically suggest[] combining d-amphetamine with L-lysine." *Id.* For example, the list of 18 amino acids cited by defendants "states they can belong to the D- or L-series. Even this list, therefore, does not limit itself to 18 amino acids." *Id.* AU '168 further "suggests posttranslational modifications of the amino acids . . . thus further increasing the potential amino acid groups to be utilized." *Id.* (citations omitted). Although AU '168 states a preference for acids of the L-series, it "actually describes numerous D-series amino acids," such that "[r]ead in context of the whole reference, a person of skill in the art would . . . not focus exclusively on amino acids with the L stereochemistry." *Id.*

No disclosure of claimed LDX mesylate compound by prior art because a selection of (1) one of 17 amino acids (including lysine) from a first list and (2) one of over 100 combinations of amino acids and protecting groups in the second list is not a selection from a "finite and limited class."

The court next found that "the Formula IV of AU '168 . . . does not teach a finite and limited class including LDX." Formula IV is depicted as follows:



"For Formula IV to disclose LDX, 'A' must be selected to be L-lysine and the amphetamine must be in the d-configuration." *Id.* The court found "no genuine issue of material fact that AU '168 does not disclose L-lysine as part of a limited class of compounds for 'A'." Rather, "AU '168 suggests that 'A' can be selected from one of three lists" and "Formula IV 'does not indicate any preference' among the different options." *Id.* The court thus concluded that

> Formula IV discloses all the compounds from all three lists, the first of which lists 17 amino acids (including lysine), the second of which teaches over a hundred possible combinations of amino acids and protecting groups and the third of which does not even provide a definite list of compounds. This too is not a definite and limited class.[17]

Even though removal of tosyl protecting group from prior art compound would result in claimed LDX, there was no motivation to remove such group because the prior art compound is a final product.

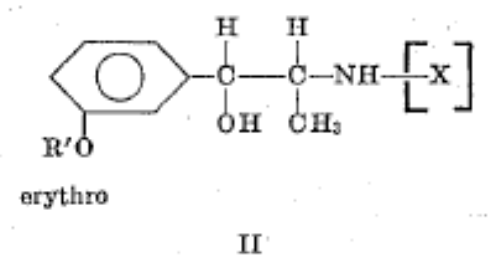
The court found that Example 24, which discloses NαTosyl-L-lysine[D(+)-1-phenyl-propyl-(2)]-amide, differs from LDX in that it contains a removable tosyl "protecting" group. Because example 24 is a final product and not an intermediate synthesis product, the court rejected defendants' argument that there was a motivation to modify example 24 to make LDX. The court found confirmation in the "hindsight nature" of defendants' argument "by the fact that out of the thousands of possible compounds it discloses, AU '168 actually provides thirty specific examples, none of which is LDX." *Id.*

Secondary reference still requires a large number of selections and thus does not overcome deficiencies of primary reference to disclose LDX.

The court further found that the secondary reference "Miller does not overcome the deficiencies of AU '168." *Id.* Defendants focused on Formula II of Miller:

16 *Id.* at 1307.

17 *Id.*



II

"which describes a molecule with two Markush groups, [R'] and [X]", where "[X] can be one of twenty amino acids–including L-lysine–or their derivatives." *Id.* However, the court found that

> 'Defendants have offered no rationale why a person of skill in the art would focus on the specific embodiment of Formula II comprising L-lysine and 'even if [X] were chosen to be L-lysine, Miller's compound is still different from LDX in [that] Miller has an OR' where LDX has an H and Miller has a C-OH where LDX has a CH–i.e., the base compound in Miller is not amphetamine.'

Id. at 1309. The court concluded that "[t]he record provides no reason or motivation why one of skill in the art would combine AU '168 with Miller." *Id.*

It is hard to not to wonder how the *Ineos* court concluded that behenamide was disclosed, yet the court here did not find LDX to be disclosed. Indeed, here the reference disclosed a specific preference for the L-amino acids, limited that class to just 18 selections. It might boil down to the fact that in both cases, the Federal Circuit was affirming the district court, though it is important to recall that *Ineos* was a review of a summary judgment decision, and there was no dispute as to what the prior art disclosed, so it would seem that this cannot be explained away solely by deference.

Because evidence established that acetaminophen degrades by hydrolysis and not by oxidation followed by hydrolysis, prior art teaching that deoxygenation to less than 0.05 ppm stabilizes pyrogallol does not suggest such deoxygenation would stabilize acetaminophen.

In *Cadence Pharm. Inc. v. Exela Pharmsci Inc.*, 780 F.3d 1364 (Fed. Cir. 2015), the court reviewed the validity of Cadence's claims directed to a method for preparing an aqueous solution of the drug acetaminophen, which is susceptible to oxidation, comprising deoxygenation of the solution until the oxygen content is below 2 ppm. The claims differed from Cadence's own prior art patent in that the prior art does not disclose decreasing the oxygen content to below 2 ppm.

Exela argued that deoxygenating below 2 ppm would have been obvious based on the prior art's disclosure that the stability of acetaminophen solutions depends on removal of oxygen dissolved in the carrier, and the teaching of the secondary reference, Palmieri, that deoxygenating pyrogallol solutions to below 0.05 ppm leads to increased stability. Because both the prior art and expert testimony established that skilled artisans understood acetaminophen to be primarily degraded via hydrolysis, rather than by oxidation, followed by hydrolysis, the court rejected Exela's argument. The court concluded "that it would not have been obvious to combine the Palmieri article with [Cadence's prior patent], because the Palmieri article addressed the degradation of pyrogallol–which degrades primarily by oxidation–and did not address the degradation of acetaminophen [which] degrades primarily by hydrolysis." *Id.* at 1375. Accordingly, "a person of ordinary skill in the art would [not] have attempted to deoxygenate an acetaminophen solution to below 2 ppm with a reasonable expectation of 'preserving [the acetaminophen] for a prolonged period.'" *Id.*

Because the difference between deoxygenating solvent before addition of acetaminophen versus after its addition is insubstantial, evidence of commercial success for product made by pre-addition deoxygenation is relevant for claimed product made by post-addition deoxygenation.

The court found that secondary considerations relating to the marketing of Ofirmev® are not per se irrelevant to the non-obviousness of the claims of the patent, despite the fact that the claims do not literally cover Ofirmev®, because "whether a solvent is deoxygenated before or after the active ingredient has been dissolved is an insubstantial difference." *Id.* at 1375-76.

> Thus, there is no reason to believe that any secondary considerations attendant to Ofirmev®, in which the solvent is deoxygenated prior to the addition of the active ingredient, would not also be present in formulations literally covered by the claims, i.e., where the solvent is deoxygenated after the addition of active ingredient.

Id. at 1376. Finally, the court found no clear error in the district court's finding that that the claimed process achieved unexpected stability relative to the prior art and in finding that the licensing of the patent is probative of non-obviousness. In particular,

> Formulations made pursuant to the methods described in the [patent] were stable for two years, whereas plaintiff's expert testified that the formulation taught in the [prior art] patent only achieved several months' stability. Even if these results were only somewhat unexpected, they are still evidence of non-obviousness, albeit less so than if the results were vastly unexpected.[18]

18 *Id.*

Because the previously known contact lens material, PMMA, was known to be impermeable to oxygen, it was obvious to further include siloxane based cross-linking agents because they were known to increase oxygen permeability of the lens.

In *Dome Patent L.P v. Lee*, 799 F.3d 1372 (Fed. Cir. 2015), the court reviewed the validity of Dome's claims covering a method of making an oxygen permeable material for the manufacture of contact lenses comprising making a siloxane-based compound known as "Tris" and then copolymerizing it with an ester of acrylic or methacrylic acid (e.g., methyl methacrylate ("MMA")), a surface wetting agent, and an oxygen permeable siloxane-based cross-linking agent. The Patent Office ("PTO") found Dome's claim obvious during reexamination and the district court affirmed.

In reviewing the merits of the obviousness rejection based on a combination of references, the court noted that (1) Gaylord teaches that the previously used contact-lens material, polymethyl methacrylate ("PMMA"), is rigid and durable but relatively impermeable to oxygen and that it would be highly desirable to provide a contact-lens material that has increased oxygen permeability, is wettable, and has improved mechanical properties and (2) to meet that need, Gaylord further discloses using siloxane-based compounds, including Tris-type monomers. Although Gaylord does not teach a hydrophobic siloxane cross-linking agent to increase oxygen permeability as claimed, Tanaka employs siloxane-based cross-linking agents, including some that are hydrophobic, to increase oxygen permeability. Further, Dome's expert testified that those in the field were turning to siloxane-based compounds to enhance a polymer's oxygen permeability. The court therefore found that the district court did not clearly err in finding that the evidence disclosed a motivation to combine the prior art.

Although certain prior art taught against use of Tris polymers to increase oxygen permeability of contact lens polymers because cross-linkers used to make Tris hydrophilic also made it opaque, other prior art suggested that such opacity issues could be overcome, thus negating any teaching away.

Dome also argued that "a person of ordinary skill would have been inclined to introduce hydrophilic cross-linking agents, instead of hydrophobic siloxane-based cross-linking agents, to offset the hydrophobicity of Tris, but Tanaka warned against this approach" and instead "suggested designing a new amphiphilic or hydrophilic monomer to replace Tris altogether." *Id.* at 1381. In particular, "Tanaka discloses potential disadvantages associated with using Tris-type monomers," explaining that "if hydrophilic monomers are copolymerized with hydrophobic Tris-type monomers to offset hydrophobicity, the copolymer 'is liable to become opaque.'" *Id.* Tanaka explains that opacity is a "fatal defect" for the copolymer's use as a material for contact lenses, and thus offsetting hydrophobic Tris-type monomers with hydrophilic monomers "is limited." *Id.* Tanaka thus proposed an alternative for Tris-type monomers. However, the district court found that while Tanaka warns that constructing a lens with Tris-type materials can be difficult, other references "plainly teach that Tris could be used effectively to make contact lenses" such that "a person of ordinary skill would not have been dissuaded from combining the prior art." *Id.* at 1382.

This case represents yet another data point which demonstrates that whether at the P.T.A.B., the district court, or the Federal Circuit, reliance on teaching away to negate obviousness rarely is convincing.

Prior art's topical use of erythromycin to treat ocular infections does not make obvious the substitution of azithromycin in view of "innumerable" options for such treatments, including some known to be better, concerns of azithromycin's suitability and general unpredictability regarding ocular penetration.

In *InSite Vision Inc. v. Sandoz, Inc.*, 783 F.3d 853 (Fed. Cir. 2015), the court reviewed several InSite patents relating to both methods and formulations for treating eye infections by the topical administration of azithromycin to the eye. Prior to the invention, azithromycin was commonly administered orally for the treatment of bacterial infections, but was not known to be effective when topically administered to the eye.

Sandoz argued that the topical use of azithromycin to treat eye infections was obvious because erythromycin, an active ingredient similar to azithromycin, was already being used as a topical formulation in the product Ilotycin®. Sandoz further relied on Zithromax®, an oral azithromycin formulation used to treat conjunctivitis, and argued that:

> [I]t would have been obvious to try azithromycin as a topical treatment of bacterial conjunctivitis, with a reasonable expectation of success [because] azithromycin was the "newer iteration" of erythromycin, with remarkably effective properties and . . . it would have been common sense to substitute a new and improved antibiotic for the antibiotic present in Ilotycin®. *Id.* at 860.

The Federal Circuit disagreed, finding no clear error in the district court's conclusion "that there were 'innumerable' options for ophthalmic treatments, including fluoroquinolones" which "'were known to be a better option than azithromycin,' because they 'were bactericidal[,] could act on a broad range of bacteria [and] were known to penetrate ocular tissue." *Id.* at 861. In addition, "those of skill in the art would have been concerned

that azithromycin might not penetrate ocular tissue based on its high molecular weight, charge and insolubility in water." *Id.* The court also found no clear error in expert testimony that successful administration of a drug systemically did not ensure success topically. The court further found no clear error in the district court's discounting (1) the relevance of Ilotycin®, given that there was conflicting expert testimony on whether it had fallen out of favor by the time of the invention; and (2) expert testimony that erythromycin formulations would make azithromycin formulations obvious, given that the expert's own patent for topical ophthalmic treatments listed 24 potential antibiotics, including erythromycin, but did not list azithromycin.

Not obvious to substitute claimed azithromycin/polymeric suspending agent combination for treating topical eye infections for prior art erythromycin/polymer combination because the latter combination is merely one of a "laundry list," is not exemplified, and would be expected to give rise to solubility and stability problems.

The court next reviewed InSite's claims reciting various formulations and methods of using topical azithromycin as a gel eyedrop for treating eye infections, including azithromycin in a polymeric suspending agent for topical ophthalmic use. The court rejected Sandoz's obviousness argument relying on a prior art patent "which mentions the possibility that erythromycin could be combined with polycarbophil," finding no error in the district court's conclusion that the "patent discloses a 'laundry list of active ingredients' and . . . a researcher would focus on the patent's examples, none of which mention erythromycin." *Id.* at 862. Sandoz cited *Merck & Co. v. Biocraft Labs., Inc.'s*[19] holding that a "patent disclos[ing] a multitude of effective combinations does not render any particular formulation less obvious" but the court found that

> Sandoz overreads *Merck*. In *Merck*, one reference expressly taught the combination of the compounds claimed in the patent . . . . Here, by contrast, selecting from the laundry list of potential active ingredients listed in the [prior art] patent at best teaches that polycarbophil can be combined with erythromycin.

783 F.3d at 863. Because the prior art "does not mention azithromycin,"[20] the skilled artisan would still need to change erythromycin to azithromycin but would have been concerned about azithromycin's solubility and stability in water. A second prior art patent disclosing azithromycin and water-based polymers also did not render the claimed combination obvious in view of the concerns raised by patentee's experts as to their stability and as to the significant differences between Carbopol disclosed in the prior art and the polycarbophil claimed.

It is interesting to see the contrast with how the court treated the lack of exemplification here versus in *Kennametal*. Given that it should be harder to establish anticipation than obviousness, one would think that the lack of exemplification of the PVD process in *Kennametal* should have carried more weight than the lack of exemplification here, which was merely an obviousness scenario.

Because gatifloxacin is an improved fluoroquinolone, it was obvious to substitute it for the ophthalmic quinolones used in prior art topical ocular formulation; corneal permeability property not relevant to obviousness inquiry because claim at issue is a product claim.

In *Senju Pharm. Co. v. Lupin, Ltd.*, 780 F.3d 1337 (Fed. Cir. 2015), the court reviewed Senju's claims directed to an aqueous liquid pharmaceutical eye drop composition comprising from about 0.3 to about 0.8% Gatifloxacin and about 0.01% disodium edetate, wherein the composition has a pH from about 5 to about 6. Senju also claimed a method for raising corneal permeability of an aqueous pharmaceutical Gatifloxacin eye drop solution comprising incorporating about 0.01 w/v% disodium edetate into the solution.

With respect to the product claims, the court rejected Senju's reliance on the corneal permeability limitation. Senju cited *Leo*[21] for the proposition "that it is necessary to consider corneal permeability . . . because the claimed compositions embody the method"[22] including that limitation. The court noted that *Leo* involved "a composition claim that includes as a limitation the function of the composition" whereas in Senju's composition claims, "there is no limitation denoting the function of the composition and we decline to import this limitation into the claims." 780 F.3d at 1346. The court found that it would have been obvious to employ gatifloxacin in a topical ophthalmic composition because the prior art disclosed (1) ophthalmic quinolone compositions in topical ocular formulations; and (2) that gatifloxacin was recognized as an improved fluoroquinolone. "Thus, it would have been obvious to improve the [quinolone topical ophthalmic] formulations by incorporating the . . . [improved fluoroquinolone] Gatifloxacin." *Id.* at 1347. The court noted that "[m]any of appellants' arguments on the lack of reasons to combine the teachings of [the prior art] rely on the fact that they do not disclose anything about corneal permeability of Gatifloxacin solutions" but, as "this is not a limitation of [the claims] is not relevant to the obviousness determination." *Id.*

Because EDTA is listed among eight conventional ingredients and used in the claimed concentrations in combination with quinolone solutions, it was obvious to employ the combination of EDTA with the fluoroquinolone Gatifloxacin.

19 874 F.2d 804 (Fed. Cir. 1989).

20 *Id.*

21 *Leo Pharm. Products, Ltd. v. Rea*, 726 F.3d 1346, 1349-50.

22 780 F.3d at 1346.

The court also concluded that "the use of gatifloxacin with EDTA would have been obvious to a person of ordinary skill in the art," noting that "EDTA is listed among eight 'conventional ingredients' in the [prior art] and a similar group of excipients." *Id.* The court also found "the use of 0.3 to 0.8 w/v% of gatifloxacin" as having been "outlined in the prior art" disclosing from about 0.03 to 3% in one patent and preferably about 0.3% to 5% w/v% in a second patent. Additionally, the use of 0.01 w/v% EDTA was also known from prior art which discloses an exemplary formulation of 0.3% quinolone solution that incorporates 0.01 w/v% EDTA, and teaches using from about 0.03 to 3% and especially 0.15% to 0.6% of medicament although higher or lower dosages can be employed.

Method of increasing corneal permeability of gatifloxacin by incorporating 0.01% EDTA in a topical formulation obvious in view of prior art suggesting that EDTA concentrations lower than 0.5% result in increased corneal permeability.

The court also concluded that the district court properly held Senju's method claim reciting use of 0.01 w/v% EDTA to increase corneal permeability to be obvious in view of prior art suggesting "that EDTA concentrations lower than 0.5 w/v% would be effective in view of the increased corneal permeability of the 0.5 w/v% EDTA formulation to which calcium was added." *Id.* at 1351. This "would lead one of ordinary skill to apply this teaching in conjunction with the pre-existing quinolone formulations, which incorporated between 0.05 and 0.1 w/v% EDTA, in arriving at a gatifloxacin formulation characterized by increased corneal permeability." *Id.* The court rejected Senju's arguments that "the prior art teaches that the use of 0.01 w/v% EDTA fails to increase corneal permeability," finding instead that "the prior art actually teaches that adding EDTA to any polar compound will increase corneal permeability dose-dependently." *Id.* At bottom, the court was reluctant to overturn the district court's analysis finding Lupin's experts to be more credible than Senju's experts on the question of whether the prior art taught that 0.01 w/v% EDTA would be effective to increase corneal permeability.

The composition claims in neither *Senju* nor *InSite* recited corneal permeability, yet it was given no weight by the *Senju* panel and significant weight by the *InSite* panel. In particular, the *Senju* panel concluded "that the district court properly found that corneal permeability is not relevant in the discussion of composition claims 12-16 because these claims do not contain the corneal permeability limitation," However, the *InSite* paneal concluded that "[T]he district court did not clearly err in determining that those of skill in the art would have been concerned that azithromycin might not penetrate ocular tissue" As claim construction is a question of law, the Federal Circuit did not owe deference to the lower court so it is difficult to explain this difference in treatment. Add to this the fact that in the *Ineos* case, the court read the claim to include properties of lower malodor and good slip properties for the plastic. This leaves the practitioner somewhat in the wilderness regarding the question of whether properties not recited in a claim will or will not be given patentable weight.

Although Galderma[23] *held that where a claimed invention falls within a prior art range, the burden shifts to the patentee to show a teaching away or secondary consideration, no such shift occurred here because the prior art range was broader and the amounts materially and unpredictably affected the claimed formulation.*

In *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293 (Fed. Cir. 2015), the court reviewed the validity of Allergan's claims directed to compositions comprising 0.01% bimatoprost and 200 ppm benzalkonium chloride ("BAK") and methods of using them to treat glaucoma or to lower intraocular pressure ("IOP"). Allergan's prior commercial composition, Lumigan, comprises 0.03% bimatoprost and 50 ppm BAK.

On review, the Federal Circuit noted that "[a]lthough the prior art does not teach [a formulation comprising 0.01% bimatoprost and 200 ppm BAK], those amounts do fall within the ranges disclosed in a single reference" disclosing "0.001%–1% bimatoprost and 0–1000 ppm of a preservative, including BAK." *Id.* at 1304. Quoting from its previous decision in *Galderma*[23], the court explained that "where there is a range disclosed in the prior art, and the claimed invention falls within that range,"[24] "the burden of production falls upon the patentee to come forward with evidence that (1) the prior art taught away from the claimed invention; (2) there were new and unexpected results relative to the prior art; or (3) there are other pertinent secondary considerations."[25] The court however distinguished Galderma[23], finding that "in this case, the prior art ranges are broader than the range in *Galderma*[23], and the record shows that the claimed amounts of the two different ingredients could and did materially and unpredictably alter the property of the claimed formulation." *Id.* The court added that

> It may also be true here that "the disclosed range[s are] so broad as to encompass a very large number of possible distinct compositions," . . . such that they do not teach any specific amounts or combinations and that the burden of producing evidence of teaching away, ***unexpected*** results, and other pertinent secondary considerations did not shift to Allergan.[26]

23 *Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731 (Fed. Cir. 2013).

24 796 F.3d 1304-05.

25 *Id.* at 1305.

26 796 F.3d at 1305 (emphasis added).

Known adverse side-effects of BAK preservative would have taught away from increasing the BAK concentration from the prior art 50 ppm to the claimed 200 ppm, especially where the 50 ppm worked adequately

The court further found that "the prior art taught away from using 200 ppm BAK in a bimatoprost formulation" by teaching "that BAK should be minimized in ophthalmic formulations to avoid safety problems," such as "increased IOP, hyperemia, dry eye, and damage to corneal cells, and to exacerbate other eye disorders." *Id.* at 1305. Thus, "[i]t is not clearly erroneous to find that those known side effects would have discouraged a person of ordinary skill from using higher concentrations of BAK in a [0.01%] bimatoprost formulation, especially when 50 ppm BAK was known to be an adequate preservative in Lumigan 0.03%." *Id.* Although the prior art disclosed ophthalmic formulations containing 200 ppm BAK, the court still found a teaching away because most of the prior art formulations were not for chronic long-term use and would teach nothing about whether it was safe to use 200 ppm BAK with a lifelong glaucoma drug. As for the formulations suitable for long-term chronic use, the court found that the majority of BAK formed complexes such that it was not free in solution cause negative effects.

Because the claimed formulation as compared to the prior art maintained the therapeutic efficacy while reducing adverse side effects, i.e., the difference between an effective and safe drug and one with significant side effects, this was a unexpected difference in kind supporting patentability.

The court further found no error in the district court's finding that the claimed formulation exhibited "unexpected results," which differed in kind, not just in degree, from the prior art. The prior art taught that 200 ppm BAK would either have no impact on the permeability of bimatoprost or decrease it, whereas "Allergan's inventors surprisingly determined that the opposite was true, namely, that 200 ppm BAK enhanced the permeability of bimatoprost. That is an unexpected difference in kind that supports nonobviousness." *Id.* at 1306. The prior art also taught that reducing bimatoprost from 0.03% to 0.01% resulted in significantly reduced efficacy, but without a reduction in hyperemia. However, "[t]he claimed formulation, which comprises 0.01% bimatoprost and 200 ppm BAK, unexpectedly maintained the IOP-lowering efficacy of Lumigan 0.03%, while exhibiting reduced incidence and severity of hyperemia, even though the prior art taught that BAK could cause hyperemia at high concentrations." *Id.* at 1306-07. The court characterized those results as "an unexpected difference in kind, *viz.*, the difference between an effective and safe drug and one with significant side effects that caused many patients to discontinue treatment." *Id.* at 1307.

Once again, there is a curious inconsistency with other cases, as the court considered suitability for long term use as a factor in its holding of non-obviousness over the prior art, even though the claim included so such requirement.

Board erred in not considering reference disclosing background knowledge of the art, even though not included in the combination of references relied upon for showing obviousness in the original IPR petition, because such reference was included as exhibit with expert declaration; sufficient reasoning not given by Board to determine if properly considered.

In *Ariosa Diagnostics v. Verinata Health, Inc.*, 805 F.3d 1359 (Fed. Cir. 2015), the court reviewed the Board's holding in an *inter partes* review upholding the patentability of Verinata's claims directed to methods of noninvasive prenatal testing for the presence of fetal chromosomal abnormalities, such as aneuploidy. The patent describes and claims a counting technique applied to an overall pool of DNA segments, selected for comparing a chromosome of concern (say, chromosome 21) with a reference chromosome (or chromosomal region), and making the comparison by identifying the respective DNA sequences.

In its Petitions, Ariosa argued for obviousness based on combinations of Dhallan's teachings about cell-free fetal DNA with Binladen's indexing and sequencing techniques and Shoemaker's method of determining aneuploidy. The Board ultimately found that the Petition and accompanying Declarations lacked the required "articulated" reason with some rational underpinning to support the legal conclusion of obviousness, and the Board declined "to search through the record and piece together those teachings that might support Petitioner's position." *Id.* at 1364. The Board rejected Ariosa's attempt, through a second declaration accompanying its Reply, to bolster the reliance placed in the Petitions on a brochure that describes indexing and massively parallel sequencing using a commercially available Genome Analyzer System, finding that Ariosa failed to explain why the additional evidence could not have been presented as part of the asserted ground of unpatentability in the first instance with the Petition. The Board therefore accorded this testimony no weight.

On appeal, Ariosa argued that the Board erred in refusing to consider the additional evidence for what it showed about the background knowledge that a skilled artisan would have possessed, particularly about DNA indexing. The court agreed, finding that if the Board refused to consider such evidence simply because the brochure had not been identified at the petition stage as one of the pieces of prior art defining a combination for obviousness, it was error. The court noted that Ariosa included the exhibit with its Petitions as an exhibit to an expert declaration which discussed the state of the art. The court concluded that "[g]iven those references in the Petitions and supporting declarations, [the exhibit] had to be considered by the Board even though it was not one of the three pieces of prior art presented as the basis for

obviousness"[27] as "we cannot confidently discern whether the Board, in its consideration of [the exhibit], was actually relying on a legally proper ground rather than the erroneous ground just noted." *Id.* at 1366. The court faulted the Board for not sufficiently articulating the "grounds for its rejection of Ariosa's reliance on [the exhibit] or other grounds independent of the incorrect ground suggested by the Board's language" and "we cannot do so for the Board where, as here, the matter is not purely legal." *Id.* The court therefore was not ready to draw a "conclusion about whether [the exhibit], if considered for what the Petitions (and supporting declarations) adequately presented about it, could have filled the explanatory gap that was the heart of the Board's reason for finding Ariosa's case unproved." *Id.*

Because Petitioner failed in its initial Petition to both identify those portions of a secondary reference which could be combined with the primary reference, as well as provide an explanation as those portions, Board properly excluded such evidence when only presented at the Reply stage of the IPR.

Finally, Ariosa challenged the Board's determination that the teachings of Binladen and Dhallan could not be combined because Binladen's indexing (i.e., tagging) scheme could not be used with Dhallan's restriction-digestible amplification primers. Ariosa argued that the Board erred in failing to consider some embodiments of Dhallan—those which do not require a restriction-enzyme digestible primer—embodiments that could be combined with Binladen. "The Board declined to consider those embodiments because the cited 'portions of Dhallan were not identified or discussed in the Petition or the accompanying Declarations'" and, in any event, "Ariosa's explanation was lacking even as to those portions." *Id.* at 1367. The court saw no error, finding that "[n]ot until [the] Reply declaration did Ariosa identify specific embodiments of Dhallan that do not use restriction-enzyme digestible primers." *Id.* The court noted that the Board may exclude or give no weight to the evidence where a party has failed to state its relevance or to identify specific portions of the evidence that support the challenge in the Petition.

Where a reference discloses a method of treating elevated levels of homocysteine using a suitable active metabolite of folate, it would have been obvious to use L-5-MTHF as the metabolite in view of secondary reference disclosing that L-5-MTHF is a natural metabolite of folate useful to treat folate deficiencies.

In *Merck & Cie v. Gnosis S.P.A.*, 808 F.3d 829 (Fed. Cir. 2015) ("*Gnosis I*"), the Federal Circuit for the first time addressed on appeal the merits of a Board decision in an *inter partes* review involving a pharmaceutical patent. The court provided insight as to the standard of review to be applied in such cases, which garnered a dissent by Judge Newman regarding the appropriate degree of deference.

The patent at issue claimed a method of preventing or treating disease associated with increased levels of homocyteine levels in the human body comprising administering 5-methyl-(6S)-tetrahydrofolic acid ("L-5-MTHF"), or a salt thereof to a human subject, as well as claims further reciting that the increased levels of homocysteine are associated with a deficiency of methylene tetrahydrofolate reductase, an enzyme that helps generate L-5-MTHF for the methionine cycle. Homocysteine was linked to severe cardiovascular, ocular, neurological, and skeletal disorders. The compounds of the invention replaced the enzymes associated with the methionine cycle, through which the body naturally converts homocysteine to methionine.

The Board found the claims obvious in light of Serfontein, Marazza and Ubbink et al. To treat high levels of homocysteine associated with various diseases, "Serfontein discloses a preparation that includes 'folate or a suitable active metabolite of folate,' along with vitamins B6 and B12." *Id.* at 832. "Although Serfontein does not specify what constitutes a 'suitable active metabolite of folate,' Marazza identifies L-5-MTHF as a 'natural metabolite' that may be used 'as at least one active compound' in a treatment for folate deficiency" and, given the problems with the unnatural D-stereoisomer, "teaches a process by which a mixture of these 5-MTHF stereoisomers may be separated into pure L-5-MTHF and D-5-MTHF forms." *Id.* Ubbink links elevated homocysteine, caused by enzyme defects, with vascular disease and suggests use of vitamin supplements containing folic acid to treat these conditions.

On review, the court found that "[t]he record amply supports the Board's finding of a motivation to combine Serfontein and Marazza,"[28] holding that "Serfontein discloses a method of treating elevated levels of homocysteine using a 'suitable active metabolite of folate' and B-vitamins"[29] and Marazza "highlights L-5-MTHF as a 'natural metabolite' of folate in which there is an 'increasing interest' for the treatment of folate deficiencies."[30] Accordingly, "as the Board found, a person of ordinary skill viewing Serfontein and Marazza would have been motivated to use L-5-MTHF as the 'suitable active metabolite of folate' called for by the method disclosed in Serfontein." *Id.* at 834.

Although some prior art teaches away from substituting the 5-MTHF of the secondary reference for the folate metabolite of the primary reference, for reducing homocysteine levels, such teaching away negated by later art showing earlier problems had been overcome.

27 *Id.* at 1365.

28 *Id.* at 833.

29 *Id.*

30 *Id.* at 834.

The court also rejected Merck's argument that the prior art teaches away from this combination by suggesting: (1) administering 5-MTHF would actually increase levels of homocysteine, (2) 5-MTHF would be too unstable for therapeutic use, and (3) L-5-MTHF is a poor substrate for polyglutamation, a process that facilitates retention and use of L-5-MTHF in the cell. While acknowledging that some of the cited prior art does indeed teach away from the invention as argued by Merck, the court found that Merck took the references out of context and also disregarded subsequent references which mitigated against the teaching away. For example, when "considered as a whole," "the Board's finding that a person of ordinary skill would not have thought that 5-MTHF was too unstable for pharmaceutical use is supported by substantial evidence." *Id.* at 835.

Prior art discloses L-5MTHF as a natural alternative to folic acid to treat elevated homocysteine levels associated with enzyme deficiencies.

The court also agreed with the Board that one of ordinary skill in the art would have been motivated to use the method disclosed in Serfontein and Marazza to treat elevated homocysteine levels associated with certain enzyme deficiencies, as disclosed in Ubbink. Merck noted that Ubbink used folic acid, not reduced folates such as L-5-MTHF as used in the other references, to treat elevated levels of homocysteine associated with certain enzyme deficiencies. The court disagreed, noting that a deficiency in folic acid was tied to a deficiency in methylenetetrahydrofolate reductase ("MTHF") which in turn was tied to a deficiency in 5-MTHF, such that "a person of skill would have known that administering 5-MTHF directly would accomplish a similar result." *Id.* at 836. "Thus, the record supports the Board's finding that the method of using L-5-MTHF disclosed in Serfontein and Marazza was a natural alternative to using folic acid when elevated homocysteine levels are associated with enzyme deficiencies, as disclosed in Ubbink." *Id.*

The court's narrative in affirming the Board is rather simple and appealing: (1) The primary reference teaches that folic acid as well as its metabolites are known to treat the host of problems associated with elevated levels of homocysteine; and (2) the secondary reference teaches that L-5-MTHF is a "natural metabolite" of folate in which there is an "increasing interest" for the treatment of folate deficiencies. Taken with the conflict in the teaching away, we have a simple substitution of one metabolite used in folate deficiencies for another.

The problem is that the Board glossed over a lot here, and the court seems to have taken on the role of being a "P.T.A.B. enabler." For example, the entire disclosure of the primary reference relates to folic acid by itself (including every example), and there is only a fleeting reference to folate metabolites in the general disclosure, along with compounds that release folates in vivo. This hardly teaches suitability of folate metabolites in the process, and even if it did, it only then amounts to a disclosure of an extraordinarily large list including both folate metabolites and compounds that release folates. Further, in citing a specific passage of the secondary reference, the court actually exaggerates the teaching of the reference, stating that it "identifies ***L***-5-MTHF as a 'natural metabolite' that may be used 'as at least one active compound' in a treatment for folate deficiency"[31] when in fact the passage cited does not refer to the L form at all, much less its use in reducing homocysteine levels.[32] The court also glosses over the fact that Marazza's entire focus is on enantiomer separation and use of the L-enantiomer for cancer treatment, which hardly supports the court's overstated and unsupported conclusion that "Serfontein specifically calls for a 'suitable active metabolite of folate' to help lower homocysteine levels, and Marazza provides that L-5-MTHF ***is one such metabolite***."*Id.* at 836 (emphasis added).

So not a single folate metabolite is disclosed in the primary reference, and while the secondary reference does disclose a folate metabolite, it is for a completely different purpose despite the Board and court's characterizations to the contrary.

Even though the Board never made an express finding as whether one of ordinary skill would have had a reasonable expectation of success in combining the references, court finds that Board "impliedly" made such finding when addressing the lack of a teaching away.

Interestingly, as pointed out by Merck, the Board never made an express finding as to whether a person of ordinary skill would have a reasonable expectation of success in combining Serfontein and Marazza, or in further combining Serfontein, Marazza, and Ubbink. ***So in other words, even if the substantial evidence standard is applicable, there were no findings to which to apply that standard***. Although acknowledging *KSR*'s[33] requirement that "a factfinder's analysis of a reason to combine known elements in the art 'should be made explicit,'"[34] the court manipulated *KSR*'s[35] mandate of "flexibility" to excuse both itself and the Board from providing an explicit statement of a reasonable expectation of success in every case, holding that because "the Board addressed Merck's arguments against a reasonable expectation of success in the context of its teaching away arguments," "the Board impliedly found a reasonable expectation of success." 808 F.3d at 836. So despite the fact

31 *Id.* at 832 (emphasis added).

32 The relevant disclosure of the secondary reference reads as follows "N5-Methyl-5,6,7,8-tetrahydrofolic acid, herein sometimes abbreviated with the denotation N5-methyl-THF, is the predominant circulating form of reduced folates in mammals. There exists an increasing interest for the application of this natural metabolite as at least one active compound in a therapeutical agent, for example as vitamin in folate deficiency states."

33 *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

34 808 F.3d at 836.

35 *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007).

that a teaching away is a factual finding completely distinct from a reasonable expectation of success, the court declined to overturn the Board's decision for failure to state expressly that a person of ordinary skill would have had a reasonable expectation of success.

So the Board failed to ever make findings regarding a reasonable expectation of success and despite the Supreme Court's admonition to the contrary, the court not only gave the Board a free pass, but added fuel to the fire by selectively citing to the record in a way that was not true to what was actually taught. As a result, the court did not in the end carry out a meaningful review of the Board's decision. We can only hope that this case will prove an outlier and not reflect this court's inability and/or unwillingness to properly police pharmaceutical IPRs.

No nexus shown between commercial success and claimed invention where the commercial products include components in addition to those claimed, such that success cannot be attributed to the claimed component.

The court next reviewed the Board's consideration of Merck's evidence of secondary considerations and agreed with the Board that (1) Merck's evidence of commercial success was deficient for failing to provide the requisite nexus between the invention and its evidence; and (2) Merck's evidence of long-felt but unmet need was unpersuasive. The court found that Merck's commercial products "go further and contain a specific combination of specific forms of B-vitamins and other active ingredients,"[36] such as vitamins B6 and B12 , and thus "Merck failed to establish that the commercial success of these products was due to the claimed method–using L-5-MTHF and 'at least one B-vitamin'–as opposed to the specific formulations in the mixed products."[37]

If commercial success is due to an element in the prior art, no nexus exists.

As for Merck's product containing only the L-5-MTHF, the court cited *Tokai Corp. v. Easton Enters., Inc.*, 632 F.3d 1358, 1369 (Fed. Cir. 2011) for the proposition that "[i]f commercial success is due to an element in the prior art, no nexus exists." 808 F.3d at 838. Here, the court agreed that substantial evidence supports the Board's finding "that the use of 5-MTHF for treating major depressive disorder and schizophrenia was known in the prior art, and therefore Merck could not show a sufficient nexus between the commercial success of the Deplin® products and the novel features in the asserted claims." *Id.*

The quote from *Tokai Corp.* is that "If commercial success is due to an element in the prior art, no nexus exists." 632 F.3d at 1369. This certainly makes sense, but only taken in context. For example, if a cleaning composition containing X exists in the prior art, and then an inventor achieves great commercial success by modifying the compound to further include Y, it makes sense to ensure that it is not the presence of X alone which is responsible for the success. However, in this particular case, the so called prior art used 5-MTHF (note not the ***L***-5-MTHF, which the court seems to have disregarded) for treating mental illness yet presumably no one buying the product at issue here was buying and taking it for such purpose (if they were, they would not be infringers in any event and it would not be covered by the claim). Given that virtually every invention includes within the claim an element found in the prior art, the court's use of this doctrine in this situation seems to create a dangerous "fudge" factor to let a panel so inclined to dismiss the probative value of commercial success in all but the most extreme situations.

Where licensing agreements include several patents in addition to the one for which commercial success is alleged, no nexus established.

The court found Merck's evidence of licensing to be similarly unavailing because "[a]lthough Merck successfully licensed the '040 patent to Pamlab, the licensing agreement also covered several other patents" and "[i]t is therefore difficult to determine the extent to which the licensing agreement was a result of the novel features in the '040 patent, as opposed to the other patents involved." 808 F.3d at 838. In light of this ambiguity, the court concluded that the Board's finding was reasonable.

Patentee has not established the requisite "nexus" to show commercial success or industry praise for a method to treat symptoms associated with folate deficiencies using L-5-MTHF where the element responsible for the commercial success or praise, the L-5-MTHF, is already known in the prior art for treatment of mental health disorders.

In *S. Ala. Med. Sci. v. Gnosis S.P.A.*, 808 F.3d 823 (Fed. Cir. 2015) ("*Gnosis II*"), a case closely related to the *Merck*[38] case reported immediately above, the court again reviewed patents relating to administering the "natural" stereoisomer L-5-MTHF and other vitamins to treat symptoms associated with folate deficiency, such as cardiovascular disease, neurological disorders, birth defects, and skeletal disorders. As in *Gnosis I*, the court affirmed the Board's finding of obviousness based on the combination of Serfontein and Marazza, based on Serfontein's teaching of using folate metabolites to treat disorders associated with folate deficiencies and Marazza's identification of L-5-MTHF as a "natural metabolite" of folate.

As in *Gnosis I*, the court also rejected evidence of secondary considerations such as industry praise because, as was

36 808 F.3d at 837.

37 808 F.3d at 837-38.

38 *Merck & Cie v. Gnosis S.P.A.*, 808 F.3d 829 (Fed. Cir. 2015).

the case with commercial success, this evidence was "not reasonably commensurate with the scope of the claims." 808 F.3d 827. The court found substantial evidence for the Board's finding that "the praise was particularly directed to the use of L-5-MTHF, an element already known in the prior art." *Id.* Thus, patentee "failed to connect the evidence of industry praise to the novel elements of the claims." *Id.*

Evidence that L-5-MTHF was unexpectedly superior to folate for a certain subset of the population not persuasive of non-obviousness because (1) the claims were not limited to that subset; and (2) administering L-5-MTHF was generally known in the prior art.

Patentee further argued that its inventors were the first to recognize that a subset of the population had difficulty processing folic acid, and that L-5-MTHF would therefore be an effective alternative. However, because "the claims are not limited to treating this subset of the population,"[39] and because "administering L-5-MTHF generally was known in the prior art,"[40] the court once again found that the Board's finding that this evidence was not adequately tied to the novel features of the claimed invention was supported by substantial evidence.

Although the Board improperly dismissed evidence of commercial success by focusing on the nexus between the patent and the licensee's products rather than the nexus between the patent and the licensing activity itself, the error was harmless in view of the strong evidence of obviousness.

The court did find that the Board improperly discounted the probative value of SAMSF's licenses to Merck, and Merck's sublicenses to Pamlab, "because SAMSF failed to show a nexus between the claimed inventions and Pamlab's products." 808 F.3d at 827. The court framed the relevant inquiry as "whether there is a nexus between the patent and the licensing activity itself, such that the factfinder can infer that the licensing 'arose out of recognition and acceptance of the subject matter claimed' in the patent." *Id.* Thus,

> Although evidence that the licensee ultimately manufactured a product that embodies the claimed invention may be probative of a nexus between the claimed invention and the licensing activity, the patentee is not necessarily required to establish an independent nexus between those products and the claimed invention for the licensing activity to be relevant.

Id. at 827-28. Nonetheless, the court found the Board's error was harmless because "[e]ven if the Board had correctly considered SAMSF's evidence of licensing, that evidence is not enough to overcome the strong evidence of obviousness found in the prior art and the expert testimony, relied upon by the Board to reach its conclusion of obviousness." *Id.* at 828.

This is certainly not the first time that this court has found probative evidence of secondary considerations to be insufficient to overcome "strong" evidence of obviousness, so that aspect of the case is not particularly shocking given the court's more recent precedent. What is questionable, however, is how the court found "strong evidence of obviousness"[41] in a review where it had to infer a reasonable expectation of success from a teaching away in view of the Board's failure to make the requisite findings. If mere inference is evidence of a "strong" case of obviousness, one must wonder what this panel would consider to be a weak case.

A comparison of *Ariosa* with the two *Gnosis* cases makes it hard to understand why the Federal Circuit was so critical of the Board in the former case to make sure it dotted its I's and crossed its T's, but extremely forgiving despite numerous lapses in the latter two cases.[42] The two decisions are irreconcilable in their approach. The best advice to IPR parties is the following—win your case at the Board or risk a panel that will review your case with a rubber stamp.

A compound comprising 92-95% purity of the (6S) diastereoisomer of leucovorin is obvious over the 50/50 prior art racemate because if it was known that the desired activity all lied in the (6S) isomer, there is motivation to obtain the purest compound possible.

In *Spectrum Pharm., Inc. v. Sandoz Inc.*, 802 F.3d 1326, (Fed. Cir. 2015), the court reviewed the obviousness of Spectrum's claims directed to a mixture of leucovorin diastereoisomers comprising 92% of the (6S) diastereoisomer and the balance the (6R) diastereoisomer (and pharmaceutically acceptable salts and esters thereof). The compound ameliorates the toxic effects of methotrexate during chemotherapy treatment, to treat folate deficiency and to enhance the efficacy of a 5-fluorouracil cancer treatment.

The question reviewed by the Federal Circuit was whether the district court erred in holding that the claimed *substantially pure* compound would have been obvious when both the 50/50 mixture and the pure compound were known in the art. The court found that "one of skill would have been motivated to modify the prior art 50/50 mixture to make the claimed mixture," because "[i]f it is known that the desired activity all lies in one isomer, surely, it is better, and there is generally motivation, to try to obtain the purest compound possible." *Id.* at 1334. In such cases "there is always

39 808 F.3d at 827.

40 *Id.*

41 808 F.3d at 828.

42 Indeed, the current rate of affirmance is almost 90%, as recently reported in Law 360.

… a motivation to aim for obtaining a pure, resolved material." *Id.*

The compound comprising 92–95% purity of the (6S) diastereoisomer of leucovorin is obvious over the pure material because it was known that the (6S) isomer provided the desired effect and the less-than-pure material did not possess unexpected advantages over the pure material.

The court also rejected Spectrum's argument that there was no reason why one would be motivated to obtain a material of 92-95% purity in view of the known pure material, holding that

> Because the desirable properties of the prior art 50/50 mixture are attributable to only one component, and the slightly impure mixture . . . has not been shown to possess unexpected advantages over the prior art pure material, the less-than-pure material, and any others of similar concentration, cannot be found to have been nonobvious.

Id. at 1335. Here, "there was no need to find an express teaching to prove sufficient motivation to modify the prior art to arrive at the claimed invention," because "various techniques to purify the isomers were reported in the art and . . . it was known that the (6S) isomer alone provided the therapeutic effect." *Id.*

Prior art disclosing that administration of drug daptomycin at higher doses and lower intervals would have good antibacterial activity suggests claimed invention even though the art is merely predictive, i.e., based on laboratory studies, not clinical trials.

In *Cubist Pharm. Inc. v. Hospira, Inc.*, 805 F.3d 1112 (Fed. Cir. 2015), the court reviewed the validity of Cubist's claims reciting methods of administering the antibiotic daptomycin at high doses and with large intervals between doses, such as at 4 or 6 mg per kg of patient weight once every 24 or once every 48 hours. Eli Lilly had developed daptomycin and found that high doses were effective against *S. aureus*, but suspended further testing when they discovered that such high doses administered every twelve hours resulted in skeletal muscle toxicity in some patients. Cubist discovered that the toxic side effects of daptomycin could be reduced by administering the drug less frequently but at higher doses while maintaining the desired therapeutic activity.

Hospira cited prior art disclosing, that "doses of 4 to 6 mg/kg/day, possibly in divided doses, are predicted to be effective"[43] based on the pharmacokinetics and antibacterial activity of daptomycin. The article further reported data suggesting "that good antibacterial activity would be produced from single doses of 4 to 6 mg/kg,"[44] and that the drug's long half-life in the body would "allow [] once- or twice-daily administration with the proper doses."[45] Although the article did not mention minimizing skeletal muscle toxicity, the district court found such effect was inherently disclosed as a necessary accompaniment to the other disclosed claimed limitations. The court rejected Cubist's argument that because the article is based on laboratory studies, not clinical trials, it is not predictive as to the likely effects of the drug in patients, holding that

> While it is true that the [article] is predictive in nature, it is based on extensive laboratory research, and its predictions of the efficacy of a dosage regimen of 4 mg/kg to 6 mg/kg at daily intervals give rise to a reasonable expectation that dosages in that amount would be effective in patients.[46]

Although not highly effective, prior art administering 2 mg/kg once daily or 3 mg/kg twice daily produced no skeletal muscle toxicity such that there would have been a reasonable expectation of success that higher doses at lower frequency would be both safe and effective.

The court also found that because Lilly's administration of 2 mg/kg once daily produced no reported side effects and 3 mg/kg twice daily produced no symptoms of skeletal muscle toxicity, albeit not highly effective, there would have been a reasonable expectation of success that somewhat higher doses administered less frequently than twice daily could be expected to be both safe and effective. Finally, the court made reference to four known characteristics of daptomycin as suggesting the invention, i.e, (1) daptomycin is especially effective at killing bacteria when it is found in high concentrations in the patient's body; (2) it has a long half-life, which allows it to act in the body over an extended period of time before being cleared by the kidneys; (3) it has a long post-antibiotic effect, i.e., it continues to suppress bacteria after leaving the body (those three characteristics suggest that it is not necessary to administer daptomycin frequently); and (4) muscle toxicity resulting from daptomycin was known to be reversible in most cases (suggesting that administering doses at greater intervals would allow the muscles more time to repair between doses, thus reducing the cumulative toxic effect of the drug).

This is a case where the court found a proposed example to be more persuasive than actual evidence. In particular, Lilly's actual work showed that administration at high doses twice daily caused muscle toxicity and discontinued that regimen for that reason. The court however relied on an article that merely proposed that high doses, possibly in divided doses, were effective against bacteria but was silent about muscle toxicity. This is completely consistent with what Lilly found, i.e., its twice

43 805 F.3d at 1122.

44 *Id.*

45 *Id.*

46 *Id.* at 1124.

daily high dose was effective against *S. aureus* but had an adverse side effect. Clearly, in suggesting that the dose could just as well be divided, the article had no clue whatsoever regarding the beneficial effects on fewer doses regarding toxicity. Nonetheless, the court forayed into inherency of that aspect, i.e., "a necessary accompaniment to the other disclosed claimed limitations." *Id.* at 1123. What does that even mean?

To the extent the court is referencing its recently minted "obviousness inherency" approach, the case is hard to follow. Obviousness by inherency states that if a combination is obvious, one cannot obtain a patent with properties that necessarily follow from that combination. The problem here, however, is that the property of reduced toxicity does not necessarily follow from following the prior art article, because the article proposes both twice daily and single administration of the drug as alternatives. Nor was the court bound by the clear error standard here, as it was a legal error to find inherency where record indisputably taught that the prior art article disclosed alterative administration modes, such that lower toxicity could not be the necessary result.

Claim limiting treatment of irritable bowel syndrome ("IBS") using alosetron to women is obvious over prior art disclosing use of drug to treat a general population of patients, as the majority of IBS patients were women and it was known that women responded better to the drug.

In *Prometheus Labs., Inc. v. Roxane Labs., Inc.*, 805 F.3d 1092 (Fed. Cir. 2015), the court reviewed the validity of Prometheus' claims directed to a method for treating a particular type of irritable bowel syndrome ("IBS") with alosetron and, particularly, IBS-D (diarrhea-predominant) as opposed to IBS-C (constipation-predominant), IBS-M (mixed) or IBS-A (alternating). The claim under review limits the treatment to a subset of those IBS patients–those who (1) are women (2) with IBS-D (3) who have experienced symptoms for at least six months and (4) who have had moderate pain. The particular limitations were the result of the FDA requiring a more restrictive label in view of severe side effects necessitating withdrawal of the drug from the market when administered to all IBS patients.

The prior art, Prometheus's own '800 patent, claims a method of treating a condition such as IBS which is ameliorated by antagonism of 5-HT3 receptors which comprises administering to a patient an effective amount of alosetron as well as a method for the treatment of irritable bowel syndrome. Thus, the claims under review recite a species of the genus method claimed in the '800 prior art patent. Although acknowledging that a narrow species can be non-obvious over a patent to a genus, the court found that "that is not the situation here." *Id.* at 1098. Regarding the limitation of the treatment to women, the court found it undisputed "that a majority of IBS patients were women"[47] and "[e]ven if the claims should be read as focusing treatment on women . . . the district court found the prior art taught precisely that,"[48] for example "that women would have a greater response to the drug than men."[49] Therefore, "it would have been obvious to a person having ordinary skill in the art to treat women as a separate group of IBS patients." *Id.*

Claim limiting treatment of IBS using alosetron to only a single type of IBS, IBS-D, is obvious because the class of drugs of which alosetron is a part, 5-HT3 antogonist drugs, is known to be particularly effective against IBS-D.

The court next reviewed the limitation directed to only treating patients suffering from IBS-D. Prometheus argued that "that the district court simply relied on studies suggesting that the class of 5-HT3 antagonist drugs, of which alosetron is a part, should be used to treat IBS-D and not IBS-C." *Id.* at 1099. The court disagreed, finding that

> While those studies were not focused on alosetron, but the class of drugs, there is ample testimony that a person of ordinary skill would have understood the studies as equally applicable to alosetron . . . . We do not think the district court clearly erred in concluding that the lessons drawn with regard to a class of drugs (5-HT3 antagonists) are applicable to a species (alosetron) within that class."[50]

Claim limiting treatment of IBS using alosetron to patients exhibiting symptoms for at least six months is obvious, because longer waits known to lead to higher confidence in the diagnosis, despite prior art recommendation of three months.

"As to the claim limitation requiring symptoms for 'at least six months' before administering alosetron,"[51] the court noted that "it was common practice at the time of the . . . patent to determine whether a patient had suffered symptoms for longer than six months."[52] The court relied on testimony to the effect that the benefit of the six-month limitation was having "a greater confidence in the diagnosis"[53] and cited studies suggesting using a six-month standard for the diagnosis of IBS. In so finding, the court rejected Prometheus' argument that three months was the diagnostic standard at the time of the invention, holding that "the district court's finding as to the six-month standard is amply supported by the record and is not clearly erroneous." *Id.* at 1100.

47 805 F.3d at 1098.

48 *Id.*

49 *Id.*

50 805 F.3d at 1099.

51 *Id.*

52 *Id.*

53 *Id.*

Claim limiting treatment of IBS using alosetron to patients exhibiting at least moderate pain is obvious, because pain was known as a main symptom of IBS and even though some IBS patients do not exhibit pain, those with severe IBS, who are the object of the claims, would be expected to have pain.

"Regarding the limitation directed to at least moderate pain," the court found that "at the time the patent issued, it was well-known to evaluate patients for pain in order to diagnose IBS." *Id.* The court noted that "[p]ain is in fact a main symptom of IBS (along with diarrhea and constipation)." *Id.* Although Prometheus conceded "that it would have been obvious to use alosetron to treat pain," it argued "that it would not have been obvious to administer alosetron only to patients suffering from at least moderate pain." *Id.* The court disagreed, citing Prometheus's own expert's testimony that because a candidate for the drug was a patient with severe IBS, it's pretty obvious that a physician will assess for at least moderate pain. Expert testimony also showed that a person of ordinary skill would have adopted a conservative approach in treating IBS patients, and avoided drug intervention for a patient with mild symptoms.

In sum, the "limitations are directed to a known type of IBS, to treating the gender that predominantly experiences IBS, to treating patients with a characteristic that is always or almost always evaluated in establishing IBS, and to assessing symptoms for a duration of time that was common in diagnosing patients with IBS." *Id.* at 1101. Thus, "there was a limited number of known parameters and it would have been obvious to combine the teachings as to each parameter." *Id.*

Because it was not the patent that was responsible for the commercial success of the claimed product, but marketing and pricing, patentee's evidence of unexpected results not sufficient.

The court also rejected Prometheus's reliance on secondary considerations. As for commercial success, the district court determined that it was not the patent that was responsible for the commercial success of reintroduced Lotronex, but instead "Prometheus's actions in marketing, increasing the price of Lotronex, and introducing a series of rebates to stimulate sales of the drug, rather than from the treatment method claimed in the . . . patent." *Id.* The district court further found a lack of an analysis showing

> [C]ommercial success for the . . . patent on its own merits, control[ling] for other variables and separat[ing] the treatment instructions from the drug compound and the method in the [prior] patent that already existed, nor any analysis to control for other changing variables, such as marketing campaigns, new drug warnings, pricing changes, *etc.*'"

Id. The court also rejected Prometheus's argument that the district court erred by placing the burden of proof on Prometheus to demonstrate the nexus between Lotronex's commercial success and the patent, holding that once a challenger has presented a *prima facie* case of invalidity, the patentee has the burden of going forward with rebuttal evidence.

The statute, 35 U.S.C. § 103, explicitly states that it is the invention "as a whole" that must be obvious. That makes this decision hard to understand, as the court carved the claim up like a turkey at Thanksgiving and simply found each element in isolation obvious. One question that arises is the following—even if all of these limitations individually were obvious, where was the suggestion that all four criteria were necessary at the time of the invention? Maybe it would have been sufficient if the population had been limited to women, without the other three requirements. Ultimately based on the decision itself, it is impossible to judge whether, had a correct review been carried out, the invention would have been non-obvious. However, the court should have at least conducted its review using the correct standard.

Obviousness-Type Double Patenting

Even though a divisional CIP, which was not entitled to rely on the safe harbor of section 121, was amended by reissue to exclude the new matter and be a simple divisional of the originally restricted parent application, the safe harbor of section 121 still does not apply.

In *G.D. Searle LLC v. Lupin Pharm., Inc.*, 790 F.3d 1349 (Fed. Cir. 2015), the court reviewed whether the patentee Pfizer was entitled to invoke the safe harbor of section 121 as a defense against a claim of obviousness-type double patenting ("ODP") against Pfizer's reissue patent, which was based on Pfizer's U.S. 5,760,068 ("the '068 patent").

Pfizer filed an application claiming compounds, compositions, and methods of use regarding the treatment of pain and inflammation without the harmful side effects associated with certain traditional anti-inflammatory drugs. After a three-way restriction requirement, Pfizer elected the compound claims and pursued composition claims in a divisional application. Both cases ultimately issued into patents. However, rather than filing a second divisional application, Pfizer pursued the restricted-out method-of-use claims in a continuation-in-part ("CIP") of the original application with the same three classes of claims, for which Pfizer received another three-way restriction requirement. Pfizer then filed a second CIP from the first CIP, also containing all three classes of claims and also receiving a three-way restriction requirement, where Pfizer prosecuted method-of-use claims. Both CIPs issued into patents. However, the Federal Circuit

invalidated the second CIP on the grounds of ODP in view of the patent issuing from the original application,[54] holding that even though both patents traced their lineage back to the same original application where there was a restriction requirement, the statutory safe harbor provision was inapplicable because "the protection afforded by section 121 to applications (or patents issued therefrom) filed as a result of a restriction requirement is limited to divisional applications," whereas "the [second CIP] patent issued from a continuation-in-part, not a divisional application." *Id.* at 1352.

Pfizer then availed itself of the reissue process in an attempt to turn back the clock and convert its second CIP divisional into a straight divisional by deleting those portions of the specification not present in the original application: designating the application as a divisional, removing the priority claim to the first CIP application, and amending the claims to recite only subject matter disclosed in the original application. The PTO eventually allowed the changes, which issued as a reissue patent. On review, the court noted that "[t]he safe harbor provision of section 121 protects a patent issuing on an application with respect to which a restriction requirement has been made, or on an application filed as a result of such a restriction requirement." *Id.* at 1354. Here, "[t]he challenged [reissue] patent . . . is not entitled to safe harbor protection, because it did not issue on either the [original] application or a divisional of the [original] application"[55] and it "cannot be a divisional of the [original] application, despite being designated as such in the reissue patent, because it contains new matter that was not present in the [original] application."[56]

Finally, "[s]imply deleting that new matter from the reissue patent does not retroactively alter the nature of the [second CIP] application,"[57] because "when the [second CIP] application issued . . . , Pfizer obtained patent protection for the new matter that was not present in the [original] application"[58] such that "[f]or years thereafter, the public was not free to practice that new matter (e.g., the now cancelled claims…) because of that patent protection."[59] "Pfizer cannot now identify the [second CIP] application as a divisional of the [original] application (for purposes of section 121) and retroactively relinquish the new matter in the [second CIP] application, after having enjoyed years of patent protection for it"[60] because "[f]airness to the public does not permit Pfizer to convert the [second CIP] application into a division of the original . . . application, and thereby take advantage of the safe harbor provision, simply by designating it as a divisional application years after the fact."[61]

Because the reissue of the CIP divisional and the reference patent forming the basis of the obviousness double patenting rejection are not derived from the same restriction requirement, the safe harbor does not apply.

The court also found that the reissue patent and the ODP reference patent are not "derived from the same restriction requirement." *Id.* at 1356. Thus, "[w]hen separate restriction requirements are imposed on separate applications and the record does not show that any of the various restriction requirements carried forward from one application to the next, the earlier restriction requirement cannot be viewed as having continued in effect with respect to the later-filed application." *Id.* Here, the reissue patent identifies itself as being descended from the two CIP applications, which were subject to a separate restriction requirement between compounds, compositions, and methods of use. "The record thus shows that two separate restriction requirements affected the chain of applications involved in this case." *Id.* However, "[i]n order for section 121 to protect the [reissue] patent against the invalidating effect of the [reference] patent, the [earlier] restriction requirement must have 'carried forward' from the [original] application to the [second CIP]application. . . . No such showing has been made, however." *Id.* at 1356-57 (citations omitted).

The problem here for Pfizer is that this was not a simple case of filing the divisional CIP with the method claims in response to the restriction requirement in the original parent. To the contrary, Pfizer filed all three types of claims in its CIP divisional and elicited a completely new restriction requirement. Further, Pfizer added new matter to the claims itself, which may have raised consonance issues though this was not addressed in the opinion. There are, however, two potential issues with this case and the 2008 case. First, it seems that the addition of new matter to a divisional should not per se be a disqualifier for reliance on the safe harbor. For example, if an applicant filed a divisional of a parent application in response to a restriction requirement and did not change the claims at all from those that were restricted, why should the addition of an example (especially if not necessary for 112 support) disqualify the applicant from the safe harbor? Certainly the language of the statute referencing divisional applications does not explicitly exclude CIP divisionals so the court had maneuvering room here. Second, the court's concern regarding the prejudice to the public for the period where Pfizer received protection for the new matter is hard to follow–after all, any time a patentee files a narrowing reissue, it enjoyed the benefit of coverage of the broader scope prior to reissue, yet the court has not raised the same prejudice issue there to preclude patentee's reliance on reissue. This case also reinforces a point we've made before that unless a patentee follows the strictest letter of the rules regarding ODP issues, this court will find a way to apply ODP.

54 *Pfizer, Inc. v. Teva Pharm. USA, Inc.*, 518 F.3d 1353 (Fed. Cir. 2008).

55 790 F.3d at 1354.

56 790 F.3d at 1354-55.

57 790 F.3d at 1355.

58 *Id.*

59 *Id.*

60 *Id.*

61 *Id.*

Written Description

Even though the written description does not disclose efficacy or hyperemia data for the claimed formulation, such clinical profile information is supported because the formulation itself is described and the profile information is an inherent property of the formulation.

In *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293 (Fed. Cir. 2015), the court reviewed the validity of Allergan's claims directed to compositions comprising 0.01% bimatoprost and 200 ppm benzalkonium chloride ("BAK") and methods of using them to treat glaucoma or to lower intraocular pressure ("IOP"). Appellants argued that the claims reciting clinical profile limitations are not adequately supported because the written description does not disclose any efficacy or hyperemia data of a formulation comprising 0.01% bimatoprost and 200 ppm BAK.

The court disagreed, finding that the "specifications specifically describe a formulation comprising 0.01% bimatoprost and 200 ppm BAK as one of the best modes of the invention"[62] and that while the claims "recite clinical profile limitations and the specifications do not explicitly describe the clinical efficacy and hyperemia profile of the claimed formulation,"[63] "the Appellants have emphasized . . . that the inherent properties of a formulation comprising 0.01% bimatoprost and 200 ppm BAK produce the claimed clinical profile."[64] The court noted that "[a] claim that recites a property that is necessarily inherent in a formulation that is adequately described is not invalid as lacking written description merely because the property itself is not explicitly described." *Id.*

Correction of formula to recite the D- form rather than L-form of asparagine did not violate the written description requirement because a person skilled in the art would have understood that the inventors possessed and were working with the D-form.

In *Cubist Pharm. Inc. v. Hospira, Inc.*, 805 F.3d 1112 (Fed. Cir. 2015), the court reviewed whether Cubist violated the written description requirement when it amended its claim reciting daptomycin of "formula 3" to correct the improperly depicted L-isomer of asparagine to the D-isomer. At the time the application was filed, and well after issuance, it was universally believed that the asparagine in daptomycin was the L-isomer. In addition to the formula 3, the specification described daptomycin as an A-21978C cyclic peptide prepared from A-21978C antibiotics described in a specifically referenced patent and by the code name LY146032, assigned to the compound by Lilly and known in the art to refer to daptomycin.

62 796 F.3d at 1308.

63 *Id.* at 1309.

64 *Id.*

On review, the court held that notwithstanding the error in the structural diagram of Formula 3, one skilled in the art would have understood that the inventors possessed and were working with the naturally occurring fermentation product, i.e., the daptomycin molecule containing D-asparagine. In this case, the applicants claimed only what they had produced–the daptomycin molecule–which they identified in several ways. The court found that "[i]t was enough that the specification disclosed relevant identifying characteristics that distinguished daptomycin from other compounds and thus showed that the inventors had possession of daptomycin, even though they may not have had an accurate picture of the entire chemical structure of that compound." *Id.* at 1120.

Enablement

Unpredictability of the utility of a claimed invention is not inconsistent with enablement, even in the absence of efficacy data, where there otherwise is sufficient in vivo and in vitro data that would convince a skilled artisan of efficacy.

In *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293 (Fed. Cir. 2015), the court reviewed the validity of Allergan's claims directed to compositions comprising 0.01% bimatoprost and 200 ppm benzalkonium chloride ("BAK") and methods of using them to treat glaucoma or to lower intraocular pressure ("IOP"). Appellant asserted non-enablement because the specifications contain no actual efficacy and hyperemia data, but merely provide a research proposal.

Appellant argued that Allergan was trying to have it both ways--if the invention was non-obvious as argued by Allergan because it was unpredictable that the claimed formulation would exhibit comparable efficacy but less hyperemia as compared to its prior Lumigen formulation, then "the skilled artisan would not accept the asserted utility of the claimed formulation"[65] without data. The court disagreed, noting that "efficacy data are generally not required in a patent application. Only a sufficient description enabling a person of ordinary skill in the art to carry out an invention is needed." 796 F.3d at 1310. Here, the court found the invention enabled because "[t]he specifications disclose actual *in vitro* and *in vivo* data, showing that increasing the amount of BAK unexpectedly increased the permeability of bimatoprost across ocular membranes," and a constructive example teaches that a 0.015% bimatoprost/125 ppm BAK formulation "would effectively reduce IOP and also exhibit less hyperemia than Lumigan 0.03%." *Id.* The court found "no tension in the district court's decision that the asserted claims would not have been obvious and also are not invalid for lack of enablement," noting that "[t]he obviousness inquiry turns on what the prior art would have taught a person of ordinary skill in the art and whether the claimed invention would have been obvious in view of the prior art," whereas "the

65 796 F.3d at 1310.

enablement inquiry turns on whether the skilled artisan . . . would be able to make and use the claimed invention without undue experimentation, based on the ordinary skill in the art." *Id.*

Indefiniteness

A claim that recites "molecular weight" but fails to recite which one of three possible ways it can be measured is indefinite where the specification fails to resolve the ambiguity and prosecution statements from two related cases contradict each other.

In *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335 (Fed. Cir. 2015), on remand from the Supreme Court (discussed *infra*) and in view of *Nautilis, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120 (2014), the Federal Circuit reconsidered whether the term "molecular weight" was indefinite.

Teva's claims recite "copolymer-1" that has a "molecular weight of about 5 to 9 kilodaltons." 789 F.3d at 1338. There are several methods to measure molecular weight, including peak average molecular weight ("M_p"), number average molecular weight ("M_n") and weight average molecular weight ("M_w"). The claims, however, do not specify which measure to use and the specification does not define "molecular weight." *Id.* at 1341, 1344-45. The district court accepted the testimony of Teva's expert that Example 1 of the patent suggests to one of ordinary skill in the art that the "molecular weight" is M_p, and concluded therefore that the claims were not indefinite. In its original decision, the Federal Circuit reviewed all aspects of the district court's decision *de novo*, and reversed. The Supreme Court vacated the decision and held that if a district court resolves factual disputes over evidence extrinsic to the patent, then the Federal Circuit must review these factual findings for clear error. The Court reiterated, however, that "the ultimate question of the proper construction" of a patent claim is "a question of law" and thus reviewed *de novo*. *Id.* at 1339.

On remand, the Federal Circuit concluded that the district court's factual determination, and specifically its acceptance of the testimony of Teva's expert, were not clearly erroneous, but again held the claims were invalid as being indefinite. The court initially looked at the claims, specification, and prosecution history "to ascertain if they convey to one of skill in the art with a reasonable certainty the scope of the invention claimed." *Id.* at 1341. The court concluded that neither the claims nor the specification specifies which of three possible measures to use, M_p, M_n, or M_w. Further, the parties agreed that M_p, M_n, and M_w are each calculated differently and would typically yield a different result for a given polymer. *Id.* at 1341, 1344-1345. As for the prosecution history, the court noted that, in response to indefiniteness rejections regarding the term "molecular weight" during prosecution of two related patents, Teva stated that this term meant M_w in one case and M_p in the other case. The Federal Circuit found no clear error in the district court's acceptance of Teva's explanation that its statement regarding M_w during prosecution was scientifically erroneous, but held that "[r]egardless of the scientific accuracy of the statement, a person of ordinary skill in the art would have understood that the applicants defined the term 'molecular weight' as M_w to gain allowance of the claims." *Id.* at 1344. The court further explained that "[t]his is a legal conclusion unaffected by the scientific error made during prosecution." *Id.*

Accordingly, even accepting Teva's expert testimony regarding the specification and its explanation of the error that occurred during prosecution as not being clearly erroneous, the court held that as a matter of law, given the inconsistent treatment of the terms during prosecution, there is not reasonable certainty that "molecular weight" should be measured using M_p. The court therefore found the claims invalid as being indefinite.

Under Nautilus, *a claim is indefinite when it recites a value that can be determined using multiple methods that yield different results, but the patent and prosecution history fail to identify which method should be used.*

In the *Dow Chem. Co. v. Nova Chem. Corp. (Can.)*, 803 F.3d 620 (Fed. Cir. 2015), the Federal Circuit considered whether, in view of *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120 (2014), the district court's award of supplemental damages should be reversed because the phrase "slope of strain hardening coefficient greater than or equal to 1.3"[66] is indefinite. In its prior, pre-*Nautilus* decision, the Federal Circuit held that this phrase was not indefinite.

Dow's claims recite an ethylene polymer composition comprising an ethylene/α-olefin interpolymer having a "slope of strain hardening coefficient greater than or equal to 1.3." 803 F.3d at 631. The patents explain that the "slope of strain hardening coefficient," a previously unknown construct, is calculated by multiplying the "slope of strain hardening" with another value. *Id.* Strain hardening is a property where a material becomes harder as it is stretched. The patents teach that strain hardening may be tested using a Instron Tensile Tester, and the resulting measurements are plotted on a graph, such as that on the following page.

66 803 F.3d at 624.

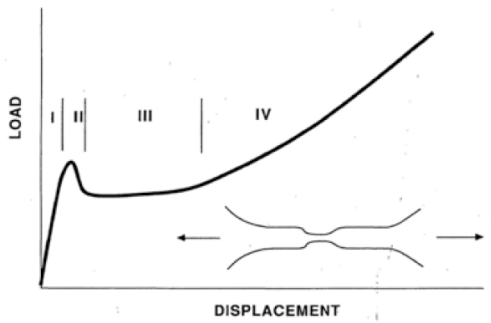


Figure 8. A typical load-displacement curve.

At issue was region IV of the graph. Nova argued that the phrase "slope of strain hardening coefficient" was indefinite because the patent specifications did not teach, with a reasonable certainty, where and how the "slope of strain hardening" should be measured. *Id.* at 633. Dow's expert testified that even though the slope in the region IV of the graph was not constant, the skilled person would know that the slope would have to be measured at its maximum value. However, three methods were known in the art to determine the maximum slope and, for purposes of the case, Dow's expert developed his own method. Each of these four methods may produce different slopes and thus different results.

Citing *Nautilus*, the court noted that although some modicum of uncertainty may be tolerated, *the patent and prosecution history must either* (1) disclose a single known approach; or (2) establish that, where multiple known approaches exist, a person having ordinary skill in the art would know which approach to select. The Federal Circuit thus framed the issue as "whether the existence of multiple methods leading to different results without guidance in the patent or the prosecution history as to which method should be used renders the claims indefinite." *Id.* at 634. In its earlier, pre-*Nautilus* decision, the court held that "the mere fact that the slope may be measured in more than one way does not make the claims of the patent invalid." 803 F.3d at 634. (*Dow*, 458 F. App'x at 920). However, under *Nautilus*[67], the court concluded that "this is no longer sufficient." 803 F.3d at 634. The court analogized this case with its remanded *Teva* decision (discussed above). Here, like *Teva*, there are multiple measurement methods that can produce different results, and the claims, specification, and prosecution history do not clearly identify which method should be used. Moreover, unlike *Teva*, Dow's expert developed his own measurement method rather than use one of three established methods. Accordingly, the court determined that "[t]he claims here are even more clearly indefinite than those in *Teva*." *Id.* at 635.

67 *Id.*

Certificate of Correction/Reissue

Although a Certificate of Correction cannot broaden a claim, the change of formula here from the L- to D-stereoisomer did not change the scope of the claim; rather it simply conformed the structural formula to the compound described in the specification and covered by the claims.

In *Cubist Pharm. Inc. v. Hospira, Inc.*, 805 F.3d 1112 (Fed. Cir. 2015), the court reviewed the validity of Cubist's claims directed to an antibiotic composition comprising a combination of (1) anhydrodaptomycin; (2) the beta isomer of daptomycin; and (3) daptomycin (Formula 3). The specification describes the Formula 3 compound in three ways: (1) an A-21978C cyclic peptide prepared from A-21978C antibiotics described in a specifically referenced patent; (2) by the code name LY146032, assigned to the compound by Lilly and known in the art to refer to daptomycin; and (3) by a particular chemical formula depicted in the application. However, the formula mistakenly identified the stereoisomer of the asparagine amino acid as the "L" stereoisomer rather than the "D" steroisomer. At the time the application was filed, and well after issuance, it was universally believed that the asparagine in daptomycin was the L-isomer.

Citing a journal article depicting the correct D-isomeric form, Cubist received a Certificate of Correction from the PTO. Hospira argued that the change was not "of minor character"[68] amenable to correction by Certificate of Correction under 35 U.S.C. § 255 because it broadened the scope of the asserted claims. On review, the court noted that "[o]nce the PTO has issued a certificate of correction, a court may invalidate the certificate only upon a showing of clear and convincing evidence that it was improperly issued." 805 F.3d at 1118. Here, the change in the diagram did not change the scope of the claim at all. Instead, the change simply conformed the structural diagram of Formula 3 to the compound described in the specification and covered by the claims. Noting that a chemical structure is not the invention itself but rather is simply a means of describing a compound, the court agreed with Cubist. In addition, "the Formula 3 compound is defined not only by the structural diagram, but also by other portions of the specification." *Id.*

Recapture rule prohibiting a patentee from regaining through reissue subject matter surrendered to obtain allowance of claims is not implicated where the applicants did not surrender subject matter to avoid prior art.

Relying on the proposition that a patentee may not regain through reissue the subject matter that he surrendered in an effort to

68 805 F.3d at 1117.

obtain allowance of the original claims, Hospira argued that the asserted claims of the reissued patent are impermissibly broader than the corresponding original claims. The recapture rule applies if (1) the reissue claims are broader than the original patent claims; and (2) the broader aspects of the reissued claims relate to subject matter that was surrendered in the prosecution of the original patent. Here, the court found that the applicants did not surrender subject matter in the prosecution of the patent to avoid prior art, noting that the applicants withdrew claim 24 from the application because of the indefiniteness rejection, not to avoid prior art. Accordingly, the recapture rule does not render claims 18 and 26 of the patent invalid.

Biologics Price Competition & Innovation Act

Failure of a Biologics Price Competition and Innovation Act of 2009 ("BPCIA") Applicant to give the Reference Product Sponsor ("RPS") its abbreviated Biologics License Application ("aBLA") within 20 days of the FDA's acceptance of the application does not violate the BPCIA but does give the RPS the right to file a declaratory judgment action.

In *Amgen Inc, v. Sandoz Inc.*, 794 F.3d 1347 (Fed. Cir. 2015), the court addressed an issue of first impression relating to the Biologics Price Competition and Innovation Act of 2009. Amgen, who was the reference product sponsor of the approved product, alleged that the BPCIA required an "information exchange process,"[69] during which Sandoz was required to give Amgen confidential access to Sandoz's Abbreviated Biologics License Application within 20 days after acceptance of the application under subsection (k) by the FDA. Sandoz responded that the "shall" provision of the statute is not an absolute requirement but rather only a "condition precedent to engaging in the information-exchange process,"[70] which gave Sandoz the option of foregoing the information-exchange process by refusing to give its aBLA to the RPS. This in turn gave the RPS the right to immediately sue and then obtain the information in the aBLA during the litigation discovery process.

On review, the court found that "read in isolation, the 'shall' provision . . . appears to mean that a subsection (k) applicant is required to disclose its aBLA and manufacturing information to the RPS by the deadline specified in the statute." *Id.* at 1355. However, the court further noted that "the BPCIA explicitly contemplates that a subsection (k) applicant might fail to disclose the required information by the statutory deadline" because it "specifically sets forth the consequence for such failure: the RPS may bring an infringement action." *Id.* "Those latter provisions indicate that 'shall' in paragraph (*l*)(2)(A) does not mean 'must.'" *Id.* The court therefore concluded that "filing a subsection (k) application and failing to disclose the required information under paragraph (*l*)(2)(A) is an artificial 'act of infringement' of 'a patent that could be identified.'" The remedy in such case is that "the RPS, but not the subsection (k) applicant, may bring a declaratory judgment action on 'any patent that claims the biological product or a use of the biological product.'" *Id.* However, because Sandoz took a path expressly contemplated by the BPCIA, its failure to disclose its aBLA and the manufacturing information by the statutory deadline was not a violation of the BPCIA.

The BPCIA permits an Applicant to give notice of commercial marketing only after the FDA licenses the product, not before.

Amgen also alleged that by giving notice of commercial marketing before approval of its biosimilar product, Sandoz violated the statute which permits a subsection (k) applicant to give notice of commercial marketing only after the FDA has licensed the biosimilar product. Amgen argued that Sandoz's premature notice denies the RPS time to seek a preliminary injunction and to resolve patent disputes in a timely fashion. Sandoz argued that the word "licensed" only means that, at the time of commercial marketing, the product must be licensed, but it does not limit the timing of the notice, which can be given before FDA licensure. Sandoz argued that Amgen's construction would result in an automatic, additional, six-month bar against marketing of every licensed biosimilar product, which improperly extends the twelve-year exclusivity period.

The court agreed with Amgen, that "notice, to be effective under this statute, must be given only after the product is licensed by the FDA." *Id.* at 1357. The court found that "[w]hile it is true that only a licensed product may be commercially marketed, it does not follow that whenever the future commercial marketing of a yet-to-be licensed product is discussed, it is the 'licensed' product. It is not yet 'the licensed product.'" *Id.* at 1357-58. The court noted that

> When a subsection (k) applicant files its aBLA, it likely does not know for certain when, or if, it will obtain FDA licensure . . . Giving notice after FDA licensure, once the scope of the approved license is known and the marketing of the proposed biosimilar product is imminent, allows the RPS to effectively determine whether, and on which patents, to seek a preliminary injunction from the court [and] ensures the existence of a fully crystallized controversy regarding the need for injunctive relief.[71]

69 794 F.3d at 1368.

70 *Id.* at 1355.

71 *Id.* at 1358.

A requirement in the BPCIA that an Applicant file its Notice of Commercial Marketing no later than 180 days before commercial marketing of the licensed product is mandatory, to permit the RPS sufficient time to assess and act upon its patent rights.

The court next considered the provision of the statute indicating that the subsection (k) applicant "shall provide"[72] notice of commercial marketing to the RPS no later than 180 days before commercial marketing of the licensed product. The court took the notice date as the one that occurred after the FDA approved Sandoz's aBLA, in view of discussion above. However, the court found that "[a] question exists . . . concerning whether the 'shall' provision . . . is mandatory"[73] and concluded that it is. Unlike the provision regarding providing an aBLA to the RPS, where the statute specifically contemplated what happens if an applicant fails to comply, no such provision for non-compliance exists for the 180-day notice requirement. The court found the purpose of the notice requirement to be clear–"to allow the RPS a period of time to assess and act upon its patent rights." *Id.* at 1360. Accordingly, "where, as here, a subsection (k) applicant completely fails to provide its aBLA and the required manufacturing information to the RPS by the statutory deadline, the [notice] requirement . . . is mandatory"[74] and Sandoz may not market its generic before passage of the 180 days from the notice.

Claim Construction & Infringement

"Buffering agent" properly construed per its ordinary meaning as an agent resisting pH changes and not as an agent resisting "material changes in pH," because more specific definition in specification is optional and addition of term during prosecution merely required its inclusion, and not a specific amount.

In *Cadence Pharm. Inc. v. Exela PharmSci Inc.*, 780 F.3d 1364 (Fed. Cir. 2015), the court construed Cadence's claim reciting a stable, liquid acetaminophen formulation dispersed in an aqueous medium containing *a buffering agent,* a free radical scavenger and/or a radical antagonist. The district court construed "buffering agent" to mean "[a]n agent that helps the formulation resist change in pH," and rejected Exela's proposed construction that the buffering agent be present "in an effective concentration to resist material changes in pH," because "nothing in the patent limits the scope of the claimed buffering agent to an 'effective concentration' or one that resists 'material changes in pH.'" *Id.* at 1369.

On review, the Federal Circuit agreed that the plain and ordinary meaning of "buffering agent" is "an agent that helps the formulation resist change in pH" and saw "nothing in the intrinsic record to warrant adding requirements of effective concentration or resistance to material change." *Id.* The court found the statement in the specification that the concentration of the buffer "may be" between 0.1 and 10 mg/ml to be "not limiting" because "even if 'all of the embodiments discussed in the patent' included a specific limitation, it would not be 'proper to import from the patent's written description limitations that are not found in the claims themselves'". *Id.* The court further found that amendment of the claim during prosecution to add the term "buffering agent" in response to a rejection "does not show that the phrase requires a minimum concentration or resistance to material change" but only that a buffering agent is necessary. *Id.*

Accused process deoxygenating solvent prior to addition of active ingredient is equivalent to claimed process deoxygenating solvent after addition of active ingredient because the timing of addition did not affect the product's stability, making the difference "insubstantial."

The district court construed the claimed step of "deoxygenation of the solution" as covering only solutions into which the active ingredient has already been dissolved. Because Exela's process first deoxygenates the solvent and only then adds an active ingredient, the district court found no literal infringement, but did find infringement under the doctrine of equivalents because "the timing of the addition of the active ingredient did not matter and ruled that the differences between the claimed steps and Exela's method were insubstantial." *Id.* at 1370. On review, the Federal Circuit found that the expert testimony that adding acetaminophen before or after the deoxygenation step would have no impact on the stability of the final product "supports the district court's finding that changing the timing of the deoxygenation step was an insubstantial difference" as confirmed by the fact that Exela's formulation is, in fact, stable. *Id.* at 1370-71.

Doctrine of claim "vitiation" is a legal conclusion of lack of equivalents and not an exception or threshold determination that forecloses resort to the doctrine of equivalents, such that argument that accused teaching is a vitiating "antithesis" of claim is nothing more than a conclusion, not an argument.

Exela argued that because deoxygenating after adding the active ingredient is the "antithesis" of deoxygenating before adding the active ingredient, a finding of equivalence would "'vitiate' the claim limitation." *Id.* at 1371. The Federal Circuit disagreed, concluding that "Exela fundamentally misunderstands the doctrine of claim vitiation" which "is not an exception or threshold determination that forecloses resort to the doctrine of equivalents, but is instead a legal conclusion of a lack of equivalence based on the

72 *Id.*

73 *Id.* at 1359.

74 *Id.* at 1360.

evidence presented and the theory of equivalence asserted." *Id.* Thus, Exela's "[c]haracterizing an element of an accused product as the 'antithesis' of a claimed element is . . . a conclusion that should not be used to overlook the factual analysis required to establish whether the differences between a claimed limitation and an accused structure or step are substantial *vel non*." *Id.* at 1372. Accordingly, "[s]ince a reasonable trier of fact could (and, in fact, did) conclude that Exela's process is insubstantially different from that recited in the claims, the argument that a claim limitation is vitiated by the district court's application of the doctrine of equivalents is both incorrect and inapt." *Id.*

No unmistakable disavowal of ordinary meaning such that claimed "optional" topping step is required, as specification teaches such step as advantageous, but not essential, and reference made to such step during prosecution was not to distinguish the prior art.

The court next construed the phrase "optionally topped with an inert gas … and placed in a closed container." *Id.* The court rejected Exela's argument that the steps are mandatory, concluding that "[t]he plain and ordinary meaning of 'optionally … topped … and placed' is that both the topping and placing steps are optional." *Id.* Further, in disclosing the "the four parameters that have to be taken into consideration as essential for preservation,"[75] the specification did not include stoppering and further provided examples exhibiting prolonged stability without stoppering. The specification's description of stoppering under vacuum as "a distinct advantage . . . cannot be read to imply that the invention is limited to such embodiments." *Id.* Nor was there "a clear and unmistakable disavowal of the unambiguous recitation of the vacuum stoppering step as being optional"[76] during prosecution. Although applicants cited the vacuum stoppering step "as a factor in providing a stable solution,"[77] during prosecution, "there is no clear indication that the vacuum stoppering step was the 'contrast' that applicants were trying to make over the cited reference,"[78] which relied on obtaining below 2 ppm oxygen in the solution. The court found that, "[a]t bottom, the language of [the claim] is unambiguous that the vacuum stoppering step is optional, and the prosecution history does not reflect a clear and unmistakable disavowal of the plain and ordinary meaning of that language." *Id.*

No literal infringement of claim requiring a quantity of drug sufficient to provide multiple doses of 2000 mg/dose by product provided in vials of 175 or 250 mg each.

In *Spectrum Pharm., Inc. v. Sandoz, Inc.*, 802 F.3d 1326 (Fed. Cir. 2015), the court reviewed the construction of the phrase "said composition being of a quantity at least sufficient to provide *multiple* doses of said mixture of (6S) and (6R) diastereoisomers *in an amount of 2000 mg per dose*." *Id.* at 1336. The district court held that Sandoz's ANDA product, in vials of 175 mg or 250 mg of levoleucovorin, would not meet the limitation of at least two doses of 2000 mg each, finding that the patent applicant had explicitly disclaimed smaller dosage amounts during prosecution. The court noted that the likely product to be sold following FDA approval is single-use vials with 175 mg or 250 mg of substantially pure levoleucovorin, indicated only for methotrexate rescue at doses between 7.5 mg and 75 mg per dose, which would be far less than at least two doses of 2000 mg each. Accordingly, there was no literal infringement.

Where applicant made amendments and statements to distinguish the prior art based on specific limitations as to the quantity of materials, applicant has made a clear and unmistakable surrender which estops it from asserting infringement under the doctrine of equivalents.

The court also held that Spectrum was estopped in view of its claim amendments and statements made to distinguish the prior art during prosecution, citing applicant's assertion that its "newly added claims 'include specific limitations as to quantities of materials,' and distinguished the prior art by pointing to the 'quantities of these specific mixtures specified in the claims.'" *Id.* at 1338. The court also cited Spectrum's reliance on the dosage limitation during an appeal to the Board by "stating that the claims 'require a minimum of four grams,' the 'quantity limitations set forth in the claims' which 'define an aspect of the invention that is of great practical significance.'" *Id.* The court found such statements to be "clear and unmistakable expressions of the applicants' intent to surrender coverage of quantities of the compound in lower doses." *Id.*

"At least one component" means "two or more," and the "totality of the specification" outweighs the district court's factual findings that formed the basis of its claim construction decision.

In *Enzo Biochem, Inc. v. Applera Corp.*, 780 F.3d 1149 (Fed. Cir. 2015), the court considered whether a chemical moiety "A" that represents "at least one component of a signaling moiety capable of producing a detectable signal"[79] means that "A" can be detected without an additional compound (i.e., direct detection), or requires another compound for detection (i.e., indirect detection).

The claim at issue recites an oligo- or polynucleotide containing a nucleotide having a nitrogenous base "B" is covalently attached to a chemical moiety "A," wherein

75 780 F.3d at 1372.

76 *Id.*

77 *Id.*

78 *Id.*

79 780 F.3d at 1154.

> A comprises at least three carbon atoms and represents ***at least one component*** of a signaling moiety capable of producing a detectable signal;
>
> B and A are covalently attached directly or through a linkage group that does not substantially interfere with the characteristic ability of the oligo- or polynucleotide to hybridize with a nucleic acid and does not substantially interfere ***with formation of the signalling moiety or detection of the detectable signal***.

Id. at 1157 (emphasis added).

The district court determined that "A" "is one or more parts of a signalling moiety, which includes, in some instances, the whole signalling moiety," and that a "signalling moiety" is "a chemical entity capable of producing a detectable signal." *Id.* at 1153. In other words, the district court concluded that "A" was capable of being directly detected. The Federal Circuit disagreed. First, the court determined that term "component" means a "multipart system" and thus the phrase "at least one component of a signalling moiety" means that "the signalling moiety is composed of multiple parts." *Id.* at 1154. Second, the court reasoned that since "A" is attached to a linkage group that "does not substantially interfere ***with formation of the signalling moiety***," "A" cannot be the whole signaling moiety. *Id.* The court reasoned that "if 'A' alone could be the signaling moiety," then "the requirement that 'A' not interfere with the formation of the signalling moiety would be read out of the claim, as the signalling moiety would be formed by the sole presence of 'A.'' *Id.* Accordingly, the court concluded that claims only cover indirect detection.

Even though it read an embodiment disclosed in the specification out of the claim, the court construes the entity "A" as not being a signalling moiety by itself, but rather requiring combination with another moiety to carry out signalling.

The court found support for its conclusion in the specification. The specification describes "A" as capable of forming a signalling moiety only in conjunction with other chemicals, and not that "A" alone can be a signalling moiety. In particular, the specification describes that "A" interacts with proteins, such as avidin or antibodies, to form a detectable unit. The court acknowledged that, based on expert testimony, Example 9 of the specification was an example of direct detection. But the Federal Circuit concluded that "this sole factual finding does not override our analysis of the totality of the specification, which clearly indicates that the purpose of this invention was directed towards indirect detection, not direct detection." *Id.* at 1156.

Judge Newman dissented on two principle grounds. First, citing *Howmedica Osteonics Corp. v. Wright Med. Tech., Inc.*, 540 F.3d 1337, 1344 (Fed. Cir. 2008), Judge Newman explained that the Federal Circuit had previously held that "at least one" means "one or more." As such, the majority erred in concluding that "*at least one* component" means a "mulitpart system," i.e., that "at least one" means "two or more." 780 F.3d at 1158. Second, citing expert testimony, the district court found that the specification includes an example of direct detection. The district court also highlighted concessions made by Applera's expert that "several parts of the original application disclosed compounds that allowed for direct detection." *Id.* at 1159. Accordingly, under *Teva*, Judge Newman argued that these factual findings are entitled to deference.

When a district court's claim construction decision does not involve factual findings, the Federal Circuit owes no deference under Teva.

In *Shire Dev., LLC v. Watson Pharm., Inc.*, 787 F.3d 1359 (Fed. Cir. 2015), on remand from the Supreme Court, the Federal Circuit again considered the district court's construction of phrase "lipophilic matrix" applying the standards enunciated by the Supreme Court in *Teva*. The Federal Circuit explained that, under *Teva*, it reviews a district court's claim construction *de* novo "[w]hen the district court reviews only evidence intrinsic to the patent (the patent claims and specifications, along with the patent's prosecution history)." *Teva Pharma*, 135 S. Ct. at 841. On the other hand, "if a district court resolves factual disputes over evidence extrinsic to the patent," then the court "review[s] for clear error those factual findings that underlie a district court's claim construction." *Id.* at 842.

Here, the district court construed "inner lipophilic matrix" as "a matrix including at least one lipophilic *excipient*." 787 F.3d at 1365 (emphasis added). The Federal Circuit disagreed, holding that, based on "the intrinsic evidence as a whole,"[80] the district court's construction was overly broad. First, looking at the claims, the term "lipophilic" modifies the "matrix" and thus the matrix–not just an excipient within the matrix–must exhibit the lipophilic characteristic. *Id.* Second, the specification describes a lipophilic matrix as one "in which the main component of the matrix structure" exhibits lipophilic properties. *Id.* The court also concluded that, based on the claims, specification, and prosecution history, the district court's construction of "lipophilic matrix" improperly permitted the inner and outer lipophilic matrices to be mixed in a single matrix. *Id.* at 1366. On remand from the Supreme Court, Shire argued that in view of the testimony the district court "heard" from various experts, the Federal Circuit should defer to the district court's claim construction. The Federal Circuit disagreed, concluding that "there is no indication that the district

80 787 F.3d at 1366.

court made any factual findings that underlie its constructions"[81] at issue in the appeal. Accordingly, like its prior decision, *Shire Dev., LLC v. Watson Pharm., Inc.*, 746 F.3d 1326 (Fed. Cir. 2014), the court reversed the district court's constructions.

Label for a gout-preventing drug directing a patient to contact their healthcare provider if they have an acute gout flare is too vague to inevitably lead a physician to prescribe the drug for an acute flare, and thus induce infringement, especially in view of alternative treatments.

In *Takeda Pharm. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625 (Fed. Cir. 2015), the court reviewed whether Hikma's sales of its drug Mitigare (colchicine) with the label "indicated for prophylaxis"[82] of gout induced infringement of Takeda's patent claiming use of the same drug to treat acute gout. Takeda argued that Hikma's label induced infringement because, in the case of the patient taking Mitigare for prophylaxis, the physician would likely tell the patient to use the Mitigare product to treat the acute flare.

On review, the court noted that for inducement to lie here, "[t]he label must encourage, recommend, or promote infringement." *Id.* at 631. The court further noted that "[t]his requirement of inducing acts is particularly important in the Hatch-Waxman Act context because the statute was designed to enable the sale of drugs for non-patented uses even though this would result in some off-label infringing uses." *Id.* Takeda conceded "that mere knowledge of off-label infringing uses of Mitigare's product would not establish inducement." *Id.* at 632. However, Takeda argued that Hikma's label, though indicated only for prophylaxis of gout, induces infringement by stating that "[i]f you have a gout flare while taking Mitigare, tell your healthcare provider," which "will 'inevitably' lead to physicians who are consulted to advise patients taking Mitigare for prophylaxis to simply increase their dose of Mitigare to treat acute gout flares." *Id.* The court disagreed, holding that "vague label language cannot be combined with speculation about how physicians may act to find inducement" because this "would seem to too easily transform . . . mere knowledge of infringing uses . . . into induced infringement." *Id.* The court also noted that "there are a host of alternatives for treating gout flares" and "Takeda points to no record evidence that physicians would forego these alternatives and simply increase the dose of Mitigare when it failed to work as a prophylactic." *Id.* at 633.

The court also rejected Takeda's argument that "where the physician prescribes colchicine for an acute gout flare, it would be 'impractical' for a patient already taking colchicine for prophylaxis not to 'reach for the colchicine they have on hand' and follow Takeda's patented methods" because it is "'common sense' that doctors would prescribe Mitigare for an infringing use because it is already available on the shelf of the patient taking it for prophylaxis," noting that it had already rejected that argument in *Warner Lambert.*[83] The court held that "[s]peculation or even proof that some, or even many, doctors would prescribe Mitigare for acute flares is hardly evidence of inevitability. This evidence does not show anything more than that there may be some infringing uses of Mitigare." 785 F.3d at 642.

No inducement to infringe a patent requiring a 0.3 mg dose of drug where the drug is sold in 0.6 mg capsules, where the dosage cannot feasibly be split and where reductions would likely be from twice daily to once daily, and not to once every other day.

As for Takeda's patents requiring a 0.3 mg dose of colchicine, the district court found that Mitigare would not likely be used to directly infringe because it comes in 0.6 mg capsules that cannot feasibly be split to reach a 0.3 mg dose of colchicine per day. Takeda argued that the capsules can be taken every other day to reach an average of 0.3 mg per day, citing in particular the language in Mitigare's label that warned patients to either reduce the daily dose or reduce the dose frequency if concomitant administration is necessary. The Federal Circuit, however, agreed with the district court that, given colchicine's "narrow therapeutic index"[84] whereby the margin between an effective dose and a toxic dose is narrow, this possibility was not likely. In any case, the court agreed with West-Ward that, given that Mitigare's label recites a 0.6 mg "once or twice daily" recommendation and a "maximum dose" recommendation, it is natural to read "reducing the dose frequency" as just instructing reducing 0.6 mg from twice daily to once daily and not to achieve the 0.3 mg dose by administering 0.6 mg every other day. 785 F.3d at 635.

Hatch-Waxman Cases

A party who sells an API covered by Orange Book-listed patents to ANDA filers cannot induce infringement because both the sales and the ANDA filers' use of the API for filing an ANDA are "reasonably related to the submission of an ANDA" and thus protected by the safe harbor.

In *Shire LLC v. Amneal Pharm., LLC,* 802 F.3d 1301 (Fed. Cir. 2015), the court reviewed whether the defendant induced infringement of Shire's claims directed to methods of using a mesylate salt of an L-lysine-d-amphetamine ("LDX") to treat attention deficit hyperactivity disorder ("ADHD"); and (2) the mesylate salts of LDX and crystalline forms thereof. Defendant did not itself make an ANDA filing as did other parties to the case.

81 *Id.* at 1368.

82 785 F.3d at 630.

83 *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348 (Fed. Cir. 2003)

84 785 F.3d at 635.

Rather, defendant's only involvement arose from its actions in supplying the ANDA filers with the active pharmaceutical ingredient LDX dimesylate.

The district court entered judgment that defendant "has induced infringement of the compound claims at issue"[85] by providing the LDX dimesylate used by the ANDA filers in their generic products. On appeal, defendant argued that providing the ANDA filers with the active ingredient so they could submit their ANDAs was "reasonably related to the submission of information under a federal law and was therefore within the safe harbor of § 271(e)(1)." *Id.* at 1310. Further, since it did not itself submit an ANDA, defendant argued "that it cannot be liable under § 271(e)(2) for its past actions and therefore the district court was wrong to enter judgment against it." *Id.* Finally, defendant asserted "that because no direct infringement has yet to occur, it cannot be liable for induced infringement under § 271(b)." *Id.*

On review, the Federal Circuit agreed that defendant "cannot be liable for the API it sold the ANDA defendants up to this point" because, "as an API supplier, [defendant] has thus far done nothing more than provide material for use by the ANDA defendants in obtaining FDA approval." *Id.* "[T]hese sales, and the ANDA defendants' use of the API for filing the ANDA, were 'reasonably related to the submission of an ANDA.'" *Id.* "As such, [defendant's] activities are protected by the safe harbor of § 271(e)(1), and the district court erred by entering judgment that [defendant] has induced infringement of the compound claims at issue." *Id.* "Moreover, as [defendant] did not submit an ANDA, it cannot be liable for infringement under § 271(e)(2)." *Id.*

Safe harbor is not limited to pre-approval activities, but includes studies necessary to support a supplemental new drug application seeking approval to revise a product label which are not routine post-approval reporting.

In *Classen Immunotherapies, Inc. v. Elan Pharm., Inc.*, 786 F.3d 892 (Fed. Cir. 2015), Classen alleged that Elan's conducting of a clinical study on the bioavailability of Skelaxin and its submission of the results to the FDA to revise the Skelaxin product label were not exempt under the safe harbor of § 271(e) because those activities are merely routine post-approval reporting to the FDA.

The court noted that "the statute [does not] limit the safe harbor only to those activities necessary for seeking approval of a generic version of a brand-name drug product," but can also include post-approval scientific studies where drug manufacturers voluntarily conduct "scientific studies and clinical trials to support 'supplemental' new drug applications ("sNDAs"), seeking the FDA's approval to revise the label of their products." 786 F.3d at 897. "Such post-approval studies serve similar purposes as pre-approval studies in ensuring the safety and efficacy of approved drugs" and, "[a]s an integral part of the regulatory approval process, those activities are 'reasonably related to the development and submission of information' under the [safe harbor] and are therefore exempt from infringement liability." *Id.* Here, "Elan initiated its own clinical trial to characterize the effect of food on the absorption of Skelaxin and observed a significant increase in bioavailability when Skelaxin was administered with food." *Id.* Because submission of such information was necessary to revise the Skelaxin product label "[t]hose activities were anything but 'routine' post-approval reporting." *Id.* The court therefore concluded that "[t]he district court . . . did not err in holding that Elan's clinical activities and FDA submissions are exempt from infringement under the safe harbor provision." *Id.*

Information obtained from activities protected by the safe harbor can be used for purposes other than regulatory approval, such as patent filings and label changes, provided that the subsequent disclosure or use is not itself an infringement.

The court also rejected Classen's argument that Elan's subsequent actions of reanalyzing the clinical data to identify patentable information and filing patent applications are commercial activities outside the scope of the safe harbor, noting that "the subsequent disclosure or use of *information* obtained from an exempt clinical study, even for purposes other than regulatory approval, does not repeal that exemption of the clinical study, provided that the subsequent disclosure or use is itself not an *act of infringement* of the asserted claims." Citing its earlier holding in *Telectronics*,[86] the court noted that when enacting § 271(e)(1), "Congress did not intend to prevent competitors 'from using, in an admittedly non-infringing manner, the derived test data for fund raising and other business purposes.'" 786 F.3d at 898. However, because the district court did not determine whether those post-submission activities constituted infringement of the patent or whether they were exempt under the safe harbor, the court vacated the judgment of noninfringement and remanded the case to the district court for further proceedings. As guidance on remand, the court noted that "[f]iling a patent application is generally not an infringement of a patent. It is not the making, using, offering to sell, selling, or importing of an invention." *Id.* Similarly, "placing the *information* submitted to the FDA on the product label after sNDA approval generally cannot be an infringement" because "[i]nformation obtained from exempt activities does not cease to be exempt once the sNDA is approved. It is a requirement of law that a drug product contains the labeling approved by the FDA." *Id.* at 899.

A party who carried out a patented quality control method outside the U.S. and then sold the resulting product in the U.S. is not an infringer under § 271(g), which is

85 802 F.3d at 1310.

86 *Telectronics Pacing Sys., Inc. v. Ventritex, Inc.*, 982 F.2d 1520 (Fed. Cir. 1992).

limited to products "made" outside the U.S., which means manufactured, not tested.

In *Momenta Pharm., Inc. v. Teva Pharm. USA Inc.*, 809 F.3d 610 (Fed. Cir. 2015), the court reviewed (1) whether Momenta's patent directed to a process to ensure that generic enoxaparin meets certain quality standards was infringed under Section 271(g) by Teva's use of the process overseas to test products ultimately imported into the U.S.; and (2) whether use of the quality control process in the U.S. was exempt from infringement as a use reasonably related to the FDA approval process under Section 271(e)(1). In a prior appeal by Amphastar at the preliminary injunction phase, the Federal Circuit held that it was unlikely that Momenta will succeed on the merits of its infringement claim and, on remand, the district court found that Amphastar's activities are protected by the safe harbor of § 271(e)(1).

Momenta argued that "made" means "manufactured," and that its patented method is a crucial interim step used directly in the manufacture of Teva's products because Teva used the patented method to select and separate batches of intermediate drug substance that conform to regulatory requirements for enoxaparin from batches that do not and then further processed only those selected batches for ultimate sale. 809 F.3d at 615. Momenta also pointed out that the FDA's Good Manufacturing Practice regulations define "manufacture" and "processing" of drug products as including testing and quality control of drug products. *Id.* On review, the court found that the "ordinary meaning" of "made" as used in § 271(g) means "manufacture" and extends to the creation or transformation of a product but not to testing to determine whether an already-synthesized drug substance possesses existing qualities or properties. *Id.* at 616. The court thus held that

> [I]t is more consonant with the language of the statute, as well as with this court's precedent, to limit § 271(g) to the actual "ma[king]" of a product, rather than extend its reach to methods of testing a final product or intermediate substance to ensure that the intended product or substance has in fact been made.[87]

Information routinely reported to the FDA after marketing approval has been obtained, such as routine record retention requirements associated with testing and other aspects of the commercial production process, are outside the scope of the safe harbor.

The court next addressed whether Amphastar's use of the testing method in the U.S. fell under the safe harbor of §271(e)(1). Despite the "broad contours of the exemption," the court noted that "some activities are outside its protection," such as "information that may be routinely reported to the FDA, long after marketing approval has been obtained" or "research tools or devices that are not themselves subject to FDA approval." 809 F.3d at 619 Although the court had concluded that Amphastar's activities were not routine in its initial review, and therefore subject to the safe harbor, the panel here (including two of the judges from the initial panel) reversed course and noted that "it is not improper for a court to depart from a prior holding if convinced that it is clearly erroneous and would work a manifest injustice,"[88] citing *Arizona v. California*, 460 U.S. 605, 618 n.8 (1983). "With the benefit of additional briefing in the current appeals, which reflects the full district court record developed by all parties after the preliminary injunction phase, we conclude Amphastar's submissions are appropriately characterized as 'routine.'" 809 F.3d at 620. The court contrasted Amphastar's "routine record retention requirements associated with testing and other aspects of the commercial production process" with "non-routine submissions that may occur both pre- and post-approval, such as the submission of investigational new drug applications ('INDs'), new drug applications ('NDAs'), supplemental NDAs, or other post-approval research results." *Id.*

In the 2012 Year In Review, we criticized the holding in *Momenta I*, stating that "[i]t is rather hard to understand how this court underwent the metamorphoses from a 'submission' reasonably related to approval of a drug to unsubmitted records prepared after such drug is approved in its apparent politically motivated zeal to expand the safe harbor." The present holding makes much more sense. Going forward, therefore, while it is clear that a commercial focus will not disqualify a party from reliance on the safe harbor pre-approval, the court will view such a commercial focus with disfavor if it occurs post-approval.

Patent Owner's statutory disclaimer of its Orange Book–listed patent does not prevent a second ANDA filer from seeking a declaratory judgment of non-infringement because such holding would permit the second ANDA filer to obtain earlier FDA approval and earlier marketing of product.

In *Apotex, Inc. v. Daiichi Sankyo, Inc.*, 781 F.3d 1356 (Fed. Cir. 2015), Apotex sought a declaratory judgment that it will not infringe a patent owned but disclaimed by Daiichi if Apotex manufactures or sells a generic drug bioequivalent to Daiichi's Benicar®. Although Apotex cannot infringe the claim in view of Daiichi's disclaimer, Apotex sought the declaratory judgment of non-infringement to receive FDA marketing approval and enter the market sooner than otherwise, as a consequence of Mylan's 180-day exclusivity period as the first generic ANDA filer. The district court dismissed Apotex's complaint for lack of a case or controversy.

On review, the Federal Circuit reversed, finding that "[t]he stakes over which the parties are vigorously fighting are concrete and

87 809 F.3d at 615.

88 809 F.3d at 620.

substantial: the amount of revenue there will be from sales of olmesartan medoxomil, and who will get what portions of it, during a period of at least six months." *Id.* at 1362. The court rejected Daiichi's contention that Daiichi's statutory disclaimer itself means that there is no adversity between it and Apotex over stakes of a concrete character, finding that "[t]he concrete stakes over which Daiichi and Apotex are fighting are the revenues to be earned through selling olmesartan medoxomil." *Id.* In particular, "[t]he patent disclaimer eliminates one, but only one, potential legal barrier to Apotex's ability to make such sales sooner rather than later." *Id.* The other is the listing of the patent in the Orange Book, which has the "consequence of preventing FDA approval during Mylan's presumptive exclusivity period . . . and the parties have adverse concrete interests in the truncation or preservation of that period" because "[u]ntil that period ends, Apotex cannot make sales, and delay of entry may have lingering adverse effects on market share." *Id.* "In these circumstances, by any common-sense measure, the parties have substantial, concrete stakes in whether Apotex secures the non-infringement judgment it seeks to advance its entry into the market." *Id.* at 1363.

Apotex's delayed market entry is traceable to the Patent Owner because it was the Patent Owner who listed its patent in the Orange Book; furthermore, tentative approval by the FDA is not a prerequisite for a case or controversy as such requirement is not found in the statute authorizing ANDA litigation.

The court also rejected Daiichi's argument that the delayed entry of Apotex at issue here is not "fairly traceable" to Daiichi, finding that "[i]f Daiichi had not listed the . . . patent in the Orange Book in the first place, . . . Mylan undisputedly would have no exclusivity period at present." *Id.* "Daiichi is therefore responsible for the current existence of Mylan's exclusivity-period rights." *Id. at 1364.* The court next rejected Daiichi's argument that tentative FDA approval for Apotex's proposed drug is a prerequisite for a case or controversy here, noting that "the statute authorizing the litigation upon filing of an ANDA nowhere requires tentative FDA approval as a precondition: the filing of the ANDA, with a paragraph IV certification, is itself deemed an act of infringement." *Id.* at 1366. Further, "[i]n all of our cases involving litigation over ANDA applications, we have never required tentative approval, including in suits brought almost immediately after the ANDA's filing." Accordingly, because "tentative approval of an ANDA is generally not a precondition to the existence of a case or controversy concerning patents listed in the Orange Book," "we conclude that tentative approval is not required for the present dispute to constitute a case or controversy unless there is an additional context-specific reason tied to statutory provisions that distinguishes this situation from those in which we have deemed tentative approval unnecessary to satisfy Article III." *Id.*

Because a successful declaration of non-infringement by Apotex would trigger forfeiture of the Mylan's exclusivity period as the first ANDA filer, a sufficient case or controversy exists to support a declaratory judgment action.

The court finally addressed Daiichi and Mylan's objection to justiciability based on the specific statutory provisions governing forfeiture of the exclusivity period. The court noted that Mylan currently has an exclusivity period available to it, based on the original listing of the now-disclaimed patent and Mylan's continued maintenance of its paragraph IV certification regarding that patent. It is also undisputed that the only basis asserted for Apotex to enter earlier than the end of the exclusivity period is a forfeiture of the period triggered by a "forfeiture event." *Id.* at 1367. The court concluded that "Apotex can trigger forfeiture by obtaining the non-infringement judgment it seeks in this case and, thus, that a case or controversy exists here." *Id.* The court found that "[t]here are two requirements for forfeiture: a court must have entered a final decision of non-infringement that is no longer appealable (certiorari aside), and the second (or later) filer must have received tentative approval." *Id.* at 1369. "Under that reading, Apotex can trigger forfeiture in this case by obtaining the judgment it seeks here and by obtaining tentative approval, if it does both early enough in relation to Mylan's market entry." *Id.*

Conclusion

So what's in store for 2016?

On the life science side, the big question will be whether the Supreme Court will grant *cert.* in *Ariosa v. Sequenom*. The stakes are enormous, as the current thinking at the Federal Circuit makes it hard to see how any diagnostic method will be eligible given that they overwhelmingly use conventional techniques to implement, the novelty being the discovery of a correlation or the existence of a molecule no one knew about. If the Supreme Court does not grant review, then the next question is what other types of inventions will fall victim to an expansive reading of both *Myriad* and *Mayo*. Some examiners are already taking an ever expanding viewpoint of these cases.

The other question is whether the court will continue to serve as a rubber stamp to IPRs. At least on the life science side, we have two panel decisions which are irreconcilable in their approach, one being overwhelmingly deferential and the other being much more scrutinizing. Perhaps we will get a better sense of the direction the court will be taking in 2016.

It will also be interesting to see the results of the *en banc* review on the issue of supplier's exceptions, though in this case the court could simply decide the issue by finding no sale regardless of the supplier issue.

Finally, while it would be good to be wrong on this one, the court is probably getting locked in on its new paradigm where it has interjected criticality issues into an anticipation analysis.

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Rob Schulman is a partner in Arent Fox's Intellectual Property practice group where he focuses on all phases of patent law in the areas of biotechnology, pharmaceuticals, and chemical inventions. His major focus is in the area of contested cases at the Patent Office, including interferences, reexaminations (both ex parte and inter partes), as well as inter partes reviews for all types of inventions. Rob also frequently provides advice on validity, non-infringement and claim construction issues in litigation. He has extensive experience in the area of clearance studies for both established and start-up companies.

Rob's practice includes development of patent portfolios, patent prosecution including application drafting, prosecution of applications and appellate review. Rob has also helped companies establish best practices for patent application writing and claim drafting. Rob has had a special focus in recombinant plant technology, general agricultural technology, vaccines, drug delivery technology, medical devices and polymers.

He regularly speaks at bar association meetings and in front of clients on case law developments in the biotech, chemical and pharmaceutical areas and has been publishing an annual Year in Review relating to such case developments since 2003.

Rob is registered with the US Patent and Trademark Office and is a member of the Court of Appeals for the Federal Circuit and Federal Circuit Inn of Courts. Rob has taught Interference Practice at Georgetown University Law School since 1992.

Client Work

- Responsible for compilation of patent case database of Federal Circuit and Board of Appeals and Interferences decisions starting in 1982.
- Successfully developed intellectual property portfolios for both pharmaceutical and biotech companies from inception to product launch and sale of company.
- Conducted numerous due diligence patent reviews, including validity, infringement, and right-to-use studies.
- Engaged by numerous companies to train their counsel in best practices for drafting claims and conducting prosecution and interferences.
- Successfully represented companies in using interferences to invalidate competitor's patents in all technologies but with special focus on biotech, plants, medical devices, and pharmaceuticals.
- Successfully represented both junior and senior parties in biotech, chemical, mechanical, and electrical interferences.
- Successfully represented parties in federal court appeals of interferences decisions.

Practices

Intellectual Property
Life Sciences

Bar and Court Admissions

District of Columbia Bar
US Patent and Trademark Office

Education

American University,
Washington College of Law, JD

Rutgers University, BS

- Successfully worked with trial lawyers in major biotech and pharmaceutical district court litigation.
- Representing Substantial number of domestic and foreign chemical, pharmaceutical, and biotech companies in the areas of plan biotechnology, vaccines, drug delivery, DNA screening methods, receptor binding, computer DNA analysis, gas processing, and polymers.
- Obtained numerous commercially significant patents which have been successfully enforced in judicial proceedings. Hatch-Waxman experience for patent term extension and immunity from infringement during FDA approval process.

Memberships

- Member, American Intellectual Property Association
- Member, American Bar Association
- Member, Intellectual Property Owner's Association
- Member, Biotechnology Industrial Organization
- Member, Federal Circuit Inn of Courts

Publications

- Author, "Is Obviousness The New Anticipation?," *Law360*, October 2, 2012
- Co-author, "Pharmaceutical, Chemical and Biotech Year in Review," 2007-2012
- Author, "Pharmaceutical, Chemical and Biotech Year in Review," 2003-2006
- Co-author, "Researchers Beware; Use Of Your Competitor's Patented Inventions In Your Research Is Probably Not Exempt From Infringement, Even Where Such Research Ultimately Generates Data for FDA Submission," *Intellectual Property Today*, March 1, 2004

Events

- Speaker, "Is Obviousness Becoming the New Anticipation?" The Federal Circuit's New Paradigm in Reviewing Prior Art, New Jersey Intellectual Property Law Association, December 5, 2012
- Speaker, "Subject-Matter Eligibility In The Wake of *Mayo v. Prometheus*," April 2012
- Speaker, "Highlights of the America Invents Act," Conference in Montpellier, France, October 2012
- Presenter, "Developments in Biotechnology, Chemical and Pharmaceutical IP Law," March 8, 2012
- Speaker, "Legislative and Judicial Developments Affecting Patenting of Biotech Inventions in the United States," DeClerq & Partners IP Seminar, Belgium, November 18, 2011
- Speaker, "Updates on Case Law Relating to Pharmaceutical Inventions," New Jersey Intellectual Property Law Association, November 1, 2010
- Speaker, "Federal Circuit Cases Relating to Patent Interferences," Intellectual Property Owners Meeting, Washington, DC, November 1, 2008

Awards & Recognition

- *Washington DC Super Lawyers* (Intellectual Property), 2013
- Selected for inclusion as a "Best Lawyer," Intellectual Property, *The Best Lawyers in America*, 2010-2013
- Listed as one of top intellectual property attorneys in 2010 in *Virginia Business* magazine
- Listed as one of 20 top intellectual property attorneys in *Washington Post* survey, 2010 and 2011
- Listed as one of 25 top intellectual property and technology attorneys in the December 2000 issue of *Virginia Business* magazine

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Alex Spiegler is a registered patent attorney whose practice focuses on all aspects of patent law. He has extensive experience with the US Patent & Trademark Office, specializing in patent prosecution and post-grant proceedings (e.g., *inter partes reviews*), in a wide variety of technologies, including biotechnology, agricultural technology, and pharmaceuticals. Alex also frequently provides advice on claim construction, infringement and validity issues in litigation.

Client Work

Recent matters include:

- Prepare and prosecute patent applications in the biotechnology, agricultural, pharmaceutical, and chemical arts, including inventions related to plants, herbicides, fertilizers, seeds, nucleic acids, proteins, enzymes, carbohydrates, diagnostics, bacteriophages, pharmaceuticals, methods of treatment, and methods of diagnosis and detection.
- Conduct due diligence, freedom-to-operate, validity and patentability analyses in the biotechnology, agricultural and pharmaceutical arts, and prepare formal legal opinions reflecting conclusions of such analyses. Recently served as IP opinion counsel to pharmaceutical company in IPO.
- Represent agricultural company in inter partes review involving herbicidal compositions.
- Represented lawn care company in litigation and patent office proceedings. Successfully obtained summary judgment on competitor's trade secret claim. Obtained favorable Markman ruling against competitors' patents, leading to dismissal of the patent infringement suit. Successfully provoked inter partes reviews and reexaminations against competitors' patents, and obtained decisions that competitors' patents are unpatentable.
- Represented inventor against reexamination of patent directed to methods for treating achondroplasia. Reexamination Certificate confirmed patentability of all original claims.
- Represented agricultural biotechnology company against reexamination of patent directed to methods of treating genetically modified plant with an herbicide. Reexamination Certificate issued with claims covering commercially important subject matter.
- Represented life sciences company with patents covering DNA sequencing technology. Obtained favorable Markman ruling.
- Represented life sciences company in patent office proceedings (interferences and reexaminations) relating to nucleic acid technology (e.g., sequencing, amplification).

Practices

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Bar and Court Admissions

District of Columbia
New York
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US Patent and Trademark Office

Education

Columbus School of Law at The Catholic University of America, JD

Rutgers University, BS (Biotechnology)

- Represented pharmaceutical company in a Hatch-Waxman litigation brought against it by owner of patents covering leading attention hyperactivity disorder drug.
- Prepared Paragraph IV Certification letters.
- Prepared successful third party submissions relating to agricultural technology.

Previous Work

Alex was an associate at an international law firm prior to joining Arent Fox. From 2000 to 2004, he was a Biotechnology Patent Examiner at the US Patent and Trademark Office.

Publications & Presentations

Recent publications:

- Co-author, Thinking Twice About "Comprising," AIPLA's *Biotech Buzz*, June 2015
- Co-author, *Inter Partes* Review Year in Review, 2014
- Co-author, Pharmaceutical, Chemical and Biotech Year in Review, 2014
- Co-author, Pharmaceutical, Chemical and Biotech Year in Review, 2013
- Co-author, "Patent Reform Stalled by Tech and Pharma/ Biotech Debate," Daily Business Review (2010)
- Co-author, "Recent Trends in Patent Practice: The Federal Circuit's Treatment of Pharmaceuticals," BNA Life Sciences Law & Industry (2007)

Recent presentations:

- "Intellectual Property in the United States," organized by Biomeridies and StartingBloch, Nimes, France (2015)
- "Subject Matter Eligibility of Biotech and Pharmaceutical Inventions," organized by Biomeridies and StartingBloch, Clapiers, France (2015)
- "Recent Developments in the Patent Office and Courts Affecting Life Sciences and Computer Patents in the United States," Flanders Institute for Biotechnology U.S. Patent Seminar, Gent, Belgium (2014)
- "Developments in Biotechnology, Chemical and Pharmaceutical Law," CLE Seminar, New York, NY (2012)
- "Legislative and Judicial Developments Affecting Patenting of Biotech Inventions in the United States," DeClerq & Partners IP Seminar, Sint-Martens-Latem, Belgium (2011)

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