

Recent Pharmaceutical Patent Decisions in the United States

Andreas Baltatzis† and Shoshana Marvin

Kramer & Amado, P.C. 330 John Carlyle Street, Third Floor, Alexandria VA 22314, USA

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There has been a renewed interest of the Supreme Court of the United States in patent law, particularly with regard to pharma related patents. The overall trend in US patent law is the continued tension between the Court of Appeals for the Federal Circuit (the Federal Circuit), the patent specialty court in the United States which favours broad patent rights, and the Supreme Court of the United States, which uses its supervisory authority to reign in the strong patent rights advocated by the lower court. In this paper, recent important decisions with regard to pharmaceutical patents that highlight the Supreme Court's oversight of the Federal Circuit's patent decisions are reviewed. A survey of recent decisions that exemplify the Federal Circuit's broad view of patent rights, by expanding patent-holders' rights whether affirming or reversing District Court decisions that found patents invalid or unenforceable is also covered in the paper. These decisions may face appeal at the Supreme Court and result in similar reversal.

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The US patent system is in a state of flux due to the interplay between the Federal Circuit and the US Supreme Court. The Federal Circuit hears and decides patent cases frequently. Their decisions tend to read patent holders' rights expansively. By contrast, the US Supreme Court, whose opinions are binding authority over the Federal Circuit, hears patent cases rarely. However, when they do, the decisions tend to restrict patent holders' rights. As a result, this conflict between broad and limited patent rights has wide ranging implications for patent practitioners.

The following cases provide an overview in which the Supreme Court overruled Federal Circuit decisions, and cases in which the Federal Circuit broadened patent holders' rights by either reversing obviousness or invalidity findings of lower courts, or confirming District Courts' findings of non obviousness or validity.

Supreme Court Decisions

Mayo Collaborative Services v Prometheus Laboratories Inc

The landmark case of *Mayo v Prometheus*¹ applied the rapidly evolving law on 'business-method' patents enunciated in the *Bilski* case to the medical context, specifically to patents directed to diagnostic methods and tests. The scope of patentable subject matter has been a long-evolving area of US patent law. Patent eligibility can be important to patent holders, as they

determine the scope of their rights, as well as to industry practitioners faced with allegations of infringement. Therefore, application of 35 USC § 101 (ref.2) to the pharmaceutical context will have far-reaching effects.

The patent³ at issue claims methods of administering a thiopurine drug and determining the levels of a particular metabolite that indicates if the drug dose should be increased or decreased. The Supreme Court found that the claims set forth a law of nature, namely the relationship between thiopurine dose and metabolites. No human action, aside from the step of administering the drug, is needed for the relationship to exist between the drug and its metabolites. Since a law of nature itself is not patentable, the Court explained that merely applying such a law would not meet the requirement of patentable subject matter.

Patents cannot be used to cover the discovery of laws of nature because granting such a patent would 'inhibit future innovation' that is based on those laws. Although the laws of nature applied in this case are narrow, the claims would impermissibly encompass a broad scope of treatment. In particular, the claims would 'tie up' a doctor's treatment decision regardless of whether the doctor made any change in dose amount based on the test results. The broad language of 'determining' the metabolite level would cover all processes, including those that measure metabolites in

†Corresponding author: Email: abaltatzis@krameramado.com

other ways and correlate the measurements to other treatments.

Unlike a patent for a new drug or a new method of administering an existing drug, which are confined to a particular application of a natural law, the *Prometheus* claims are not limited to a particular application. The Court reasoned that the step correlating the metabolite level to treatment alteration does not necessarily implicate a transformation of the drug ‘should science develop a totally different system for determining metabolite levels.’ The Court also emphasized that the ‘machine or transformation’ test for patent eligibility is ‘an important and useful clue,’ but does not supersede the exclusion of mere applications of laws of nature from the realm of patent-eligible subject matter. Since the claims are effectively underlying laws of nature themselves, the Court held them to be invalid, thereby overruling the decision of the patent specialist court, the Court of Appeals of the Federal Circuit.

Claims that do no more than explain why a physiological phenomenon works may be subject to a *Prometheus* attack. Claims that encompass the pre-existing administration of a drug and merely correlate that administration to a pharmaceutical property should be examined for their satisfaction of the patent eligibility standard. An understanding of *Prometheus* and the basic concepts of patent eligibility can be a valuable tool for practitioners and their counsel to both strengthen their patent assets, and effectively challenge patents that do not appreciably expand on natural laws in the public domain.

Caraco Pharmaceutical Laboratories Ltd v Novo Nordisk A/S

*Caraco v Novo Nordisk*⁴ relates to the administration of the United States generic drug regime, i.e. the Hatch-Waxman Act⁵, and is of great interest to any company seeking to market a generic pharmaceutical in the United States.

The drug at issue in *Caraco* was Prandin (repaglinide), which was FDA approved for three uses to treat diabetes: repaglinide by itself; repaglinide in combination with metformin; and repaglinide in combination with thiazolidinediones (TZDs). The Court stated that the ‘358 patent was acquired by Novo ‘for one of the three FDA-approved uses of repaglinide—its use with metformin. But Novo holds no patent for the use of repaglinide with TZDs or its use alone.’ Instead the FDA listed the patent as associated with the ‘use of repaglinide in combination with metformin to lower blood glucose.’⁶ This use

was associated with a specific ‘use code’ designated by the FDA.

Under the Hatch-Waxman Act, a generic company must certify that an FDA-listed patent is invalid or not infringed. Alternatively, the generic company may submit a statement that it is not seeking approval to market the product for one or more patented methods of use covering the listed drug. This is commonly known as a ‘little viii’ statement after the subparagraph of the relevant statute. Caraco filed proposed labeling with the FDA, thereby carving out the patented repaglinide-metformin combination therapy. However, Novo then changed its use code for the ‘358 patent. Accordingly, Caraco was informed that they could no longer employ a section viii carve out. The FDA allows ‘section viii carve-outs’ only if a patent use or exclusivity code is listed in the FDA Orange Book under 21 USC. 505(j)(5)(F), also, 21 CFR § 314.94(a)(8)(iv)). Caraco filed a counterclaim seeking an order ‘requiring Novo to ‘correct’ its use code ‘on the ground that [the ‘358] patent does not claim’ two approved methods of using repaglinide—alone and in combination with TZDs.’

Therefore, the question at issue was whether Congress had authorized a generic company to challenge a use code’s accuracy by bringing a counterclaim against the brand manufacturer in a patent infringement suit. The relevant statute provides that a generic company ‘may assert a counterclaim seeking an order requiring the [brand manufacturer] to correct or delete the patent information [it] submitted ... under [two statutory subsections] on the ground that the patent does not claim ... an approved method of using the drug.’

The District Court enjoined Novo to correct the inaccurate description of the ‘358 patent. However, the Court of Appeals for the Federal Circuit reversed the holding that Caraco ‘lacked ‘a statutory basis to assert a counterclaim.’ The court interpreted the statutory phrase ‘the patent does not claim ... an approved method of using the drug,’ to require Caraco to ‘demonstrate that the ‘358 patent does not claim any approved method of use, and further held that the ‘counterclaim provision does not reach use codes because they are not ‘patent information submitted by the [brand] under subsection (b) or (c).’

The Supreme Court overruled the Federal Circuit, stating that the statutory scheme ‘contemplated that one patented use will not foreclose marketing a generic drug for other unpatented ones. Within that

framework, the counterclaim naturally functions to challenge the brand's assertion of rights over whichever discrete use (or uses) the generic company wishes to pursue.' The Court additionally stated that use codes are encompassed within the counterclaim's ambit and that overbroad use codes interfere with the FDA's ability to approve generics under the statute. The court held that Caraco 'may bring a counterclaim seeking to 'correct' Novo's use code 'on the ground that' the '358 patent 'does not claim ... an approved method of using the drug.'

Accordingly, the Caraco decision allows generic drug companies to bring counterclaims to correct overbroad use codes that cover approved uses not claimed in associated FDA listed patents.

Association for Molecular Pathology v Myriad Genetics

The biotech world had been waiting with great anticipation for the Supreme Court's decision regarding the patentability of isolated human DNA.⁷ This litigation has a long and interesting history. Also known as the *Myriad* case, after the patent holder, the case began when a collection of plaintiffs, including the Association for Molecular Pathology (AMP) and the ACLU, among others, sued for declaratory judgment of invalidity against Myriad Genetics and the USPTO with regard to patents related to the human BRCA1 and BRCA2 genes. In the District Court, the plaintiffs won a significant victory, eviscerating the entirety of the Myriad patents, and overturning 30 years of US Patent and Trademark policy. The decision sent shockwaves through the biotech community, and Myriad appealed the case to the Federal Circuit.

In the first instance at the Federal Circuit, the US government reversed course from its previous stance and refused 'to defend the (US) PTO's longstanding position that isolated DNA molecules are patent eligible, arguing instead for a middle ground.'⁸ Instead the government advocated the plaintiffs' position that isolated and unmodified genomic DNAs are not patent eligible and are in fact products of nature. The Federal Circuit disregarded this change of position by the government, and overturned the District Court decision, finding the composition claims to isolated DNA patentable, as well as a method to screening potential cancer therapeutics. However, the holding invalidating the method claims to comparing and analysing gene sequences was upheld. The case was then appealed to the United States Supreme Court.

Rather than decide the *Myriad* case, the Supreme

Court vacated the original decision, and remanded the case back to the Federal Circuit to reconsider in view of the decision in *Mayo v Prometheus*.⁹ Despite the specific instructions by the Supreme Court vacating the previous decision, the Federal Circuit issued an opinion that was identical to its previous decision. Again, the Federal Circuit reversed the District Court's decision regarding Myriad's composition claims 'because each of the claimed molecules represents a non-naturally occurring composition of matter.' The Court also reversed the District Court concerning Myriad's method claim to screening potential cancer therapeutics via *in vitro* change. Lastly, the appeals court affirmed the District Court's decision that 'Myriad's method claims directed to 'comparing' or 'analysing' DNA sequences are patent ineligible; such claims include no transformative steps and cover only patent-ineligible abstract, mental steps.' Again the decision was appealed to the United States Supreme Court.

On 13 June 2013, the Supreme Court unanimously overruled the Federal Circuit by deciding that isolated DNA is not patentable subject matter and cDNA, synthetic DNA that omits non-coding portions (exons), is patentable.¹⁰ The Court stated that Myriad's principal contribution was merely determining the location and genetic sequence of the BRCA1 and BRCA2 genes – Myriad did not create or alter the genetic information. Therefore Myriad's gene patent claims did not 'render the genes patent eligible as 'new composition[s] of matter,' as defined in Section 101 of the Patent laws.¹¹ In contrast, cDNA is not naturally occurring, but an exons-only molecule made in a laboratory. The Court emphasized what was not implicated by the decision: there were no method claims at issue – 'the processes used by Myriad to isolate DNA were well understood by geneticists at the time of Myriad's patents.' Similarly, there were no patents before the Court that claimed 'new applications of knowledge about the BRCA1 and BRCA2 genes,' or claims in which 'the patentability of DNA [wherein] the order of naturally occurring nucleotides has been altered.' The Court thus left a door open to patentability of these types of DNA-related claims.

Court of Appeals for the Federal Circuit Decisions *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litigation*

This case¹² involves plaintiffs Aptalis Pharmatech, and Cephalon (collectively 'Cephalon'), the owner and exclusive licensee of US Patent Nos. 7,387,793 ('the '793 patent') and 7,544,372 ('the '372 patent').

The claims of the '793 patent are drawn to an extended-release dosage form of skeletal-muscle relaxants, and the '372 patent covers a method of relieving muscle spasms that includes the step of administering the extended-release formulation.

Mylan Pharmaceuticals Inc (Mylan), the defendants, filed an Abbreviated New Drug Application (ANDA) for a generic version of an extended-release cyclobenzaprine hydrochloride dosage form, and Cephalon sued Mylan for patent infringement based on their ANDA filing. The District Court found that Mylan's products infringed the '793 and '372 patents, but held that Cephalon's asserted patent claims were invalid as obvious. In particular, the District Court determined that the claimed extended-release pharmacokinetic (PK) profile was bioequivalent and, therefore, obvious in view of the immediate-release PK profile. The Federal Circuit held that the District Court should have also considered the asserted claims' limitation requiring a therapeutically effective plasma concentration. The Federal Circuit indicated that the District Court should have determined whether it would have been obvious to a person of skill in the art that a bioequivalent PK value would yield therapeutic effectiveness. 'Evidence of obviousness, especially when that evidence is proffered in support of an 'obvious to try' theory, is insufficient unless it indicates that the possible options skilled artisans would have encountered were 'finite,' 'small,' or 'easily traversed,' and that skilled artisans would have had a reason to select the route that produced the claimed invention.'¹³ Accordingly, the Federal Circuit held that because therapeutic effectiveness was a claimed limitation, the District Court could not rely on bioequivalence alone absent a known relationship between PK values and therapeutic effectiveness.

Further, the Federal Circuit indicated that the District Court erred by finding that the patents-in-suit were obvious before considering the secondary considerations, and reiterated that all objective evidence must be considered before reaching such a conclusion. The defendants also argued that the specification failed to disclose the best mode by omitting a particular range of dew points for curing the coating. The Court held that the specification need not disclose the optimal dew points to enable skilled artisans to practice the best mode. Optimization of the process known to skilled artisans would produce the optimal dew points. Therefore, the disclosure is adequate without them.

This case may show an inclination of the Federal Circuit to move towards a more rigid interpretation with regard to obviousness that was previously rejected by the Supreme Court in *KSR v Teleflex*. Therefore, it will be useful to monitor whether this case is a trend or an outlier with regard to Federal Circuit case law.

Otsuka Pharm Co Ltd v Sandoz Inc

Otsuka Pharm Co Ltd v Sandoz Inc,¹⁴ focuses on an obviousness challenge to US Patent 5,006,528 ('the '528 patent'), which is listed in the FDA Orange Book for the atypical antipsychotic Abilify (aripirazole). The defendants based their obviousness challenge on several prior art compounds, none of which convinced the Court that the claims of the '528 patent were *prima facie* obvious over the prior art. Affirming the District Court, the Federal Circuit reasoned that although the prior art contained several structurally similar compounds there was no reason, absent hindsight, for a person of skill in the art at the time the invention was made, to use any of them as a lead compound.

An aspect of the Federal Circuit's analysis is related to the last compound proposed by the defendants, namely OPC-4392. On appeal the defendants argued that the inventor's own development efforts constituted evidence of obviousness, stating that Otsuka's aripiprazole development involved a 'short timeline' and 'took only a few months,' however, the Court disagreed, stating that '[t]he inventor's own path itself never leads to a conclusion of obviousness; that is hindsight.' This case highlights the difficulty of asserting an obviousness challenge to a patent that claims a new chemical entity and is unlikely to be overturned by the Supreme Court.

Merial Limited v Cipla Limited

Merial Ltd (Merial) returned to the district to seek enforcement of a permanent injunction following a permanent injunction arising from patent infringement.¹⁵ The patented compositions at issue contain pesticidal N-phenylpyrazole derivatives such as fipronil for protecting domestic dogs and cats from infestation with fleas and ticks.

Cipla is a pharmaceutical company incorporated under the laws of India with its principal place of business in Mumbai, India. Merial filed suit against Cipla alleging infringement of two patents. Neither Cipla nor any of the other defendants responded to the

complaint, or entered an appearance in the District Court. Merial therefore moved to hold the defendants in default, and the District Court granted that motion. The District Court found that Cipla had infringed each patent, and entered a permanent injunction barring Cipla from directly or indirectly infringing the patents in the future.

Velcera, a company formed by former Merial executives in 2004, began preparations to enter the market for flea and tick control products that would 'directly compete' with Merial's Frontline series 'at a substantially lower price.' 'In practice, the parties' interrelated web of agreements and intermediaries involved in producing and distributing [the competing products] functioned as follows: Velcera (through FidoPharm) would place an order for PetArmor Plus with Omnipharm, which would then pass the order to Cipla. Upon producing the product in India, Cipla would transfer ownership . . . ship the product from India to Dubai and there transfer title to QEDetal. Formal ownership of the product would transfer yet again in Dubai, from QEDetal to FidoPharm, and, finally, Fido-Pharm would import the PetArmor Plus for sale in the United States.'

Merial filed a motion for contempt in District Court, contending that Cipla's activities relating to PetArmor Plus violated the permanent injunction against infringement of the patents. Merial alleged that PetArmor Plus was merely a rebranded version of Cipla's enjoined product and that the importation and sale of the competing product violated the injunction.

Cipla sought to vacate the injunction, alleging that the District Court lacked personal jurisdiction over Cipla when it issued the Default Order.

The Federal Circuit held that the District Court had personal jurisdiction over Cipla when it entered the default judgment and injunction. The Federal Circuit further agreed with the District Court in finding no more than colorable differences between Merial's and Cipla's products. When 'infringement has been established through default, the judgment is no less binding or authoritative simply because comprehensive and painstaking factual analyses regarding every claim limitation may have been unnecessary or impractical at the time of the initial decision. As such, whether or not the default order here included an exhaustive infringement analysis, it necessarily and conclusively established that Protektor Plus met each limitation recited in the asserted claims of the patent.'

The Federal Circuit then concluded that 'Cipla's extraterritorial role in the development, production, and ultimate US sale [of the competing product] violated the District Court's injunction against induced infringement' and that 'Velcera's actions bringing PetArmor Plus to market in concert with Cipla qualified as contemptuous conduct.' Again the Federal Circuit found a broad interpretation of patent rights with regard to enforcing permanent injunctions.

Momenta Pharm Inc v Amphastar Pharm Inc

Momenta sued Amphastar for infringing US Patent Number 7,575,866 ('the '866 patent')¹⁶ which claimed methods for analysing enoxaparin.¹⁶ Momenta alleged that Amphastar 'infringed the '866 patent by 'manufacturing generic enoxaparin for commercial sale' using the claimed methods.' The District Court granted Momenta a preliminary injunction, and Amphastar appealed.

Amphastar argued that its testing fell within the scope of the Hatch-Waxman safe harbor.¹⁷ Section 271(e)(1) states that '[i]t shall not be an act of infringement to ... use ... a patented invention ... solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs' Momenta argued that the safe harbor does not apply to post-approval activity. Momenta stated that the 'availability of other acceptable testing methods means that Amphastar's alleged use of the patented method is not required by the FDA, and is therefore outside of the safe harbor provision.'

The Federal Circuit stated that the broad language of Section 271(e)(1) 'unambiguously applies to submissions under any Federal law, providing that the law 'regulates the manufacture, use, or sale of drugs.' The Court addressed the contention that the information in question was not 'submitted' to the FDA but was retained by Amphastar. The Court stated that Amphastar 'cannot sell a batch of enoxaparin unless it has established that its strength and quality is consistent with the standards set forth in the relevant official compendium,' and that FDA regulations require that 'all records associated with a produced batch of drugs,' be retained for at least one year after batch expiration and be ready for authorized inspection. The requirement to maintain records for FDA inspection satisfies the requirement that the uses be reasonably related to the development and submission of information to the FDA,' thus, the Court asserted that the information was 'submitted' for purposes of the statute.

The Federal Circuit vacated and remanded the case back to the District Court, concluding that the submissions were not ‘routine submissions’ to the FDA, but were ‘submissions that are required to maintain FDA approval,’ and that they must ‘be done according to the patented methods described in an official compendium.’ The Court held that Amphastar’s post-approval studies were ‘reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use or sale of drugs,’ fell within the scope of the § 271(e)(1) safe harbor, and vacated the preliminary injunction.

In view of the *Momenta* decision, drug testing or studies that are conducted according to a patented method are protected under the safe harbor provision of 35 USC. § 271(e)(1) if such testing is required by the FDA to maintain approval to market the drug. In contrast, infringing studies not mandated by the FDA, i.e., investigator-initiated studies conducted to assess adverse side effects, are not protected under the safe harbor provision of the statute. While many commentators considered this decision to be an overbroad interpretation of the Federal Statute, the Supreme Court has declined to review this decision, which restricts patent rights with regard to drug testing or studies.

Alcon Research Ltd v Apotex Inc

Apotex Inc (Apotex) submitted an ANDA to the Food and Drug Administration seeking approval to market a generic version of the anti-allergy eye drop Patanol®.¹⁸ Alcon Research Ltd (Alcon), sued Apotex for patent infringement, of US Patent No. 5,641,805 (‘805 patent) which is listed in the FDA Orange Book for Patanol®. The ‘805 patent is directed to a method for treating allergic eye disease by topically administering 0.1% w/w olopatadine, which stabilizes conjunctival mast cells in the eye.

Apotex asserted that the claims would have been obvious over the prior art, which discloses eye drops with olopatadine concentrations that overlap with the claimed ranges. Alcon argued that the prior art does not supply a ‘reason to focus on olopatadine instead of many other promising antihistamines,’ that there would not have been a reasonable expectation of success,’ that the ‘prior art teaches away from using olopatadine as a mast cell stabilizer.’

The Federal Circuit found that the District Court incorrectly compared the ‘805 patent claims and the prior art. The Court looked to the dependent claims for ascertaining the concentration of olopatadine

covered by claim 1. Alcon argued that ‘some olopatadine concentrations covered by the claims do not stabilize human conjunctival mast cells to a clinically relevant extent and should therefore be excluded from the claims’ scope.’ However, the Federal Circuit stated that ‘[t]his is not how patent law works ... you can’t simply disavow the invalid portion and keep the valid portion of the claim. If everything up to 0.001% w/v is admittedly not enabled, then the entire claim is invalid.’ The Court emphasized that it will not ‘rewrite the claims to narrow them for the patentee to cover only the valid portion.’

The Federal Circuit concluded that the prior art rendered the claims obvious because it discloses olopatadine concentrations that overlap with the ranges in those claims, but it does not teach the 0.1% w/v composition recited in claims 4 and 8 of the ‘805 patent. Apotex argued that even though the prior art does not disclose the claimed 0.1% w/v concentration; routine experimentation would have led a skilled artisan to try this formulation. While the ‘805 claims are limited to using formulations with an olopatadine concentration of about 0.1% w/v, the prior art only tested formulations with olopatadine concentrations up to 0.01% w/v and thus does not disclose this limitation. Thus, the Court held that claims 4 and 8 would not have been obvious.

Eli Lilly and Co v Teva Parenteral Medicines Inc

The Federal Circuit declined to find obviousness type double patenting between patents directed to pharmaceutical compounds.¹⁹ US Patent 5,344,932 (‘the ‘932 patent’) issued from an application filed on 11 December 1989 and discloses and claims the antifolate chemotherapy drug perimetrexed. US Patent 5,028,608 (‘the ‘608 patent’) issued from an application filed on 24 May 1990 as a continuation-in-part of the ‘742 application. The ‘608 patent discloses and claims a compound (‘the ‘608 compound’) that differs from perimetrexed only in that it contains a thiophene ring (a five membered, aromatic, sulfur containing heterocycle) where perimetrexed contains a benzene ring. US Patent 5,248,775 (‘the ‘775 patent’) issued from an application filed on 31 January 1992 and discloses a family of intermediates that can be used to make various antifolates, including perimetrexed. In particular, the ‘775 patent claims a compound (‘the ‘775 intermediate’) that differs from perimetrexed only in that it contains 3 protecting

groups and has a carbon-carbon triple bond where perimetrexed has a benzene ring.

The defendants each asserted that perimetrexed is an obvious variant of either the '608 compound or the '775 intermediate and therefore the '932 patent is invalid for obviousness type double patenting. With respect to the '608 compound, the court found that a person of ordinary skill in the art would not have been motivated to make modifications that would have led to perimetrexed and that a complicated molecule like the '608 compound provides many possible opportunities for modification and there was nothing that would have motivated a person of skill to substitute a phenyl group for the thiophene.

The Court did not agree that the '932 patent was invalid for obviousness type double patenting, and stated that the cases the defendants relied on each dealt with a case where a first patent claimed a compound and disclosed a use for that compound, and a second patent claimed a method of using the compound for the use disclosed in the first patent. The Court further stated that in the instant case the patents dealt with two distinct compounds and that therefore these cases do not apply.

Santarus Inc v Par Pharmaceutical Inc

The Federal Circuit recently clarified how negative claim limitations can be adequately supported in patent specifications, such that they satisfy the written description requirement.²⁰ In this case, the Federal Circuit held that negative claim limitations are adequately supported when specification describes a reason to exclude the relevant limitation.

The patents at issue in this case involve formulations of omeprazole proton pump inhibitors (PPIs). These formulations inhibit gastric acid secretion to prevent and treat stomach acid-related diseases and disorders.

The inventor filed a first provisional application on 4 January 1996, to which the first patent, US Patent No. 5,840,737 ('the '737 patent'), claimed priority. Par filed an ANDA to market a generic product with the same formulation as the Zegerid® PPI. The lower court found some of the claims of its continuation patent US Patent No 7,399,772, to be invalid as failing the written description requirement, and that all claims were invalid as obvious.

One set of amended claims included an exclusionary (negative) limitation, stating that, 'the composition contains no sucralfate.' The original specification provided reasons why omeprazole was preferable to sucralfate, another gastrointestinal

medication. The lower court stated that because the inventor's composition was only described as advantageous in the specification, the negative limitation could not also be used to exclude sucralfate without evidence that sucralfate is contraindicated. Therefore, the District Court held that the negative limitation did not satisfy the written description requirement.

On appeal, the Federal Circuit rejected this reasoning and emphasized that '[n]egative claim limitations are adequately supported when the specification describes a reason to exclude the relevant limitation.' Because people skilled in the art would understand that the disadvantages of including sucralfate could be avoided by the claimed formulation, the written description was satisfied. Further, the Court noted that '[s]uch written description support need not rise to the level of disclaimer. The Court therefore held that the statements in the parent patent were sufficient to support the exclusionary limitation, and thus, the parent patent was not a proper prior art reference against the claims because they were supported by the original specification.

Pozen Inc v Par Pharmaceutical Inc

In this case,²¹ the District Court found that the asserted claims of US Patent No. 6,060,499 ('the '499 patent'), US Patent No. 6,586,458 ('the '458 patent'), and US Patent No. 7,332,183 ('The '183 patent'), were not invalid as obvious under 35 USC. § 103.

Pozen developed a method for treating migraines by combining two drugs, sumatriptan and naproxen, in a single tablet. Sumatriptan is a 5-HT receptor agonist that was developed in the late 1980s and is widely accepted as an effective medicine for migraines, and Naproxen is a well known nonsteroidal anti-inflammatory drug. Pozen and GlaxoSmithKline (GSK) market sumatriptan and naproxen combination called Triximet®. Pozen filed an ANDA to market Triximet® and listed the '499, '458, and '183 patents in the FDA Orange Book.

Pozen, Par and DRL (appellants) sought to obtain FDA approval to market generic forms of Triximet® before the expiration of Pozen's patents asserting the claims were invalid as obvious and argued that the claims were obvious over the prior art.²²

After reviewing the relevant claims and prior art, the Federal Circuit agreed with the District Court that the prior art did not render the patents obvious. Additionally, the court found that 'Par's ANDA

product ... satisfies the [limitations] under ... the doctrine of equivalents.’ The court reiterated that ‘the doctrine of equivalents is not foreclosed with respect to claimed ranges.’²³ The Court concluded that ‘[u]nder the doctrine of equivalents, a tablet layer with 85% of the agent can be fairly characterized as an insubstantial change from a tablet layer with 90% of the agent.’

In re Rosuvatin Calcium Patent Litigation

The Court of Appeals for the Federal Circuit affirmed the District Court’s decision finding that Astrazeneca’s patent for its Crestor cholesterol-lowering drug was valid, enforceable and infringed by several ANDA filers.²⁴ The decision clarified the standard for showing error without deceptive intent supporting a reissue patent application and the definition of an FDA approval application ‘submitter’ who may be subject to infringement liability.

FDA-approved Crestor, used to control high cholesterol, is covered by US Reissue Patent No. 37,314 (the ‘314 patent). The defendants argued that the ‘314 patent was invalid on the ground of improper reissue, the patent was unenforceable based on inequitable conduct before the USPTO, and the patent was invalid on obviousness grounds. Defendant Apotex further argued that it could not be liable for infringement because it did not submit the ANDA within the meaning of Section 271(e)(2)(A) of the Patent Act. The District Court ruled that the ‘314 patent was valid, enforceable and infringed.

The defendants argued that the alleged error supporting the reissue patent application occurred with deceptive intent and that the US subsidiary of one of the defendants was a submitter of the ANDA under the Hatch-Waxman Act where the subsidiary signed and filed the ANDA on behalf of a foreign affiliate and intended to benefit from the ANDA.

The Federal Circuit first affirmed the District Court’s decision that the defendants had not proved that the patent was unenforceable due to inequitable conduct. The Court found that while Patentee Shionogi’s employees made deliberate decisions to withhold material references from the USPTO during the prosecution of the original patent application from which the ‘314 patent was reissued, the plaintiffs did not establish deceptive intent. Although deceptive intent may be inferred from circumstantial evidence under *Therasense Inc v Becton Dickinson & Co*,²⁵ the Federal Circuit noted that inference must be ‘the single most reasonable inference one could draw from

the evidence’ and that such an inference could not be drawn from patentee employees’ credibility during testimony. Instead, the Court emphasized that Shionogi’s patent department had a heavy work load and was understaffed, employee oversights resulted from confusion, error, and misunderstanding of the rigor of the US patent examination process leading to a failure to disclose the documents at issue.

Secondly, the Federal Circuit affirmed the District Court’s finding that Shionogi’s claiming of subject matter in the original patent that overlapped the prior art in order to try for broader patent coverage, did not intentionally create the error for which it sought reissue, and the reissue application was promptly filed upon discovery of the error.

Thirdly, the Federal Circuit addressed the issue of patent infringement, specifically defendant Apotex’s argument that it did not ‘submit’ its ANDA within the meaning of Section 271(e)(2)(A) of the Patent Act because it merely signed and filed the ANDA on behalf of its Canadian affiliate, and therefore it could not infringe the US patent. The Federal Circuit held that Apotex was properly named as a defendant, since lower courts have applied liability to the ANDA ‘submitter’ who signs the ANDA and intends to directly benefit from the ANDA.

Cephalon Inc v Watson Pharmaceuticals Inc

The enablement requirement of US patent law is met when a person of skill in the art can read the disclosure of a patent and practice the invention without undue experimentation.²⁶ In this case, the Court examined whether a person of skill in the art would have understood the term ‘effervescent agent’ to mean a single gas-evolving compound that is used in an oral mucosa drug delivery formulation, or alternatively, to mean two compounds that evolve gas through a chemical reaction in the presence of water.

The lower court held that the patent specification did not sufficiently describe a single gas-evolving compound that satisfied the enablement requirement. The enablement challenge was based primarily on expert testimony that it would have required undue experimentation to formulate an oral mucosa tablet with only one gas-evolving agent. According to the expert, such a formulation would have been ‘very difficult’ and ‘complicated’ to achieve. The lower court emphasized that it would have required experimentation to determine the correct proportion of an outside acid source that would be used with a single gas-evolving agent.

The Federal Circuit noted that some experimentation may be required and that a patent fails the enablement requirement when the amount of experimentation is ‘unduly extensive.’²⁷ The fact that a clinician would be required to calculate the amount of the single gas-evolving compound and the amount of the outside acid source does not mean that the quantity of experimentation is undue. Additionally, the defendant and patent challenger did not provide evidence showing why the alternative disclosures of an effervescent ‘couple’ ‘do not provide sufficient guidance for a skilled artisan to calculate formulations for single compound effervescent agents.’ Since there was insufficient evidence to show undue experimentation the Federal Circuit reversed the lower court’s nonenablement determination.

Conclusion

These cases highlight the continued conflict between the decisions of the United States Supreme Court and the Court of Appeals for the Federal Circuit. The renewed interest in patent law by the Supreme Court ensures an evolving landscape with regard to pharmaceutical patent law. A skilled patent attorney can provide sound counsel and potentially help avoid costly litigation by grounding his/her opinion in a conservative reading of applicable authority, applying sound scientific analysis, and avoiding hidden traps inherent in such a dynamic evolution of the case law.

References

- 1 *Mayo Collaborative Services v Prometheus Laboratories Inc*, 132 S.Ct. 1289 (2012).
- 2 Title 35 United States Code; 35 USC. § 101.
- 3 Seidman *et al.*, Method of treating IBD/Crohn's disease and related conditions wherein drug metabolite levels in host blood cells determine subsequent dosage, US Patent No. 6,355,623 (to Hopital-Sainte-Justine, Canada) 12 March 2002.
- 4 *Caraco Pharmaceutical Laboratories Ltd v Novo Nordisk A/S*, 132 S.Ct. 1670 (2012).
- 5 United States Public Law 98-417; US Federal Food, Drug, and Cosmetic Act, Section 505(j) 21 USC. 355(j).
- 6 Muller, NIDDM regimen, US Patent No. 6,677,358 (to Novo Nordisk A/S, Denmark) 13 January 2004
- 7 *Association for Molecular Pathology v Myriad Genetics*, 133 S.Ct. 2107 (2013).
- 8 *Ass'n for Molecular Pathology v USPTO*, 653 F.3d 1329, 1349–1350.
- 9 *Mayo Collaborative Services v Prometheus Laboratories Inc*, 132 S.Ct. 1289, 1294 (2012).
- 10 *Ass'n for Molecular Pathology v Myriad*, 133 S.Ct. 2107, 2109 (2013).
- 11 Myriad, 133 S.Ct. at 2110; see also Title 35 United States Code; 35 USC. § 101.
- 12 *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litigation*, 676 F.3d 1063 (Fed. Cir. 2012).
- 13 *In re Cyclobenzaprine*, 676 F.3d citing KSR, 50 US at 421.
- 14 *Otsuka Pharmaceutical Co Ltd v Sandoz Inc*, 678 F.3d 1280 (Fed. Cir. 2012).
- 15 *Merial Limited v Cipla Limited*, 681 F.3d 1283 (Fed. Cir. 2012).
- 16 *Momenta Pharmaceuticals Inc v Amphastar Pharmaceuticals Inc*, 686 F.3d 1348 (Fed. Cir. 2012).
- 17 35 USC. § 271(e)(1).
- 18 *Alcon Research Ltd v Apotex Inc*, 687 F.3d 1362, 1363 (Fed. Cir. 2012).
- 19 *Eli Lilly and Co v Teva Parenteral Medicines Inc*, 689 F.3d 1368 (Fed. Cir. 2012).
- 20 *Santarus Inc v Par Pharmaceutical Inc*, 694 F.3d 1344 (Fed. Cir. 2012).
- 21 *Pozen Inc v Par Pharmaceutical Inc*, 696 F.3d 1151 (Fed. Cir. 2012).
- 22 35 USC. § 271 (e)(2)(A).
- 23 *Pozen*, 696 F.3d citing *Adams Respiratory*, 616 F.3d at 1291-92.
- 24 *In re Rosuvastatin Calcium Patent Litigation*, 703 F.3d 511 (Fed. Cir. 2012).
- 25 *Therasense Inc v Becton Dickinson & Co*, 649 F.3d 1276, 1290 (Fed. Cir. 2011) (en banc).
- 26 *Cephalon Inc v Watson Pharmaceuticals Inc*, 707 F.3d 1330, 1336 (Fed. Cir. 2013) citing *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988).
- 27 *Cephalon*, 707 F.3d citing *Chiron Corp v Genentech Inc*, F.3d 1247, 1253 (Fed. Cir. 2004).