INSIDE THE MINDS

Patent Enforcement Best Practices

Leading Lawyers on Evaluating a Patent's Scope, Investigating Infringement Claims, and Developing Strategies for Prosecution and Defense

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Defining Patent Law

Patent law can be broken down into four main areas of concern with reference to assertion of rights: claim construction (proper scope of the subject matter of the claim), validity (the patent claim meets the statutory requirements for patentability under the current judicial interpretation of Title 35 of the United States Code), enforceability (the patent claim was obtained without intentional misrepresentation or omission of facts material to the patentability), and infringement (the accused subject matter meets all the limitations of the asserted claim either literally or under the doctrine of equivalents) including contributory and/or inducing infringement.

Claim construction is critical in due diligence, freedom to operate, and litigation matters, since the proper construction of the claim dictates the scope of the right to exclude others from making, using, selling, offering for sale, or importing the subject matter of the claim. Claim construction is a matter of law (for the judge to decide) and has been the subject of a large amount of recent judicial scrutiny. Accordingly, it is very important to study and apply recently articulated language and rationale from the Federal Circuit to the facts intrinsic to the patent (i.e., the claims, specification, and file history) in view of the state of the art at the time of the original application for patent.

The next issue is **validity** (i.e., is the properly construed claim valid). Validity, in contrast to construction, is a matter of fact (for a finder of fact, such as the jury, to decide). Validity is of critical relevance in due diligence, freedom to operate, and litigation matters. Validity analyses primarily concern the statutes 35 U.S.C. §§101, 102, 103, and 112 (i.e., is the subject matter new, useful, and non-obvious, and has the patentee described the "best mode" of practicing the invention at the time of filing and taught one of ordinary skill the fundamental scope of the subject matter of the claim—within the specification and claims—so one of ordinary skill in the art would recognize possession of the invention at the time of the filing and be able to make and use the invention). The novelty requirement under 35 U.S.C. §102 is paramount and is frequently problematic for patent holders.

Enforceability of a patent is absent if the patent was obtained by fraud (misrepresentation or omission of a fact that is material to the patentability under the patent statute) on the U.S. Patent and Trademark Office. Intent, and therefore fraud, can be inferred from the evidence of an act or omission that is material to the patentability of the invention. The materiality and intent factors of fraud are inversely related. In a due diligence project, for example, in evaluating the exclusivity aspect of the patent, it is important to evaluate the facts of the technology and the acts of the owners to determine that the patent should be enforceable (i.e., that no material information was withheld or misrepresented to the U.S. Patent and Trademark Office during prosecution).

Infringement is present if the accused subject matter meets every limitation of a properly construed claim, either literally or under the doctrine of equivalents. A patent is a grant from the U.S. government that provides the owner the right to exclude others from making, using, selling, offering for sale, or importing subject matter defined by the claims of the patent. A patent claim may be infringed either literally or under the doctrine of equivalents.

Under the doctrine of equivalents, "a product or process that does not literally infringe upon the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused product or process and the claimed elements of the patented invention." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997) (citing *Graver Tank*, 339 U.S. at 609).

The doctrine evolved in recognition of the fact that:

> [t]he language in the patent claims may not capture every nuance of the invention or describe with complete precision the range of its novelty. If patents were always interpreted by their literal terms, their value would be greatly diminished. Unimportant and insubstantial substitutes for certain elements could defeat the patent, and its value to inventors could be destroyed by simple acts of copying.

> *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 731 (2002).[1]

Inducing infringement exists under 35 U.S.C. §271(b) if a party actively and knowingly assisted in direct infringement. The patent owner has the burden of showing the party's actions induced infringing acts and the party knew or should have known their actions would induce actual infringement. Proof of actual intent to induce infringement is a requirement for liability under 35 U.S.C. §271(b). The patentee must establish that the accused infringer purposefully caused, urged, or encouraged another individual to infringe the patent with knowledge of the likely infringing result. The patentee may prove the accused infringer's intent to induce infringement by showing a number of actions from which the trier of fact could infer such intent, including giving a direct infringer instructions, for example, on how to use a patented process.

Contributory infringement exists if a party aids or abets direct infringement:

> Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination, or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use, shall be liable as a contributory infringer.
>
> 35 U.S.C. §271(c).

[1] According to the Supreme Court in *Festo*, "A narrowing amendment made to satisfy any requirement of the Patent Act may give rise to an *estoppel*." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 736 (2002) (*Festo VIII*). Such a narrowing amendment, whether made to avoid prior art or to comply with §112, creates a presumption that the patentee surrendered the territory between the original claims and the amended claims. *Id.* at 741. The patentee may rebut that presumption by showing that the alleged equivalent could not reasonably have been described at the time the amendment was made, or that the alleged equivalent was tangential to the purpose of the amendment, or that the equivalent was not foreseeable (and thus not claimable) at the time of the amendment. *Id.* at 740–41. *See, also, Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 344 F.3d 1359 (Fed. Cir. 2003).

Importation, sale, offer for sale, or use of a product that was produced using a patented process is an act of infringement. The product is presumed by the court to have been made by the patented process if a substantial likelihood exists that the product was made by the patented process, and the patent owner has made a reasonable effort to determine the process actually used in the production of the product and was unable to so determine. However, a product made by a patented process will not be considered to be so made if it is materially changed by subsequent processes or it becomes a trivial and non-essential component of another product. 35 U.S.C. §§271(g), 295.

Filing of an abbreviated new drug application (ANDA), for example, is an act of infringement under 35 U.S.C. §271(e)(2)(A).[2] The Hatch-Waxman Act sets a thirty-month stay to Food and Drug Administration (FDA) approval of an ANDA that has been filed with Paragraph IV certification with regard to a patent that is properly listed in the FDA Orange Book [3, 4] if a lawsuit is filed under 35 U.S.C. §271(e)(2)(A) asserting infringement of that patent within forty-five days of notice of the certification.[5, 6] Particularly, the ANDA may

[2] It shall be an act of infringement to submit an application under §505(j) of the Federal Food, Drug, and Cosmetic Act or described in §505(b)(2) of such act for a drug claimed in a patent or the use of which is claimed in a patent.

[3] Any patent that claims the drug for which the applicant submitted the application or claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. 21 U.S.C. §355(b)(1). The holder of an approved new drug application must file the same information with respect to similar patents that are obtained after the application is approved. 21 U.S.C. §355(c)(2).

[4] Each patent "which claims the [drug previously approved by the FDA] or which claims a use for [that] drug for which the [ANDA] applicant is seeking approval…and for which information is required to be filed" for listing in the FDA Orange Book. 21 U.S.C. §355(j)(2)(A)(vii), referring to 21 U.S.C. §§355(b)(1) and 355(c)(2).

[5] 21 U.S.C. §§355(j)(2)(A)(vii), 355(j)(2)(B)(i), and (ii), 355(j)(5)(B)(iii).

[6] The ANDA applicant, however, does not have to seek approval for all uses approved for the reference listed drug. If a method of using the approved drug is patented and is listed in the Orange Book, but the applicant is not seeking approval for the patented use, the applicant must state in the ANDA that the method of use patent does not claim the use for which the manufacturer is seeking approval ("Section viii statement"). 21 U.S.C. §355(j)(2)(A)(viii). The Section viii statement permits the ANDA applicant to avoid certifying to a patent by stating that it is not seeking approval for the use claimed in the listed patent. A proper Section viii statement must "carve out" from the proposed ANDA

not be approved until the date the court determines invalidity or non-infringement, the date the patent expires, or thirty months from the date the patent holder receives notice of the certification (subject to judicial discretion), whichever occurs first.[7] *See*, *e.g.*, Federal Trade Commission, *Generic Drug Entry Prior to Patent Expiration: An FTC Study*, 1–8 (July 2002).

Clients most often face paramount issues with respect to patent law when a certain patent suddenly appears to control an exclusive market position in a growingly attractive (e.g., lucrative) industrial market. Suitors and competitors emerge in abundance at this time to carefully and critically evaluate the controlling patent or portfolio for scope, validity, and enforceability. An approach to this problem, from the patent owner side, is proper management of discovery assets (i.e., strategic portfolio development toward maintaining market exclusivity). Due diligence projects, including comprehensive freedom-to-operate opinions of counsel, are of great importance to suitors and competitors at this time in the life cycle of a product that commands a lucrative market. Our firm recommends carefully positioning and asserting select instruments of a patent portfolio in a timely manner.[8]

Serving Clients

The following are the major patent-related issues our firm deals with on behalf of our clients:

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labeling, the labeling protected by the listed patent. A Section viii statement does not carry the requirement for notice to the new drug application holder and patent owner, and the related opportunity for a thirty-month stay.

[7] A single opportunity exists for a thirty-month stay in the approval date of each ANDA. Once the single thirty-month stay has been imposed, ANDA applicants filing Paragraph IV certifications to subsequently listed patents need not notify the new drug application holder of such certifications.

[8] Timeliness is important also due to the equitable doctrines of *laches* and *estoppel*. To successfully invoke *laches*, a defendant must prove the plaintiff delayed filing suit an unreasonable and inexcusable length of time after the plaintiff knew or reasonably should have known of its claim against the defendant and that the delay resulted in material prejudice to the defendant. The defense of *estoppel* bars recovery for infringement when the owner represents that the patent will not be enforced against the infringer and the infringer reasonably relies on that representation and the infringer will be materially prejudiced if the patentee is allowed to proceed with the claim.

Relevant Facts and Law

For example, what are the relevant facts and/or legal issues important to successfully asserting or defending and prevailing in a prospective lawsuit? Critical facts, often difficult to find, tend to be the most controlling elements of a patent law case. Knowledge of the developing law is important to know what facts are critically relevant and therefore important to find.

Claim Construction

This includes proper meaning (legal construction of the overall scope) of the patent claim in view of the evidence intrinsic to the patent, as well as validity of the properly construed claim in view of relevant facts as well as current judicial interpretation of the patent statute.

Freedom to Operate

The ability to make, use, sell, offer for sale, or import a certain entity, for example, usually within the proper exclusivity of a client's current and/or prospective patent claim. This issue regularly comes up with respect to third-party or competitor patents wherein clients seek to evaluate and control any risk of adverse exposure to litigation.

FRCP Rule 11 Basis to Commence an Action

It is generally important to have a written legal conclusion, based upon review of the facts, that to the best knowledge, information, and belief, formed after an inquiry reasonable under the circumstances, that commencing an action in a U.S. district court under Title 35 of the United States Code to enforce a U.S. patent is in accord with Rule 11 of the U.S. Federal Rules of Civil Procedure.

Antitrust and Patent Misuse Issues

It is very important to carefully evaluate the facts of the prospective lawsuit to ensure that, in the case of a plaintiff asserting a patent, for example, no valid antitrust or patent misuse counterclaims are present.

The financial implications of patent law are large indeed. About $800 million in research and development resources, for example, are required in the pharmaceutical industry to bring a new drug to market. However, by the time a new drug is approved by the FDA, only about six years remain on the term of the original compound patent. Accordingly, the innovative side of the pharmaceutical industry relies significantly on life cycle planning through data exclusivity and patent portfolio management to protect large research and development investments. The Hatch-Waxman Act,[9] however, provides significant incentive in terms of certain market exclusivity in reward for a successful challenge to patents that otherwise block generic competition.[10]

Our practice is in portfolio development, market exclusivity, and freedom to operate in the pharmaceutical industry. We generally provide counsel in the industry toward leveraging discovery assets to obtain and preserve market exclusivity through patent protection, enforcement, defense, and closely related FDA issues. The following are the major areas we focus on when trying to attain a successful outcome for our clients:

Portfolio Development

First, it is important to identify and understand the market a client seeks to occupy. Then, as a corollary, it is very important strategically to identify competing technologies to properly evaluate, ascertain, and protect a valuable market niche. Similarly, it is important to know and understand the Food, Drug, and Cosmetic Act, the Code of Federal Regulations, as well as the antitrust laws and authoritative judicial precedent to properly advise clients how to manage market exclusivity through tools, laws, and regulations other than the patent statute.[11]

[9] The FDA regulates pharmaceuticals under the Food, Drug, and Cosmetic Act. Congress passed the Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act in 1984 to create a balance between the brand-name and generic sectors of the pharmaceutical industry.

[10] An ANDA may be filed if certification is provided, for example, that an otherwise relevant patent listed in the FDA Orange Book is invalid, unenforceable, or not infringed. 21 U.S.C. 355(j)(2)(A)(vii) (IV) (Paragraph IV certification).

[11] The listability of patents, for example, in the FDA publication of approved drug products with therapeutic equivalence, known in the industry as the Orange Book.

Due Diligence

Pharmaceutical clients need to know, when evaluating a target company for purchase, whether a patent portfolio owned by the target company will provide an exclusive market position with regard to a valuable compound in clinical trials, for example. In other words, the buyer generally needs to know the proper scope and term of patent claims that encompass valuable subject matter in the portfolio and whether the claims are valid and enforceable under the current judicial interpretation. Since patents merely provide the right to exclude others, in addition to the issue of exclusivity, a due diligence project necessarily addresses the issue of freedom to operate. In other words, a prospective purchaser of a compound in clinical trials, for example, needs to know, in the event the company is acquired, whether they, as a new owner, will have freedom to operate (i.e., the ability to make, use, sell, offer for sale, and import the compound and formulations).

Assessment

Know and fully understand the facts of the competition and the infringing subject matter. Assess the facts of the relevant patents and the proper scope of the claims to be asserted against the competition. Evaluate the options for providing notice, if necessary, to the competition. Counsel the client to proceed carefully to avoid exposure, including: (1) providing the competition with the option to file for declaratory judgment in their home forum,[12] (2) potentially serious and costly antitrust counterclaims and/or patent misuse issues, as well as (3) equitable defenses including unclean hands, unenforceability, *laches*, and *estoppel*.

We have developed several procedures to expedite the analysis of patent infringement cases. For example, in anticipation of ANDA litigation as a plaintiff,[13] we become very familiar well in advance with the evidence

[12] The patent holder, in providing notice, must be careful in bringing patents to the attention of a suspected infringer so as not to trigger a reasonable apprehension of a lawsuit on their behalf. If a party can exhibit evidence that they expect to be sued, a declaratory judgement action may be filed by that party in their local district court. The patent holder is then forced to defend a lawsuit based on an assertion of non-infringement and/or invalidity of the patent(s) as well as related antitrust claims, for example, in a forum that is likely to be favorable to the suspected infringer.

intrinsic to the patent(s) that are likely to be asserted against an ANDA filer. We review and confirm the listability of the claims in the FDA Orange Book. We then carefully review the reference listed drug, the FDA-approved label, and respective indications, in view of the properly construed claims and history of the patent(s) likely to be asserted. We identify and characterize basic facts that must be present in the ANDA to support arguments of literal infringement or infringement under the doctrine of equivalents, as well as facts for inducing, and/or contributory infringement. Depending upon the patents to be asserted, and possible creative attempts to avoid those patents, we continuously look to developing judicial authority toward guidance in efficaciously asserting a client's portfolio in fact to maintain legal market exclusivity in a prudent and cost-effective manner.

We generally advise our clients who receive a letter, for example, that creates a "reasonable apprehension" of an infringement lawsuit to authorize an action for declaratory judgment of non-infringement and/or invalidity, if the facts are amenable, in a local district court. First, of course, we evaluate the facts of the patent(s) and the accused operations. However, our counsel is generally to dispose of such threats sooner in a local forum, rather than engaging in almost certainly prolonged and unproductive negotiations. We generally recommend that any current or prospective issues related to exclusivity and/or freedom to operate should be fully evaluated and resolved sooner rather than later in a results-oriented manner to manage assets and control exposure, particularly when the facts could be relevant to formulations in clinical trials.

Serving our clients to the best of our ability means keeping up on developments and precedent in the industry. Some of the ways we do that include regularly reading Federal Circuit slip opinions as they are handed

[13] A lawsuit must be filed within forty-five days of receiving a Paragraph IV ANDA notice letter. It is important also to have a legal conclusion, based upon review of the facts, that to the best knowledge, information, and belief, formed after an inquiry reasonable under the circumstances, commencing an action in a U.S. district court under Title 35 of the United States Code to enforce a U.S. patent is in accord with Rule 11 of the U.S. Federal Rules of Civil Procedure. It is also important to carefully evaluate the facts of the prospective lawsuit to ensure that, in the case of a plaintiff asserting a patent, for example, no valid antitrust or patent misuse counterclaims, for example, are present.

down before they are formally published. We also participate and study *amicus* briefs filed in pending U.S. Supreme Court cases.

We have learned in our practice that the one most important factor that contributes to success is an intimate knowledge of a client's business, current and prospective exclusive markets, and the competition. Without that knowledge, all our skills, experience, research, and training are effectively handicapped.

Protecting an Investment

When patent holders suspect their patent is being infringed, the communication of a carefully worded cease-and-desist letter, aggressively putting the infringer on notice, and/or the filing of a carefully pleaded patent infringement complaint in a district court is the most important action a patent holder can take. Notice to the infringer, in some cases, is important to preserve all potential claims for damages, including lost profits, and potentially treble damages and attorneys' fees for willful infringement and bad faith. A cease-and-desist letter, however, must be carefully worded to avoid creating a reasonable apprehension of a lawsuit from the perspective of the recipient; otherwise, a recipient (accused infringer) could file for declaratory judgment in a local district court.

Specific notice issues must also be addressed in ANDA litigation. For example, if a Paragraph IV certification letter includes omissions or errors, the patent holder should immediately put the filer on notice to preserve so that it may pursue bad faith claims, including attorneys' fees, against the infringer. *See*, *e.g.*, *Takeda Chemical Industries Ltd. v. Ourlan Laboratories Inc.*, 2006 WL 2686779 (S.D.N.Y. Sept. 20, 2006) (attorneys' fees awarded to patent holder where baseless Paragraph IV certifications filed by defendants, and other litigation misconduct engaged in). Timing of the filing of the infringement suit is important. For example, in ANDA litigation, a new drug application holder and owner of a patent listed in the FDA Orange Book must file an infringement action against the ANDA filer within forty-five days of receiving Paragraph IV notice to obtain a thirty-month stay of the FDA's approval of the ANDA.

The biggest threat to the exclusivity of a patent is a holding of invalidity. Indeed, the patents most likely to require enforcement are patents that block access to a lucrative market. This is because the prospect of large monetary gain from access to the market is frequently used to justify the expense in challenging the proper scope, validity, and enforceability of the patent(s). This is particularly true in the pharmaceutical industry, wherein a successful challenger to a blocking patent listed in the FDA Orange Book is awarded six months of generic market exclusivity.

The Steps of Patent Enforcement

Evaluation of the Patent

A patent to be asserted against an infringer must be evaluated to legally determine the proper scope of the claims (and the remaining term of the grant). The construed claims are then applied to the accused subject matter. If the accused subject matter meets all the limitations of the claims, the patent may properly be asserted.

Claim construction is an issue of law.[14] Claims define the scope of the right to exclude. Claim construction inquiries, therefore, begin and end in all cases with the actual words of the claim.[15] It is a "bedrock principle" of patent law that "the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (*en banc*) citing *Innova/Pure Water Inc. v. Safari Water Filtration Sys. Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004); *Vitronics Corp. v. Conceptronic Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). The written description part of the specification itself does not delimit the right to exclude. That is the function and purpose of claims. "[W]e look to the words of the claims themselves…to define the scope of the patented invention." *Id.*, citing *Markman v. Westview Instruments Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996). It is the person of

[14] *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 970–71, 34 USPQ2d 1321, 1322 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996).

[15] *See, Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313, 63 USPQ 2d 1374 (Fed. Cir. 2002) citing *Renishaw PLC v. Marposs Societa' Per Azioni*, 158 F.3d 1243, 1248, 48 USPQ2d 1117, 1120 (Fed. Cir. 1998).

ordinary skill in the field of the invention through whose eyes the claims are construed. Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of particular claim terms ("the context of the surrounding words of the claim also must be considered in determining the ordinary and customary meaning of those terms"). *Id.*, citing *Vitronics*, 90 F.3d at 1582.

To construe a patent claim, a court principally consults the evidence intrinsic to the patent, namely the claims themselves, the written description, and the prosecution history. A claim term has the meaning the term would have to a person of ordinary skill in the art at the time of the invention. This meaning is ascertained "in the context of the entire patent." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (*en banc*); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 79 USPQ 2d 1705 (Fed. Cir. 2006). Arguments made during prosecution regarding the meaning of a claim term are relevant to the interpretation of that term in every claim of the patent. The prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution. *Atofina v. Great Lakes Chemical Corporation*, 441 F.3d 991, 78 USPQ 2d 1417 (Fed. Cir. 2006) citing *Phillips*, 415 at 1317.

The court, incidentally, must ensure that any reliance on extrinsic evidence, (e.g., dictionaries) accords with the intrinsic evidence. *Atofina v. Great Lakes Chemical Corporation*, 441 F.3d 991, 78 USPQ 2d 1417 (Fed. Cir. 2006), citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (*en banc*). A court should discount any expert testimony that is clearly at odds with the claim construction mandated by the claims themselves, the written description, and the prosecution history, in other words, with the written record of the patent (i.e., the evidence intrinsic to the patent). *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (*en banc*).

Evaluation of the Facts of the Operations of the Suspected Infringer

In the event of an ANDA, since the patent holder and new drug application owner receives a copy of the ANDA, the ANDA must be compared to the proper scope of the subject matter of the patent claims to determine if the filing of the ANDA in fact infringes the patent under 35 U.S.C. §271(e)(2)(A).

This is also important under Federal Rule of Civil Procedure 11 to file a lawsuit.

Efforts should be directed to obtaining all facts that may provide information as to the operations of the suspected infringer, including available descriptions of research and market information. Information may be gleaned from a company's published information and from U.S. government records using the Freedom of Information Act. 5 U.S.C. §552.[16]

Presumption: Product Made by Patented Process

In actions alleging infringement of a process patent based on the importation, sale, offer for sale, or use of a product that is made from a process patented in the United States, if the court finds (1) that a substantial likelihood exists that the product was made by the patented process, and (2) that the plaintiff has made a reasonable effort to determine the process actually used in the production of the product and was unable to so determine, the product shall be presumed to have been so made, and the burden of establishing that the product was not made by the process shall be on the party asserting that it was not so made. 35 U.S.C. §295.

Companies that seek to maintain a current lucrative and exclusive market position through patent protection are most likely to be involved in patent enforcement litigation. Often, industries that are research and development intensive develop and seek to maintain these markets.

After putting the infringer on notice, a patent holder may seek to negotiate a license with the infringer or seek to enforce its patent rights, including the right to seek a permanent injunction against the infringer. Determining the best strategy requires a full analysis of the litigation risks, as discussed below, as well as the business objectives of both the patent holder and the infringer. In some instances, it may be possible to negotiate an appropriate license and achieve royalties, and accept limited competition in the marketplace, particularly where, as described below, there is a serious risk

[16] Upon written request, agencies of the U.S. government are required to disclose those records unless they can be lawfully withheld from disclosure under one of nine specific exemptions in the Freedom of Information Act. This right of access is ultimately enforceable in federal court.

that litigation will result in invalidation of the patent. Thus, both legal and business considerations determine the practical advantages of filing a patent infringement action.

When clients first come to us with patent infringement concerns, we ask if the client is competing in the same market space as the suspected infringer. We ask if the patent is relevant to a current market where the client seeks to maintain exclusivity. We ask if there has been any communication or dealings with the suspected infringer. We then ask for the facts of the patent so we can review the file and the proper scope of the claims, as well as confirm the maintenance and remaining term of the patent. We then evaluate the facts of the operations of the suspected infringer.

We ask if the client is competing in the same market space as the suspected infringer because, depending upon the facts, a suspected infringer may not necessarily be a bad thing for our client's business. We generally try to productively creative a win-win situation if the facts allow our client, for example, to offer a revenue-generating license to the suspected infringer. In some cases, cross-licensing agreements are desirable wherein each party, for example, owns patents that are relevant to the other's business operations. Nevertheless, there are inevitably situations wherein a client must seek to enjoin an infringer from operating within the scope of a patent.

Generally, full discovery of all facts related to the alleged infringer's actions and defenses is necessary to successfully enforce a patent. Because most communications and data storage are now by electronic means, particular care must be taken to aggressively seek and review all electronic documents and data that may lead to the discovery of relevant information. Particular care must be taken to obtain all research data related to any expert opinions proffered in the litigation. Discovery motion practice is often required to obtain electronic discovery, and care must be taken to comply with local rules and practice to protect the record. For example, in rules promulgated by the New Jersey District Court, the parties must consult at the outset of the litigation about their electronic storage systems.

An infringer may also seek to bifurcate the trial and stay discovery on the willfulness issue, arguing that separating the liability issue of validity from willfulness will promote efficiency and convenience, and prevent injustice.

Defendants seek to avoid disclosure of privileged information and waiver of the attorney/client privilege. Courts have used various approaches to resolve this issue, but if the motion to bifurcate is denied, a defendant's failure to provide responsive discovery can subject them to sanctions.

An important issue that must be decided is whether to seek a jury trial or a bench trial (where the judge is the fact finder). Research has shown that of the relatively small percent of patent litigation outcomes that are based on jury findings, patentees have the edge. (Paul M. Janicke and LiLan Ren, "Who Wins Patent Infringement Cases?" *AIPLA Quarterly Journal*, Winter 2006, at FN 63.) Some factors we consider with our clients in deciding to request a jury trial include: Will the jury be impressed with the "ribbon and the seal" on the patent? Is there a home court advantage? Is the case complex and weak, so a jury may even the odds? How often have you observed the judge who is handling the case and his approach to patent litigations? Are there emotional issues or dramatic events that may have a greater impact on a jury? Most often, a party will not have a choice, because a jury trial is selected by at least one party over a bench trial in the majority of patent cases. Approximately 40 percent of cases that reach trial are bench trials, demonstrating that in these cases neither party wanted a jury. (Kimberly A. Moore, "Judges, Juries, and Patent Cases: An Empirical Peek Inside the Black Box," 99 *Michigan Law Review* 365 (2000).)

Preparing for the Markman Hearing

In 1996, the Supreme Court issued its landmark decision in *Markman v. Westview Instruments Inc.*, 116 S. Ct. 1384 (1996), holding that the interpretation of patent claims is an issue of law for a trial judge, not a jury, to decide. This has resulted in the district courts, under various procedures, holding what is commonly referred to as a "*Markman* hearing," where the judge (or a specially appointed master) determines the meaning of the language of the claims. Even prior to filing a lawsuit, thought should be given to hiring the best experts to prepare for the *Markman* hearing.

The outcome of the *Markman* hearing is often dispositive of the entire case, because the interpretation of the claim, or "claim construction," is usually the central issue. After the *Markman* hearing, the successful party usually files a motion for summary judgment on infringement or validity, which is

increasingly being granted by district court judges. Thus, the argument needed to prevail at the *Markman* hearing, in view of the evidence and current authoritative judicial precedent, is key to success in patent litigation.

Patent cases are often won by the legal team that makes the most effective arguments at the *Markman* hearing. From the beginning, the patent litigator must take on the role of educator and determine what will be most effective in convincing a judge of a proffered claim construction. Not only must counsel find a way to give meaning to patent claims, but the meaning must be condensed into a statement and claims chart that will convince a federal judge. Given that most judges are not familiar with the scientific or technological concepts of the patent, the carefully calculated proposed claim construction at the *Markman* hearing becomes the most important positioning event a party can take in patent litigation. *See*, *e.g.*, "The Sedona Conference Working Group on *Markman* Hearings and Claim Construction," *Report on the Markman Process*, 1–14 (June 2006, public comment version).

The entire patent file history must be scrutinized for disclaimed scope or prosecution history *estoppel*. Having construed the claims one way for determining their validity, it is axiomatic that the claims must be construed in the same way for infringement. *W.L. Gore & Assocs. Inc. v. Garlock Inc.*, 842 F.2d 1275, 1279, 6 USPQ2d 1277, 1280-81 (Fed. Cir. 1988). "[I]t is [also] axiomatic that that which would literally infringe if later anticipates it earlier." *Bristol-Myers Squibb v. Ben Venue Laboratories*, 246 F.3d 1368, 58 USPQ2d 1508 (Fed. Cir. 2001). *See*, also, *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1367 (Fed. Cir. 2005); *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 457 F.3d 1293, 79 USPQ 2d 1705 (Fed. Cir. 2006). Full discovery and analysis is the only way to limit risks. The responsive claim construction statement and claims chart similarly must track the evidence, and it is often required that the alleged infringer also indicate whether it will be relying on an "advice of counsel" defense, which would require the production of opinions of counsel in discovery.

Debate between Intrinsic and Extrinsic Evidence

Use of strategic visual and demonstrative evidence to assist the judge in understanding the proffered claim construction is key to helping the judge

understand the arguments and interpret the evidence. If the experts and litigation attorneys can crystallize the case into a single graphic that becomes the focus of the *Markman* hearing, it can help frame the "theme" of the hearing and focus the arguments in a way that favors the party proffering the graphic. Every effort must be made to hone the case down to its core, similar to the way trial attorneys are trained to focus on one theme throughout their presentation to the fact finder.

Because the *Markman* hearing essentially defines the scope of the patent, both as to validity and infringement, the availability of interlocutory appeal has been advocated. District court patent claim interpretations are frequently overturned by the Federal Circuit. For instance, in the period from 1996 to 2003, 35 percent of district court claim interpretations were overturned by the Federal Circuit. (Kimberly Moore, "*Markman* Eight Years Later: Is Claim Construction More Predictable?" 9 *Lewis & Clark Law Review* 231 (2005).) This makes the road to a final conclusion on patent infringement issues a long one.

We counsel our clients at the outset on the various strategic paths during the patent litigation process, and the potential timelines depending on the court the case is filed in. For example, research based on litigation filed in 1995 and 1997 documented that a patent litigation case remains on a court's docket for an average of fifteen months with a median of ten months. However, cases in jurisdictions with "rocket dockets" move much more quickly, skewing the statistics and front-loading litigation costs. In about 25 percent of the cases, summary judgment motions were filed, again reducing the timeline for the litigation. In the study, only 5 percent of filed cases proceeded all the way through to a court ruling on infringement. Another 80 percent of cases settled. Of the remaining 15 percent of cases, one-half (7.5 percent) were resolved on summary judgment and the other half (7.5 percent) went through trial. Around 20 percent of the verdicts resulted in damage awards, which does not take into account settlement payments. (Kesan, Jay P. and Ball, Gwendolyn G., "How Are Patent Cases Resolved? An Empirical Examination of the Adjudication and Settlement of Patent Disputes" University of Illinois Law and Economics Research Paper No. LE05-02.)

Obtaining a Finding of Infringement, Injunctive Relief, and Damages

After the *Markman* hearing, the prevailing party usually files a summary judgment motion and seeks injunctive relief. Until the recent *eBay* decision, the standard adopted by the Federal Circuit for obtaining injunctive relief was a "general rule that courts will issue permanent injunctions against patent infringement absent exceptional circumstances." *See*, *e.g.*, *MercExchange LLC v. eBay Inc.*, 401 F.3d 1323, 1339 (Fed. Cir. 2005). In *eBay Inc. v. MercExchange LLC*, No. 05–130 (May 15, 2006), slip op. 22, the Supreme Court unanimously overturned that standard, holding that district courts in infringement actions must apply the traditional four-factor test for granting an injunction. The court emphasized that "[t]he decision to grant or deny permanent injunctive relief is an act of equitable discretion by the district court, reviewable on appeal for abuse of discretion."

The Supreme Court provided further guidance when it also rejected the district court's "categorical" rule that a patent holder's "lack of commercial activity in practicing the patents" and "willingness to license its patents" sufficed to demonstrate that the patent holder would not suffer irreparable harm in the absence of an injunction. Thus, the court squarely rejected all broad categorical rules in favor of a fact-specific inquiry that takes account of the facts of each particular case. It is much too soon to observe what patterns will emerge as the district courts grapple with how to apply the *eBay* decision to distinct fact patterns. There also will be continued guidance by the Federal Circuit, as appeals are heard.

Damages Issues

Plaintiffs typically seek damages based on a percentage of the value of the entire product, even when the infringing element is only a small part of a larger, unpatented system, increasing settlement pressures.

The standards for willfulness also affect damages issues. The patent law provides that a court may award treble damages and attorneys' fees if it finds that the defendant engaged in willful infringement. The standard applied is whether "a potential infringer ha[d] actual notice of another's patent rights" and failed to satisfy his or her "affirmative duty to exercise due care to determine whether or not he is infringing." *Knorr-Bremse*

Systeme Fuer Nutzfahrrzeuge Gmbh v. Dana, 383 F.3d 1337, 1343 (Fed. Cir. 2004) (Dyk, J., concurring in part and dissenting in part) (citation and internal quotation marks omitted). The court in exceptional cases may award reasonable attorney fees to the prevailing party. 35 U.S.C. §285.

Protection from claims of willful infringement may be sought by obtaining a competent and well-reasoned opinion of counsel that states the analysis and concludes non-infringement and/or that the relevant claims are invalid. Parties, however, must be counseled to calculate the risk to waive the attorney/client privilege requiring disclosure of attorney-prepared materials. We advise clients, at times, depending upon the facts, to avoid draconian results by moving to bifurcate the liability and damages phase of a proceeding.

Facing the decision of whether to disclose an opinion and incur the risk of waiving attorney/client privilege is a common dilemma, because such claims of willful infringement have been found to be asserted in more than 90 percent of all infringement claims. (Kimberly A. Moore, "Empirical Statistics on Willful Patent Infringement," 14 Fed. Cir. B. J. 227, 232 (2004).)

The effect of an injunction against a potential patent infringer is dramatic. It may put a competitor out of business or seriously impact its profitability. Or, as Justice Kennedy observed in the *eBay* case, "[A]n industry has developed in which firms use patents not as a basis for producing and selling goods but, instead, primarily for obtaining licensing fees. For these firms, an injunction, and the potentially serious sanctions arising from its violation, can be employed as a bargaining tool to charge exorbitant fees to companies that seek to buy licenses to practice the patent." *Id.* at 2 (Kennedy, J., concurring).

Failure or Success in Enforcement

A most confusing aspect of patent enforcement for many clients is the fact that patents merely provide the right to exclude others from practicing what is claimed. A patent does not provide the right to practice what is claimed. A broad third-party patent that encompasses a certain commercial embodiment does not necessarily preclude the patentability of

that commercial embodiment. However, to practice the commercial embodiment, the proprietor of that commercial embodiment, even if patented, may need to seek a license, for example, from the holder of the broad patent or challenge the validity (seek freedom to operate).

There are several reasons why a patent holder is not successful in patent enforcement cases. One cause of failure comes from frequent, albeit subtle, changes in the judicial interpretation of the statutory requirements for patentability. Another is that issued claims may be too broad. Overly broad claims may be found to encompass something that previously existed. Claims that encompass actual commercial embodiments may not exist in the patent. Problems also exist when statements made during the prosecution phase of a case are construed to limit the scope of the claims, which then surrenders coverage of the subject matter of interest.[17] It is therefore now even more apparent that, to reduce the risk of invalidity in view of a *de jour* Federal Circuit decision, claims should be articulated in different ways to capture various aspects and perspectives of the invention within the same application. As succinctly stated in the *Exxon Inc. v. Lubrizol Corp.* concurring opinion, "[W]e are not free to read the claims as they might have been drafted, even if as drafted they do not accomplish what the inventor may have intended."[18]

Patent claims, to be valid and enforceable, fundamentally, cannot describe anything that has previously existed, regardless of whether it was known to exist. *Knowledge* of an inherent characteristic in the prior art is

[17] As articulated in *Markman*, "[C]ommonly the claims are drafted by the inventor's patent solicitor and they may even be drafted by the patent examiner in an examiner's amendment (subject to the approval of the inventor's solicitor). While presumably the inventor has approved any changes to the claim scope that have occurred via amendment during the prosecution process, it is not unusual for there to be a significant difference between what an inventor thinks his patented invention is and what the ultimate scope of the claims is after allowance by the PTO…the focus is on the objective test of what one of ordinary skill in the art at the time of the invention would have understood the term to mean. 52 F.3d 967, 985, 34 USPQ2d 1321, 1335 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370, 38 USPQ2d 1461 (1996).

[18] 64 F.3d 1553, 35 USPQ2d 1801, 1808 (Fed. Cir. 1995) (Plager, J., concurring), *cert. denied*, 116 S. Ct. 2554 (1996).

irrelevant.[19] This clarification of the doctrine of inherent anticipation was recently decided by the Federal Circuit in the case of *Schering v. Geneva* wherein the court held that a patent claim that structurally described a metabolite of loratadine (Claritin®) was inherently anticipated and hence invalid. 339 F.3d 1373 (Fed. Cir. 2003). The metabolite, descarboethoxyloratadine, is formed in the patient's body upon ingestion of loratadine. Since the claim would theoretically have precluded, for example, the prior administration of loratadine, the subject matter of the claim was found to be anticipated (i.e., "[T]hat which would literally infringe if later in time anticipates if earlier," *Schering* citing *Bristol-Ourers Squibb Co. v. Ben Venue Labs. Inc.*, 246 F.3d 1368, 1378 (Fed. Cir. 2001).)[20]

Generally, the applicant must convey in the written description of the invention, with reasonable clarity to those skilled in the art, as of the filing date, *possession* of the invention as claimed. The written description requirement does not require the applicant to describe every embodiment within the scope of the subject matter claimed; however, the description must clearly allow persons of ordinary skill in the art to recognize that what is claimed was in fact conceived.[21] Conception is the "formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice." An idea is sufficiently definite and permanent for conception if it provides one skilled in the art with enough guidance to "understand the invention," that is, "when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue." The

[19] *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373 (Fed. Cir. 2003); *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331 (Fed. Cir. 2005); *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1367 (Fed. Cir. 2005).

[20] *Bristol-Myers Squibb v. Ben Venue Laboratories*, 246 F.3d 1368, 58 USPQ2d 1508 (Fed. Cir., April 20, 2001) (inherent anticipation wherein *efficacy* was not previously realized); *Eli Lilly & Co. v. Barr Laboratories, Inc.*, 251 F.3d 955, 58 USPQ2d 1865 (Fed. Cir. 2001) (inherent anticipation wherein *mechanistic property* was not previously realized); *Verdegaal Brothers, Inc. v. Union Oil Company of California*, 814 F.2d 628, 2 USPQ2d 1051 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 827 (1987).

[21] *Moba v. Diamond*, 325 F.3d 1306, 66 USPQ2d 1429 (Fed. Cir. 2003); *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004), *rehearing denied* 375 F.3d 803, *cert denied* 543 U.S. 1015 (2004).

inventor must be able to "describe his invention with particularity." *Invitrogen Corp. v. Clontech Labs. Inc.*, 429 F.3d 1052 (Fed. Cir. 2005).

The *Rochester* decision has recently made it clear under the requirement for written description, however, that genera of small molecule compounds are not properly defined only in terms of their ability to antagonize, for example, a defined activity of a fully characterized biological molecule. A claimed genus may be satisfied through sufficient description of functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004), *rehearing denied* 375 F.3d 803, *cert denied* 543 U.S. 1015 (2004); Guidelines, 66 Fed. Reg. at 1106 (emphasis added). The plaintiff's scientists were the first to identify and characterize the biological enzymes COX1 and COX2 and to recognize the pharmacological value of the prospective ability to antagonize the elucidated biological mechanism of COX2 without affecting the activity of COX1. Although the scientists had indeed made an elegant and valuable discovery by identifying a distinct pharmacological problem as well as a path to solving that problem (i.e., compound collection screening assay(s)), no means, *per se*, of antagonizing COX2 without affecting the activity of COX1 was disclosed. Nevertheless, a claim issued to a "method for selectively inhibiting PGHS-2 [COX-2] activity in a human host" in which "the activity of PGHS-1 [COX-1] is not inhibited." The patentee asserted their claim against the proprietors of the compound Celebrex® (celecoxib) (antagonist of COX2 but not COX1) and argued *inter alia* that "no written description requirement exists independent of enablement." Importantly, the court stated, *inter alia*, that although "an invention may be enabled even though it has not been described…the description must convey what the compound is, not just what it does." *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004), *rehearing denied* 375 F.3d 803, *cert denied* 543 U.S. 1015 (2004).

The guidelines adopted by the Federal Circuit state that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics (i.e., structure or other physical and/or chemical

properties) by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means the species that are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. For inventions in an unpredictable art, adequate written description of a genus that embraces widely variant species cannot be achieved by disclosing only one species within the genus. *Invitrogen Corp. v. Clontech Labs. Inc.*, 429 F.3d 1052 (Fed. Cir. 2005).

The courts have made it clear that, to enable the scope of a claimed invention under 35 U.S.C. §112, a specification must provide more than an invitation to experiment.[22] The Federal Circuit stated in *Genentech Inc. v. Novo Nordisk*, for example, "A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Tossing out the mere germ of an idea does not constitute *enabling* disclosure…Genentech is attempting to bootstrap a vague statement of a problem into an enabling disclosure sufficient to dominate someone else's solution of the problem. This it cannot do."[23]

The requirement that the claims "particularly point out and distinctly claim" the invention is met when a person of ordinary skill in the art understands the scope of the subject matter when reading the claim in conjunction with the rest of the specification. *Default Proof Credit Card Sys. Inc. v. Home Depot U.S.A. Inc.*, 412 F.3d 1291, 1298 (Fed. Cir. 2005). Patent claims may not create zones of uncertainty into which others may enter only at the risk of infringement; "[t]o sustain claims so indefinite as not to give the notice required by the statute would be in direct contravention of the public interest which Congress therein recognized and sought to protect."[24] The primary purpose of the

[22] *Enzo Biochem, Inc., v. Calgene, Inc.*, 188 F.3d 1362, 1374, 52 USPQ2d 1129, 1138 (Fed. Cir. 1999).

[23] 108 F.3d 1361, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997) (emphasis added).

[24] *United Carbon Co. v. Binney & Smith Co.*, 317 U.S. 228, 233, 55 USPQ 381, 384 (1942).

requirement of definiteness in claims under 35 U.S.C. §112, Paragraph 2, is to provide clear warning to others as to what constitutes infringement of the patent.

If one employs means-plus-function language in a claim, one must set forth in the specification an adequate disclosure showing what is meant by that language. If an applicant fails to set forth an adequate disclosure, the applicant has in effect failed to particularly point out and distinctly claim the invention as required by the second paragraph of §112. *Default Proof Credit Card Sys. Inc. v. Home Depot U.S.A. Inc.*, 412 F.3d 1291, 1298 (Fed. Cir. 2005).[25]

Successful enforcement of a patent must begin before there is any suspected infringement. We advise clients to do several things:

- Claim the invention in a range of breadth claims (i.e., broad, medium, and narrow).
- Describe the invention from different perspectives. Carefully define in the written description of the invention all terms used in the claims.
- Comply with the duty of disclosure (i.e., to disclose all information that could be material to the patentability of the subject matter during the prosecution of the application for patent).

One of our most difficult patent enforcement cases involved an ANDA litigation matter wherein asserted claims were fundamentally drawn to a drug delivery device that accomplished a certain well-characterized function. The difficulty came from the fact that the claims were limited to certain elements defined in broad terms of structure and composition that, in unison, accomplished a specified function. Since the accused product accomplished the same function and met all the limitations of the claims

[25] A claim term that does not use "means" will trigger the rebuttable presumption that §112 Paragraph 6 does not apply. This presumption can be overcome by pointing to evidence that a claim term connotes sufficient structure to avoid application of §112 Paragraph 6. "We have held that it is sufficient if the claim term is used in common parlance or by persons of skill in the pertinent art to designate structure, even if the term covers a broad class of structures and even if the term identifies the structures by their function." *MIT v. Abacus Software*, Fed. Cir. 05-1142-1163 (decided September 13, 2006).

per our proffered construction, it infringed. The result can be attributed to the *Markman* hearing, simplified presentation, and judicial attention.

The Law Affecting Enforcement and Infringement

Several laws support patent holders in enforcement cases. (See Appendix A for additional examples.) These include:

35 U.S.C. §271 Infringement

(a) Whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States, or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.

(b) Whoever actively induces infringement of a patent shall be liable as an infringer.

(c) Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination, or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use, shall be liable as a contributory infringer.

(e)(2) It shall be an act of infringement to submit (A) an [ANDA] application under §505(j) of the Federal Food, Drug, and Cosmetic Act or described in §505(b)(2) of such act for a drug claimed in a patent or the use of which is claimed in a patent.

(g) Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during the term of such process patent…A product which is made by a patented process will, for purposes of this title, not be considered to be so made after—

(1) it is materially changed by subsequent processes; or

(2) it becomes a trivial and non-essential component of another product.

35 U.S.C. §295

In actions alleging infringement of a process patent based on the importation, sale, offered for sale, or use of a product which is made from a process patented in the United States, if the court finds—

(1) that a substantial likelihood exists that the product was made by the patented process, and

(2) that the plaintiff has made a reasonable effort to determine the process actually used in the production of the product and was unable so to determine, the product shall be presumed to have been so made, and the burden of establishing that the product was not made by the process shall be on the party asserting that it was not so made.

35 U.S.C. §282 Presumption of Validity

A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim.

Because a patent carries a statutory presumption of validity, 35 U.S.C. §282, the challenger has the burden of showing by clear and convincing evidence, after all reasonable inferences are drawn in its favor, that the patent claim is invalid. *Monsanto v. Scruggs*, 459 F.3d 1328, 79 USPQ 2d 1813 (Fed. Cir. 2006), citing *WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1355 (Fed. Cir. 1999). Anticipation, however, is a question of fact answered by the clear and convincing evidence. *See*, *e.g.*, *SmithKline Beecham Corp. v. Apotex Corp.* wherein the Federal Circuit fundamentally held that the superior chemical compound was inherently anticipated, due to the fact that it

existed, even though it may not have been previously detectable. 403 F.3d 1331 (Fed. Cir. 2005).

These laws are helpful in enforcement because the burden is high for a defendant in a patent infringement case. Invalidity must be shown by clear and convincing evidence.

Conversely, there are also laws that help patent infringers defend against patent enforcement.

Congress amended the patent laws in 1984, for example, to insulate drug research from charges of infringement so long as the research is "reasonably related to the development and submission of information" to the FDA.

35 U.S.C. §271(e)(1)

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States 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…

The U.S. Supreme Court recently clarified the scope of the statute in *Merck KGaA v. Integra Lifesciences LTD*. Particularly clarified was that the use of compounds in preclinical studies is protected under §271(e)(1) if there is a reasonable basis to believe the compound tested could be the subject of an FDA submission and the experiments will produce the types of information relevant to an investigational new drug application or new drug application. The statutory language makes clear that §271(e)(1) provides a wide berth for the use of compounds in activities related to the federal regulatory process, including uses reasonably related to the development and submission of *any* information under the Food, Drug, and Cosmetic Act. 545 U.S. 193, 74 USPQ 2d 1801 (2005); *Eli Lilly & Co. v. Medtronic Inc.*, 496 U.S. 661, 665–669, 674 (1990). This necessarily includes preclinical studies, both those pertaining to a drug's safety in humans and those related to, for example, a drug's efficacy and mechanism of action. "There is simply no room in the statute for excluding certain information from the exemption on the basis

of the phase of research in which it is developed or the particular submission in which it could be included." *Merck KGaA v. Integra Lifesciences LTD*, 545 U.S. 193, 74 USPQ 2d 1801 (2005). §271(e)(1), accordingly, exempts from infringement the use of compounds in preclinical research, even when the compounds do not themselves become the subject of an FDA submission. Further, the use of a compound in experiments not themselves included in a "submission of information" to the FDA does not, standing alone, render the use infringing. *Id.*

35 U.S.C. 286 Time Limitation on Damages

Except as otherwise provided by law, no recovery shall be had for any infringement committed more than six years prior to the filing of the complaint or counterclaim for infringement in the action.

This statute is particularly relevant in the drug discovery industry wherein research tools are generally applied early in the discovery stage (i.e., during lead identification of compounds). Development compounds generally require, however, about ten to twelve years to bring to market.

Antitrust Issues

The fundamental question of Federal Circuit antitrust law is whether or when a patentee's behavior in either procuring or enforcing a patent can give rise to antitrust liability. As a general rule, behavior conforming to the patent laws enjoys immunity from the antitrust laws.[26, 27] A patentee may be

[26] Whether a patentee's conduct in procuring or enforcing a patent is sufficient to strip the patentee of its immunity from the antitrust laws is decided under the law of the Federal Circuit. *See Nobelpharma AB v. Implant Innovations*, 141 F.3d 1059, 1068 (Fed. Cir. 1998). However, the law of the appropriate regional federal circuit continues to apply to "issues involving other elements of antitrust law such as relevant market, market power, damages, etc." *Nobelpharma AB v. Implant Innovations*, 141 F.3d at 1068.

[27] Under the *Noerr-Pennington* doctrine, a party who petitions the government for redress generally is immune from antitrust liability. *See Eastern R.R. Presidents Conference v. Noerr Motor Freight*, 365 U.S. 127 (1961); *United Mine Workers v. Pennington*, 381 U.S. 657 (1965). The doctrine has been "expanded to include litigation to protect such rights as patents." *Organon, Inc. v. Teva Pharmaceuticals USA, Inc.*, 293 F. Supp.2d 453, 457 (D.N.J. 2003) (citing *Professional Real Estate Investors v. Columbia Pictures Industries, Inc.*, 508 U.S. 49, 60 (1993)).

subject to antitrust liability, however, for the filing of a patent infringement action if the patentee obtained its patent by fraud or if the patent infringement action is a sham.

A patentee who brings an infringement action may be subject to antitrust liability for the anti-competitive effects of that action only if the alleged patent infringer proves: (1) that the asserted patent was obtained through knowing and willful fraud within the meaning of *Walker Process Equipment Inc. v. Food Machinery & Chemical Corp.*, 382 U.S. 172, 177 (1965) (the patentee obtained the patent by knowingly and willfully misrepresenting facts to the U.S. Patent and Trademark Office);[28] or (2) that the infringement action was a mere sham[29] to cover an attempt to directly interfere with the business relationships of a competitor. *See Glass Equipment Development Inc. v. Besten Inc.*, 174 F.3d 1337, 1343 (Fed. Cir. 1999); *Nobelpharma*, 141 F.3d at 1068.

Patent Misuse

The doctrine of patent misuse is a method of limiting abuse of patent rights separate from the antitrust laws. The doctrine is an affirmative defense that evolved from the equitable doctrine of unclean hands. The key inquiry under this fact-intensive analysis is whether the patentee has impermissibly broadened the scope of the patent grant with anti-competitive effect.[30] When used successfully, this defense results in

[28] Good faith attempts to behave in accordance with the patent laws should furnish a complete defense to retain antitrust exemption (e.g., an attempt to enforce a patent right the patentee reasonably believes itself to possess). *Walker Process Equip., Inc. v. Food Mach. & Chem. Corp.*, 382 U.S. 172, 174 (1965). In order to prevail on a *Walker Process* claim, the claimant must therefore establish: that the patentee attempted to enforce the patent; that the patent issued because the patentee defrauded the Patent and Trademark Office; that the patentee's attempted enforcement threatened to lessen competition in a relevant antitrust market; that the claimant suffered antitrust damages; and that all other elements of attempted monopolization are met. *Id.* These requirements frame the antitrust inquiry.

[29] The patent infringement action must be objectively baseless in the sense that no reasonable litigant could realistically expect success on the merits. *Professional Real Estate Investors, Inc. v. Columbia Pictures Industries, Inc.*, 508 U.S. 49, 61 (1993).

rendering the patent unenforceable until the misuse is purged. It does not, however, result in an award of damages to the accused infringer. If "the practice has the effect of extending the patentee's statutory rights and does so with an anti-competitive effect…the finder of fact must decide whether the questioned practice imposes an unreasonable restraint on competition…" *Virginia Panel*, 133 F.3d at 869.

Laches **and** ***Estoppel***

To successfully invoke *laches*, a defendant must prove that the plaintiff delayed filing suit an unreasonable and inexcusable length of time after the plaintiff knew or reasonably should have known of its claim against the defendant and that the delay resulted in material prejudice to the defendant. The *laches* defense has two underlying elements: first, the patentee's delay in bringing suit must be "unreasonable and inexcusable," and second, the alleged infringer must have suffered "material prejudice attributable to the delay." *Intirtool Ltd. v. Texar Corp.*, 369 F.3d 1289, 1297, 70 USPQ2d 1780 (Fed. Cir. 2004). The length of time that may be deemed unreasonable has no fixed boundaries, but rather depends on the circumstances of the case. A presumption of *laches* arises if the patentee delays bringing suit for more than six years after actual or constructive knowledge of the defendant's infringing activity. *State Contracting & Engineering Corp. v. Condotte America, Inc.*, 346 F.3d 1057, 68 USPQ2d 1481 (Fed. Cir. 2003).

The defense of *estoppel* bars recovery for infringement when the owner represents that the patent will not be enforced against the infringer and the infringer reasonably relies on that representation and infringer will be materially prejudiced if the patentee is allowed to proceed with the claim.

Litigation is often the only choice. Not only may it be the only opportunity to maintain and enforce strategic market exclusivity, but it has the incidental but important feature of putting other potential

[30] *Monsanto v. Scruggs,* 459 F.3d 1328, 79 USPQ 2d 1813 (Fed. Cir. 2006). The "policy of the patent misuse doctrine is to prevent a patentee from using the patent to obtain market benefit beyond that which inures in the statutory patent right." *Monsanto Co. v. McFarling,* 363 F.3d 1336, 1341 (Fed. Cir. 2004) quoting *Mallinckrodt,* 976 F.2d at 704 (Fed. Cir. 1992). A court of equity will not lend its support to enforcement of a patent that has been misused. *See*, *Senza-Gel Corp. v. Seiffhart,* 803 F.2d 661, 668, 231 USPQ 363, 368 (Fed. Cir. 1986).

infringers on notice of the consequences of infringement. Another benefit is that litigation can fundamentally secure a declaration of the patent's validity and scope.

However, litigation poses serious risks. It is difficult to predict the outcome of such litigation, because judges and juries frequently have little, if any, knowledge of the industry or scientific background to evaluate scientific and technical information. In fact, litigation frequently results in a judicial determination that the patent is invalid. Thus, a patent holder has to weigh the benefits against the disadvantages of filing a patent infringement lawsuit.

It is often difficult to predict the outcome of an infringement trial, since the trial judge will make legal rulings and the jury makes findings of fact before reaching a verdict. Thereafter, if there is an appeal, it is again difficult to predict the course of the appeal, since many areas of patent law are undergoing evolution as the Federal Circuit and the Supreme Court continue to shape the law and how it is applied to the complex fact patterns of each patent case.

To begin patent litigation requires filing a carefully pleaded complaint in district court based on a full examination of the facts available and a review of litigation risk issues. A very important strategic decision is where to file patent litigation. Generally, courts that reside in districts where the subject matter industry is dominant are most familiar with issues characteristic of the industry. About 65 percent of all cases are filed in ten district courts, and these courts have the most familiarity with patent matters. *See*, *e.g.*, Kimberly A. Moore, "Forum Shopping in Patent Cases: Does Geographic Choice Affect Innovation? 79 *N.C.L. Review* 934 (2001). The ten district courts are: Northern District of California, Central District of California, Southern District of New York, Northern District of Illinois, District of Massachusetts, District of Delaware, Southern District of Florida, Eastern District of Virginia, District of New Jersey, and District of Minnesota.

In the past ten years, there have been several major changes in the laws affecting patents. Claim construction is now a matter of law for the judge to decide. The authoritative judicial interpretation of the statutory

requirements for patentability have evolved significantly, particularly the requirements of novelty 35 U.S.C. §102 (doctrine of inherent anticipation) and written description 35 U.S.C. §112, Paragraph 1. These changes affect the patent holder's ability to maintain and enforce strategic market exclusivity. The claims must fundamentally be construed to avoid anticipation as well as to encompass subject matter that was sufficiently described in the specification. Thus, familiarity with the judges who will hear patent cases in a particular district court is important in terms of shaping how claim construction, for example, is presented. Given that the Federal Circuit determines that the district court judges improperly construe patent claim terms in 33 percent of the cases appealed, it becomes even more important that the claims presentation to the district court judge be presented in such a manner that the court's findings are more likely to withstand appeal. (Kimerly A. Moore, "Are District Court Judges Equipped to Resolve Patent Cases?" 12 Fed. Circuit B.J. 1 (2002).)

Education and patience are powerful tools when it comes to enforcement as well as dealing with defense issues. We counsel innovators in understanding the current authoritative judicial precedent to leverage discovery assets and to maintain and enforce strategic market exclusivity. As succinctly stated in the *Exxon Inc. v. Lubrizol Corp.* concurring opinion, "we are not free to read the claims as they might have been drafted, even if as drafted they do not accomplish what the inventor may have intended."[31]

[31] 64 F.3d 1553, 35 USPQ2d 1801, 1808 (Fed. Cir. 1995) (Plager, J., concurring), *cert. denied*, 116 S. Ct. 2554 (1996).

Patrick H. Higgins *is a shareholder in the Princeton office of the international law firm, Buchanan Ingersoll & Rooney PC. Mr. Higgins practices intellectual property law in the pharmaceutical industry, i.e., leveraging discovery assets toward developing and maintaining market exclusivity, managing closely related FDA issues, opinion work, due diligence matters, and abbreviated new drug application (ANDA) litigation. His focus is the evaluation, development, enforcement, and defense of rights in the drug-discovery industry.*

Prior to joining Buchanan, Mr. Higgins was a partner in the Princeton office of an East Coast-based law firm, where his practice concentrated on strategic portfolio development, evaluation of third-party rights in the pharmaceutical industry and ANDA litigation. Before that he was a senior attorney for AstraZeneca, responsible for strategic portfolio development, risk evaluation, and due diligence matters.

Before entering law school, Mr. Higgins worked as a research scientist in the industry. His scientific background and knowledge of the industry enables him to work with clients ranging from small biotech companies to large pharmaceutical corporations in leveraging drug discovery assets and resolving freedom-to-operate issues, as well as evaluating and maintaining market exclusivity.

Mr. Higgins is a member of the Biotechnology Council of New Jersey, the New Jersey Intellectual Property Law Association, the American Intellectual Property Law Association, and the Philadelphia Intellectual Property Law Association. He was awarded the Global Director of Research Award from a major pharmaceutical company. He is admitted to practice in Pennsylvania and California, as well as before the U.S. Court of Appeals for the Federal Circuit and the U.S. Patent and Trademark Office.

Mary Sue Henifin *is a shareholder in the Princeton office of the law firm of Buchanan Ingersoll & Rooney PC. As a member of the firm's commercial litigation section, she focuses her practice on intellectual property matters, particularly on the enforcement and defense of rights. In addition to providing risk advice to her clients, she frequently prosecutes and defends cases in both federal and state courts. Ms. Henifin writes and lectures frequently on the use of expert witnesses and other trial evidence issues, including to state and federal bar and judicial organizations across the country. She has chaired programs for the Institute of Continuing Legal Education on litigation and expert witness issues.*

She has co-authored chapters on toxicology and medical testimony for the Reference Manual on Scientific Evidence*, a treatise for federal court judges published by the Federal Judicial Center, which is frequently cited in both state and federal court opinions. She also co-authored the* New Jersey Trial and Evidence Treatise. *Martindale-Hubble has awarded her an AV rating, which identifies a lawyer with very high to pre-eminent legal ability. Ms. Henifin served as chair and is a member of the Lawyer's Advisory Committee to the Federal District Court for the District of New Jersey. She is a trustee of the Association of the Federal Bar of the State of New Jersey. She was appointed adjunct assistant professor at the Robert Wood Johnson Medical School, and was awarded the Adjunct Professor of the Year Award.*

Ms. Henifin has represented pharmaceutical companies in bringing patent infringement claims against multiple parties based on defendants submittal of ANDAs to the FDA seeking approval to engage in manufacture and sale of generic versions of prescription drugs.

Prior to joining Buchanan, Ms. Henifin was a partner with a large, Princeton-based international firm. Before that, she was an attorney with the New York office of an international firm. From 1989 to 1992, she served as a deputy attorney general for the state of New Jersey.

Ms. Henifin received a J.D. degree with honors from Rutgers University School of Law, where she served as research editor of the Law Review. After law school, she was a clerk for the Honorable Dickinson R. Debevoise of the U.S. District Court for the District of New Jersey. She graduated from Harvard College, cum laude, with a B.A. in biology, and she holds a master's of public health degree from Columbia University. Ms. Henifin is admitted to practice in New Jersey and New York.

Appendices

CONTENTS

APPENDIX A

PATENT STATUTES LIST

35 U.S.C. §100 Definitions.

When used in this title unless the context otherwise indicates -

(a) The term "invention" means invention or discovery.

(b) The term "process" means process, art, or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material.

(c) The terms "United States" and "this country" mean the United States of America, its territories and possessions.

(d) The word "patentee" includes not only the patentee to whom the patent was issued but also the successors in title to the patentee.

(e) The term "third-party requester" means a person requesting ex parte reexamination under section 302 or inter partes reexamination under section 311 who is not the patent owner.

35 U.S.C. §101 Inventions patentable.

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

35 U.S.C. §102 Conditions for patentability; novelty and loss of right to patent.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, or

(c) he has abandoned the invention, or

(d) the invention was first patented or caused to be patented, or was the subject of an inventor's certificate, by the applicant or his legal representatives or assigns in a foreign country prior to the date of the application for patent in this country on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or

(e) the invention was described in - (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language; or

(f) he did not himself invent the subject matter sought to be patented, or

(g)(1) during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

35 U.S.C. §103 Conditions for patentability; non-obvious subject matter.

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(b)

(1) Notwithstanding subsection (a), and upon timely election by the applicant for patent to proceed under this subsection, a biotechnological process using or resulting in a composition of matter that is novel under section 102 and non-obvious under subsection (a) of this section shall be considered non-obvious if-

(A) claims to the process and the composition of matter are contained in either the same application for patent or in separate applications having the same effective filing date; and

(B) the composition of matter, and the process at the time it was invented, were owned by the same person or subject to an obligation of assignment to the same person.

(2) A patent issued on a process under paragraph (1)-

(A) shall also contain the claims to the composition of matter used in or made by that process, or

(B) shall, if such composition of matter is claimed in another patent, be set to expire on the same date as such other patent, notwithstanding section 154.

(3) For purposes of paragraph (1), the term "biotechnological process" means-

(A) a process of genetically altering or otherwise inducing a single- or multi-celled organism to-

(i) express an exogenous nucleotide sequence,

(ii) inhibit, eliminate, augment, or alter expression of an endogenous nucleotide sequence, or

(iii) express a specific physiological characteristic not naturally associated with said organism;

(B) cell fusion procedures yielding a cell line that expresses a specific protein, such as a monoclonal antibody; and

(C) a method of using a product produced by a process defined by subparagraph (A) or (B), or a combination of subparagraphs (A) and (B).

(c)

(1) Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.

(2) For purposes of this subsection, subject matter developed by another person and a claimed invention shall be deemed to have been owned by the same person or subject to an obligation of assignment to the same person if -

(A) the claimed invention was made by or on behalf of parties to a joint research agreement that was in effect on or before the date the claimed invention was made;

(B) the claimed invention was made as a result of activities undertaken within the scope of the joint research agreement; and

(C) the application for patent for the claimed invention discloses or is amended to disclose the names of the parties to the joint research agreement.

(3) For purposes of paragraph (2), the term "joint research agreement" means a written contract, grant, or cooperative agreement entered into by two or more persons or entities for the performance of experimental, developmental, or research work in the field of the claimed invention.

35 U.S.C. §112 Specification.

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A claim may be written in independent or, if the nature of the case admits, in dependent or multiple dependent form.

Subject to the following paragraph, a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

A claim in multiple dependent form shall contain a reference, in the alternative only, to more than one claim previously set forth and then specify a further limitation of the subject matter claimed. A multiple dependent claim shall not serve as a basis for any other multiple dependent claim. A multiple dependent claim shall be construed to incorporate by reference all the limitations of the particular claim in relation to which it is being considered.

An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.

35 U.S.C. §271 Infringement of patent.

(a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States, or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.

(b) Whoever actively induces infringement of a patent shall be liable as an infringer.

(c) Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination, or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use, shall be liable as a contributory infringer.

(d) No patent owner otherwise entitled to relief for infringement or contributory infringement of a patent shall be denied relief or deemed guilty of misuse or illegal extension of the patent right by reason of his having done one or more of the following: (1) derived revenue from acts which if performed by another without his consent would constitute contributory infringement of the patent; (2) licensed or authorized another to perform acts which if performed without his consent would constitute contributory infringement of the patent; (3) sought to enforce his patent rights against infringement or contributory infringement; (4) refused to license or use any rights to the patent; or (5) conditioned the license of any rights to the patent or the sale of the patented product on the acquisition of a license to rights in another patent or purchase of a separate product, unless, in view of the circumstances, the patent owner has market power in the relevant market for the patent or patented product on which the license or sale is conditioned.

(e)

> (1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is

primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) 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 or veterinary biological products.

(2) It shall be an act of infringement to submit -

> (A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent, or
>
> (B) an application under section 512 of such Act or under the Act of March 4, 1913 (21 U.S.C. 151 - 158) for a drug or veterinary biological product which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques and which is claimed in a patent or the use of which is claimed in a patent, if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug or veterinary biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

(3) In any action for patent infringement brought under this section, no injunctive or other relief may be granted which would prohibit the making, using, offering to sell, or selling within the United States or importing into the United States of a patented invention under paragraph (1).

(4) For an act of infringement described in paragraph (2)-

> (A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed,
>
> (B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or

sale within the United States or importation into the United States of an approved drug or veterinary biological product, and

(C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug or veterinary biological product. The remedies prescribed by subparagraphs (A), (B), and (C) are the only remedies which may be granted by a court for an act of infringement described in paragraph (2), except that a court may award attorney fees under section 285.

(5) Where a person has filed an application described in paragraph (2) that includes a certification under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), and neither the owner of the patent that is the subject of the certification nor the holder of the approved application under subsection (b) of such section for the drug that is claimed by the patent or a use of which is claimed by the patent brought an action for infringement of such patent before the expiration of 45 days after the date on which the notice given under subsection (b)(3) or (j)(2)(B) of such section was received, the courts of the United States shall, to the extent consistent with the Constitution, have subject matter jurisdiction in any action brought by such person under section 2201 of title 28 for a declaratory judgment that such patent is invalid or not infringed.

(f)

(1) Whoever without authority supplies or causes to be supplied in or from the United States all or a substantial portion of the components of a patented invention, where such components are uncombined in whole or in part, in such manner as to actively induce the combination of such components outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(2) Whoever without authority supplies or causes to be supplied in or from the United States any component of a patented invention that is especially made or especially adapted for use in the invention and not a staple article or commodity of commerce suitable for substantial non-infringing use, where such component is uncombined in whole or in part, knowing that such component is so made or adapted and intending that such component will be combined outside of the United States in a manner that would infringe the patent if such combination occurred within the United States, shall be liable as an infringer.

(g) Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during the term of such process patent. In an action for infringement of a process patent, no remedy may be granted for infringement on account of the noncommercial use or retail sale of a product unless there is no adequate remedy under this title for infringement on account of the importation or other use, offer to sell, or sale of that product. A product which is made by a patented process will, for purposes of this title, not be considered to be so made after -

(1) it is materially changed by subsequent processes; or

(2) it becomes a trivial and nonessential component of another product.

(h) As used in this section, the term "whoever" includes any State, any instrumentality of a State, any officer or employee of a State or instrumentality of a State acting in his official capacity. Any State, and any such instrumentality, officer, or employee, shall be subject to the provisions of this title in the same manner and to the same extent as any nongovernmental entity.

(i) As used in this section, an "offer for sale" or an "offer to sell" by a person other than the patentee or any assignee of the patentee, is that in which the sale will occur before the expiration of the term of the patent.

35 U.S.C. §282 Presumption of validity; defenses.

A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. Notwithstanding the preceding sentence, if a claim to a composition of matter is held invalid and that claim was the basis of a determination of non-obviousness under section 103(b)(1), the process shall no longer be considered non-obvious solely on the basis of section 103(b)(1). The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.

The following shall be defenses in any action involving the validity or infringement of a patent and shall be pleaded:

> (1) Non-infringement, absence of liability for infringement, or unenforceability,
>
> (2) Invalidity of the patent or any claim in suit on any ground specified in part II of this title as a condition for patentability,
>
> (3) Invalidity of the patent or any claim in suit for failure to comply with any requirement of sections 112 or 251 of this title,
>
> (4) Any other fact or act made a defense by this title.

In actions involving the validity or infringement of a patent the party asserting invalidity or non-infringement shall give notice in the pleadings or otherwise in writing to the adverse party at least thirty days before the trial, of the country, number, date, and name of the patentee of any patent, the title, date, and page numbers of any publication to be relied upon as anticipation of the patent in suit or, except in actions in the United States Court of Federal Claims, as showing the state of the art, and the name and address of any person who may be relied upon as the prior inventor or as having prior knowledge of or as having previously used or offered for sale the invention of the patent in suit. In the absence of such notice proof of the said matters may not be made at the trial except on such terms as the court requires.

Invalidity of the extension of a patent term or any portion thereof under section 154(b) or 156 of this title because of the material failure-

(1) by the applicant for the extension, or

(2) by the Director, to comply with the requirements of such section shall be a defense in any action involving the infringement of a patent during the period of the extension of its term and shall be pleaded. A due diligence determination under section 156(d)(2) is not subject to review in such an action.

35 U.S.C. §283 Injunction.

The several courts having jurisdiction of cases under this title may grant injunctions in accordance with the principles of equity to prevent the violation of any right secured by patent, on such terms as the court deems reasonable.

35 U.S.C. §284 Damages.

Upon finding for the claimant the court shall award the claimant damages adequate to compensate for the infringement but in no event less that a reasonable royalty for the use made of the invention by the infringer, together with interest and costs as fixed by the court.

When the damages are not found by a jury, the court shall assess them. In either event the court may increase the damages up to three times the amount found or assessed. Increased damages under this paragraph shall not apply to provisional rights under section 154(d) of this title.

The court may receive expert testimony as an aid to the determination of damages or of what royalty would be reasonable under the circumstances.

35 U.S.C. §285 Attorney fees.

The court in exceptional cases may award reasonable attorney fees to the prevailing party.

35 U.S.C. §286 Time limitation on damages.

Except as otherwise provided by law, no recovery shall be had for any infringement committed more than six years prior to the filing of the complaint or counterclaim for infringement in the action.

In the case of claims against the United States Government for use of a patented invention, the period before bringing suit, up to six years, between the date of receipt of a written claim for compensation by the department or agency of the Government having authority to settle such claim, and the date of mailing by the Government of a notice to the claimant that his claim has been denied shall not be counted as a part of the period referred to in the preceding paragraph.

35 U.S.C. §295 Presumption: Product made by patented process.

In actions alleging infringement of a process patent based on the importation, sale, offered for sale, or use of a product which is made from a process patented in the United States, if the court finds-

> (1) that a substantial likelihood exists that the product was made by the patented process, and
>
> (2) that the plaintiff has made a reasonable effort to determine the process actually used in the production of the product and was unable so to determine, the product shall be presumed to have been so made, and the burden of establishing that the product was not made by the process shall be on the party asserting that it was not so made.

Courtesy of Patrick H. Higgins, Buchanan Ingersoll & Rooney PC

APPENDIX B

TAKEDA CHEMICAL INDUSTRIES LTD. AND TAKEDA PHARMACEUTICALS NORTH AMERICA INC. v. MYLAN LABORATORIES INC., MYLAN PHARMACEUTICALS INC., UDL LABORATORIES INC., ALPHAPHARM PTY. LTD., AND GENPHARM

U.S. DISTRICT COURT SOUTHERN DISTRICT OF NEW YORK

Takeda Chemical Industries, Ltd. and	:	
Takeda Pharmaceuticals North America, Inc.	:	
Plaintiffs	:	03 CIV. 8253 (DLC)
-v-	:	
Mylan Laboratories, Inc.,	:	
Mylan Pharmaceuticals, Inc.,	:	
And UDL Laboratories, Inc.	:	
Defendants	:	
	:	Opinion & Order
Takeda Chemical Industries, Ltd. and	:	
Takeda Pharmaceuticals North America, Inc.	:	
Plaintiffs	:	
-v-	:	04 CIV. 1966 (DLC)
Alphapharm Pty. Ltd. and	:	
Genpharm, Inc.	:	
Defendants	:	

For Plaintiffs:
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For Defendants Alphapharm Pty. Ltd. and Genpharm, Inc.:
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DENISE COTE, District Judge:

Takeda Pharmaceutical Company Limited ("Takeda") and Takeda Pharmaceuticals North America, Inc. ("Takeda North America") have brought this patent action under the Food Drug Cosmetic Act, 21 U.S.C. §§301-99, the Drug Price Competition and Patent Term Restoration Act of 1984, Pub L. No. 98-417, 98 Stat. 1585 (1984) (codified in scattered sections of titles 21, 35, and 42 U.S.C.) (the "Hatch-Waxman Act"), and under the patent laws of the United States, alleging that four generic drug manufacturers have infringed and will induce infringement of Takeda's patents protecting its product ACTOS®, a drug used to treat Type 2 diabetes.

This Opinion presents the findings of fact and conclusions of law following a bench trial held between January 17 and January 30, 2006, to resolve the challenges made by defendants to Takeda's U.S. Patent No. 4,687,777 ("'777 Patent"), which protects the invention of the chemical compound 5-{ 4-[2- (5-ethyl-2-pyridyl)ethoxy] benzyl} -2,4-thiazolidinedione ("pioglitazone"). Alphapharm Pty. Ltd. and Genpharm, Inc. ("Alphapharm") contend that the invention is obvious based on the disclosure by Takeda of a structurally similar molecule in the prior art. Mylan Laboratories, Inc., Mylan Pharmaceuticals, Inc., and UDL Laboratories, Inc. ("Mylan") contend that Takeda deceived the Patent and Trademark Office ("PTO") when it applied for the '777 Patent, principally by misrepresenting the results of efficacy and toxicity tests. Neither challenge is meritorious. The length of this Opinion is occasioned by the need to address the many iterations of the defendants' arguments, as they searched for a viable theory to attack the '777 Patent.

As described below, the '777 Patent discloses a remarkable invention. After decades of work to develop an anti-diabetic treatment, Takeda discovered a

pharmaceutical agent that was both effective and non-toxic. This represented a significant advance over compounds disclosed in the prior art. Takeda's application to the PTO for the '777 Patent reported the very analysis of test results on which Takeda itself had previously relied to select the pioglitazone molecule from the thousands it had synthesized and the hundreds it had tested. Faced with the task of proving their cases by clear and convincing evidence, both Alphapharm and Mylan have failed to make even a rudimentary showing that the invention was obvious or that Takeda engaged in inequitable conduct. Their challenges to the '777 Patent are rejected.

Trial Procedure

The trial was conducted in accordance with the Court's Individual Practices and the Scheduling Order dated July 20, 2004. The parties filed a Joint Pretrial Order and accompanying memoranda of law and proposed findings of fact and conclusions of law on November 18, 2005. The parties also served affidavits containing the direct testimony of all their witnesses, as well as copies of all the exhibits and deposition testimony which they intended to offer as evidence in chief at trial.

A science tutorial was held on December 1, 2005. Testifying for Takeda were Silvio Inzucchi ("Inzucchi"), a Professor of Medicine at Yale University and expert endocrinologist who serves as the Director of the Yale Diabetes Center; James Hendrickson ("Hendrickson"), the Henry F. Fischbach Professor of Chemistry, retired, at Brandeis University and an expert in organic chemistry; and Peter Valberg, a senior scientist at a private environmental health consulting firm, an expert in the statistical analysis of animal testing data, and formerly an Associate Professor of Physiology at Harvard's School of Public Health. Testifying for Alphapharm was Henry Mosberg ("Mosberg"), a Professor of Medicinal Chemistry at the University of Michigan, and an expert in drug design. Testifying for Mylan was Lawrence Hendry ("Hendry"), an Adjunct Professor of Physiology and Endocrinology at the Medical College of Georgia, an Associate Adjunct Professor of Medicinal Chemistry at the University of Georgia, and the founder of a chemical design firm.

The plaintiffs and defendants were each given twenty-four hours for opening statements, examination of witnesses and evidentiary arguments at trial. Of the time granted the defendants, Alphapharm was given eight hours and Mylan sixteen hours.[1] The parties were given additional time for summations.

In addition to the experts who testified on December 1, the following witnesses testified at trial. For Takeda, Richard Daly, Senior Vice President of Marketing at Takeda North America; William Kettyle ("Kettyle"), an expert endocrinologist with significant expertise in the treatment of diabetes; Loren Koller ("Koller"), a doctor in veterinary medicine, an environmental health and toxicology consultant, an expert in immunotoxicology, and an officer of the Association for Assessment and Accreditation of Laboratory Animal Care International; Takeshi Fujita ("Fujita"), a former Takeda employee who, as the Chief Scientist of Takeda's Biology Research Laboratory, was the co-inventor on the '777 Patent; Samuel Danishefsky ("Danishefsky"), a Professor of Chemistry at Columbia University who holds the Kettering Chair at the Memorial Sloan-Kettering Cancer Institute; Yasuo Sugiyama, Takeda's Manager of Strategic Research Planning and a researcher who was involved in the development of pioglitazone; Bernard Landau ("Landau"), a Professor of Biochemistry at Case and Western Reserve University, and, in 1996, a Nobel Fellow at the Karolinska Institute in Sweden; Bruce Stoner ("Stoner"), a former Chief Administrative Patent Judge; Gerard Colca ("Colca"), a former senior research scientist in metabolic disease research at The Upjohn Company ("Upjohn"), a U.S. pharmaceutical company that had worked with Takeda in the development of pioglitazone; and Douglas Morton, a former Director of Diabetes and Gastrointestinal Diseases Research at Upjohn.

Testifying for Alphapharm was Richard Wright, a Professor of Economics at the University of California at Berkeley, and a member of the Steering Committee for Berkeley's Center for Hunger and Obesity. Testifying for Mylan was Martin Ronis ("Ronis"), a Professor of Medicinal Sciences at the University of Arkansas, Associate Director of the Arkansas Childrens' Nutrition Center and an expert in chemical testing in animals. Mylan also

[1] When the defendants exhausted their time at trial, they were given a limited amount of additional time.

presented the declaration of Mark Nusbaum ("Nusbaum"), a former Examiner-in-Chief and member of the Board of Patent Appeal and Interferences.[2]

The parties also offered excerpts from the deposition testimony of some of the fact witnesses that testified at trial and of the following individuals: Michael Davis, the American patent attorney who prosecuted the '777 Patent; Yoshikazu Hasagawa, the Senior Manager in charge of Intellectual Property litigation for Takeda; Shelly Monteleone, Intellectual Property Counsel for Mylan; Brett Mooney, an Alphapharm employee involved in pharmaceutical development; Hiroyuki Odaka, a former Takeda employee who worked in Takeda's Biology Research Laboratories at the time of the development of pioglitazone; Brian Roman, an attorney and a Rule 30(b) (6) witness for Mylan; Howard Rosenberg ("Rosenberg"), the Group Intellectual Property and API Strategy Director for Generics U.K., a sister company of Alphapharm, and an Alphapharm Rule 30(b) (6) witness; Michael Rosenberg, the owner of Health Decisions, a company engaged in clinical research; Takashi Sohda, General Manager of Takeda's Pharmaceutical Research Division; Barry Spencer, a Senior Patent Officer at Alphapharm and a Rule 30(b) (6) witness for Alphapharm; Shigehisa Taketomi, a Takeda employee and Rule 30(b) (6) witness for Takeda; and Stephen Talton, a Mylan employee responsible for preparing applications to sell generic drugs.

The findings of fact based on the evidence presented at trial are scattered throughout this Opinion. The background section contains the story of the development of pioglitazone, an introduction to the prior art, a description of the relevant patents and their file histories, an introduction to the science that is necessary to understand the discussion that follows, and an outline of the procedural history of this litigation. The discussion section of the Opinion will address first the issue of obviousness and then the issue of inequitable conduct.

[2] Takeda chose not to cross-examine Nusbaum and thus he did not appear at trial.

Background

A. Diabetes

Diabetes is a disease in which the body is unable to metabolize blood sugar or glucose derived from food, primarily carbohydrates, into energy efficiently. The blood glucose level is essentially controlled by insulin, which drives the process whereby glucose enters the cells of the body and is turned into energy. Insulin is a hormone made by specialized cells within the pancreas called beta cells.

There are two types of diabetes. Type 1 diabetes is characterized by the fact that the pancreas does not produce insulin. Insulin must therefore be supplied from an external source, such as an injection or insulin pump. Type 1 diabetes compromises less than 10% of diabetes cases worldwide.

In Type 2 diabetes, the body fails to utilize effectively the insulin that is produced. This failure usually starts in the muscles, which collectively use most of the glucose produced by the body. The liver is also responsive to insulin, which instructs the liver when to stop making glucose. When the liver becomes insulin resistant, it resists those instructions and continues to create glucose. Insulin resistance also impacts the pancreas, at first by forcing it to produce more insulin than normal. Over time, the increased resistance to the action of insulin overwhelms the ability of the pancreas to produce sufficient insulin, and the symptoms of diabetes begin to appear. If Type 2 diabetes is left untreated, the demand for insulin from the pancreas can eventually lead the beta cells to become dysfunctional, a phenomenon known as "exhaustion" or "burn-out."

Diabetes can cause great damage to the body. Due to the toxic effects of high glucose on blood vessels, patients with diabetes are predisposed to chronic complications such as kidney failure, blindness, leg ulcers and amputations, heart attacks, and strokes.

B. Treatments of Diabetes

Type 2 diabetes may be treated with lifestyle changes, such as weight loss, improved diet, and exercise. These steps are rarely sufficient. A substantial

portion of patients ultimately need injections of insulin. Insulin is effective because insulin resistance in Type 2 patients is not complete—insulin may still lower blood glucose.

The past twenty-five years have seen the development of a number of oral anti-diabetic drugs ("OAD") that are used instead of, or in conjunction with, insulin. Different classes of OADs have that have been developed work in the different parts of the body affected by diabetes. It is common practice to treat diabetes with a combination of several classes of drugs.

Sulphonylureas, which became available in the 1980s, are the oldest class of drug used to treat Type 2 diabetes, and work by stimulating the pancreas to secrete more insulin. Meglitinides work very much like the sulphonylureas but differ in that their onset is more rapid and their duration of action is briefer.[3] Biguanides help to reduce the liver's production of glucose. Metformin®, a biguanide, is frequently the first drug chosen to treat a newly diagnosed Type 2 diabetes patient. It became available in 1995.

The treatment of diabetes was revolutionized in the 1990's with the introduction of a class of drugs known as thiazolidinediones ("TZDs"). TZDs were first discovered by Takeda in the 1970s. They are peripheral insulin sensitizers, working within muscles to enhance the effect of insulin in that organ, and thereby to increase the muscles' ability to take glucose from the bloodstream.

The first TZD to be marketed in the United States was troglitazone, known by the commercial name Rezulin®. Rezulin®, which was developed by Pfizer, first became available in 1997. In May of 1999, two years after Rezulin® entered on the market, the Food and Drug Administration ("FDA") approved GlaxoSmithKline's Avandia® (whose active ingredient is rosiglitazone). The drug at issue here, ACTOS®, which was approved by the FDA in July of 1999, is the only other TZD currently approved by the FDA for sale in the United States.

[3] Alpha-glucosidase inhibitors, which are used infrequently in the United States, interfere with starch absorption in the intestine, thereby slowing the increase in blood glucose levels after meals.

In March 2000, Pfizer withdrew Rezulin® from the United States market due to significant concerns about its safety. After Rezulin® was withdrawn, ACTOS® and Avandia® essentially split the TZD market in the United States. More recently, research has shown that these two TZDs have a greater positive effect in the treatment of cardiovascular disease than other anti-diabetic drugs, and that ACTOS® in particular has a greater impact than Avandia® on lowering cardiovascular risk.[4] Based in part on this research, there is evidence that ACTOS® is becoming the preferred TZD among knowledgeable doctors.

By any measure, ACTOS® has been a hugely successful commercial product. It has led the TZD market for new prescriptions written by endocrinologists since February 25, 2000. In October 2001, it became the seventh fastest product in pharmaceutical history to reach $1 billion in annual sales.

C. Takeda's Research into Diabetes

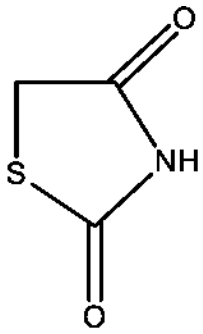
Takeda, a Japanese pharmaceutical company, is based in Osaka, Japan. Takeda North America is a wholly owned United States subsidiary of Takeda America Holdings, Inc., which is a wholly owned subsidiary of Takeda.

Takeda began its research into obesity and related diseases in the early 1960s. Working with Nagoya University in Japan, Takeda developed an animal model that exhibits the symptoms of diabetes: KKAy mice. This is an obese strain of mice that consistently exhibits symptoms of insulin resistance under normal diet conditions. Takeda researchers also developed the genetically obese and diabetic Wistar fatty rat. The development of the KKAy mouse and the Wistar fatty rat were significant steps in the effort to develop pharmaceutical treatments for diabetes since compounds could now be tested in diabetic animals.

Takeda made a pharmacological breakthrough in the 1970s. Takeda researchers discovered the first TZD derivative compound and learned that TZDs exhibited considerable blood glucose lowering effects in KKAy

[4] To reduce cardiovascular risk both trigylcerides and LDL-cholesterol should be lowered. Pioglitazone has shown better trigylceride lowering properties than rosiglitazone and also has shown less of an effect of raising LDL-cholesterol.

mice.[5] The defining characteristic of TZDs is the presence of a thiazolidinedione group at the right end or moeity[6] of a molecule. The chemical structure of this group is:



Takeda's work with TZD derivatives revealed that at least some compounds within the TZD class did not lower blood glucose in normal, non-diabetic animals. This was another important finding because it suggested that TZD derivatives did not affect the level of insulin in the body, but instead were insulin sensitizers, a term for compounds that ameliorate insulin resistance, the defining characteristic of Type 2 diabetes.

While scientists did not initially understand how TZDs work, and still debate today precisely how TZDs actually function within the body, there is a growing consensus that TZDs enhance the signal of insulin receptors that reside in the cells that require or store energy, such as muscles and fat cells. When we eat, the level of glucose rises in the bloodstream, stimulating the pancreas to secrete more insulin. The insulin which is flowing through the blood binds to insulin receptors, causing changes inside cells that allow glucose to enter the cell from the bloodstream, where it can be burned for energy or stored. Because of a negative feedback system, as the level of glucose in the blood falls, the pancreas produces less insulin so that the blood glucose returns to normal levels.

[5] Takeda's diabetes research was conducted through a partnership of Dr. Yutaka Kawamatsu, who ran the chemical research into TZDs and Fujita, who oversaw the biological research.

[6] A moiety is a "group of atoms forming a distinct part of a large molecule." Oxford English Dictionary (Draft Revision to 2d Ed. December 2003).

TZDs activate the insulin receptors by binding to a molecule within the cell's nucleus known as PPAR-gamma. Together, they bind to specific areas on the cell's DNA, producing messenger RNA and effectively stimulating the production of glucose transporters within the cell. The transporters travel to the surface of the cell and facilitate the entry of glucose into the cell from the bloodstream.

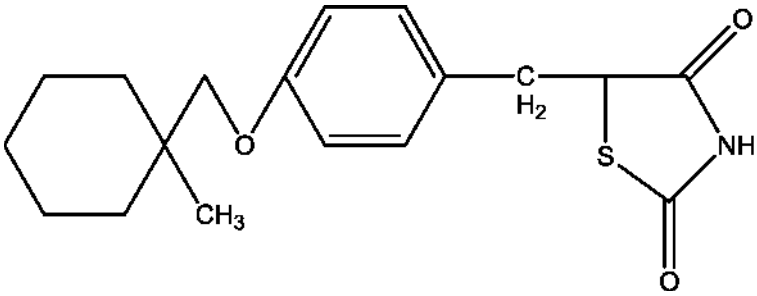
Scientists still do not fully understand how insulin resistance works at the cellular level, but it is believed that the problem relates to the interaction between the insulin receptors and that section of the DNA in the cell's nucleus that is responsible for triggering the production of glucose transporters. As noted, TZDs work by binding with a molecule in the nucleus of the cell called PPAR-gamma. When that happens, the PPAR-gamma molecule changes shape and binds to the DNA in the cell. Each TZD seems to bind differently with the PPAR-gamma. As a result, different TZDs have different metabolic effects. TZDs also bind with other PPAR molecules in the cell, such as the PPAR-alpha and PPAR-delta molecules, further contributing to the differences among TZDs.

The fact that TZDs affect the gene transcription process within DNA makes them both effective but also unpredictable. Only a fraction of the genes in the human body have been identified. It is possible that TZDs stimulate genes that are still unknown. As one of Takeda's expert endocrinologists has explained, gene transcription is "a big black box.... When you are stimulating a gene, you can do a lot of things downstream that you may not understand."

D. The Development of Ciglitazone and the '200 Patent

Takeda's research led to the synthesis of the TZD ciglitazone in February of 1978. Takeda worked for many years to develop ciglitazone, only abandoning it when it proved toxic during human clinical trials. Thereafter, Takeda's search for a TZD to develop as a commercial pharmaceutical used ciglitazone as a benchmark. Takeda searched for a compound that was more potent than ciglitazone, which required unrealistically high doses to be effective, and yet non-toxic.

Ciglitazone's chemical structure is illustrated here:



It was identified as a particularly promising compound based on its blood lowering effect in KKAy mice. Based on this research, Takeda filed a United States patent application on July 27, 1979, covering a generic class of TZD derivatives including ciglitazone. The application eventually resulted in the issuance of U.S. Patent No. 4,287,200 ("'200 Patent").

The application for the '200 Patent ("'200 Application") made eight claims. Its first claim was its broadest and covered hundreds of millions of TZD compounds through a formula that allowed for a wide variety of chemical structures on the left-hand end to be attached to the TZD structure on the right. The '200 Application represented that TZDs are "novel compounds and useful as, for example, remedies for diabetes, hyperlipemia and so on of mammals including human beings."

The '200 Application was the subject of two office actions by the PTO. The second office action allowed two of the eight claims, but rejected all of the other claims as containing "improper Markush groups." *See* Ex parte Markush, 1925 CD 126, 340 Off. Gaz. Pat. Office 839 (Comm'r. Pat. 1925).[7] The office action identified three separate groups the patent examiner believed were contained in the '200 Application.[8]

[7] The examiner cited a recent appellate decision, In re Harnisch, 631 F.2d 716 (C.C.P.A. 1980), as providing a legal basis for the rejection. Harnisch confirmed the concept of an "improper Markush group" as a basis for rejecting a patent application. Id. at 721. The decision explained that the issue underlying improper "Markush groups" was better described as a lack of "unity of invention." Id.

[8] The three groups identified were distinguished by the possible structures on the left end moiety. Group A was composed of compounds where the left end moiety contained an

In response to the second office action, Takeda amended its application to cover only the first of the three groups identified by the examiner. In the amendment Takeda noted that it might file "divisional applications" to cover the other groups.

The '200 Patent was issued on September 1, 1981. Fujita and Dr. Yutaka Kawamatsu were named as co-inventors. In addition to the generic class of TZDs, the patent also presented, as examples, sixty specific compounds covered by the generic formula. Included among those disclosed was compound 42, whose left end was a 2-pyridyl ring with a methyl at the 6-position. Compound 42 is a compound of importance to this litigation and is discussed in detail below.[9] Like ciglitazone, compound 42 had first been synthesized in 1978.

E. Two Divisional Patents

Takeda obtained two divisional patents for the '200 Patent. First, through a patent issued on July 20, 1982, as U.S. Patent No. 4,340,605 ("'605 Patent"), Takeda received a patent for the third group identified by the examiner.[10] In support of the application for that patent, Takeda presented a declaration from Fujita providing data for blood glucose and lipid lowering effects of twelve compounds tested in KKAY Mice, including compound 42 from the '200 Application.

On July 7, 1982, Takeda filed an application for a second divisional to the '200 Patent. The patent, which issued on March 20, 1984, as U.S. Patent 4,438,141 ("'141 Patent"), covered the second grouping that was identified by the examiner in the course of prosecuting the '200 Patent.

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alkyl, cycloalkyl or phenylalkyl; for Group B the left end contained a thienyl or furyl; for Group C the left end contained a pyridyl or thiazolyl. It is this last group that is of importance here; pioglitazone is a left end pyridyl.

[9] Compound 42 from the '200 Patent is compound (b) from the '777 Patent.

[10] The third group identified, compounds with a pyridyl or thiazoyl on the left end, had been designated group C by the examiner.

F. Sohda II

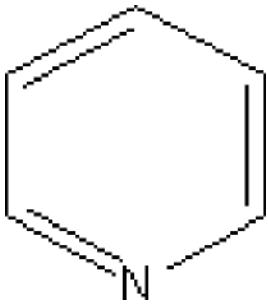
While it was securing the '200 Patent, Takeda continued its research into TZD derivatives and by early 1982 had evaluated approximately 1000 compounds for their potential as anti-diabetic agents. Important information about TZDs and Takeda's research efforts was published in a series of articles by Takeda's scientists. Of particular importance to this Opinion, because it constitutes prior art for the '777 Patent, was an article received for publication on April 22, 1982, T. Sohda et al., Studies on Anti-diabetic Agents. II. Synthesis of 5-[4-(1 Methylcyclohexylmethoxy) - benzyl]) thiazolidine-2, 4-dione (ADD-3878) and its Derivatives, Chem. Pharm. Bull., 30:3580-3600 (1982) ("Sohda II"). Sohda II did not disclose pioglitazone, but it did disclose a compound that was structurally close to pioglitazone, and which Alphapharm contends made the invention of pioglitazone obvious.

Sohda II described 101 specific TZD compounds, giving data on each compound's efficacy. As was the case in the Fujita declaration submitted in the prosecution of the '605 Patent, the data were presented as a score ranging from one to four in two categories: hypoglycemic activity (blood sugar lowering activity) and plasma triglyceride lowering activity. A higher score represented greater potency.

While the article did not present data on the toxicity or side effects of the compounds, it did comment on these issues for particular compounds. Of the 101 compounds, the article identified three compounds—compounds 47, 49 and 59—as showing the most favorable profiles "in terms of activity and toxicity." The article concluded that those three compounds "may be valuable for the treatment of maturity-onset diabetes and/or hyperlipidemia which involves obesity." Compound 49 was ciglitazone and compound 47 was a compound whose left end was structurally similar to ciglitazone's. The left end of compound 59 was different from 47 and 49, its left end terminated with a 3-pyridyl ring.

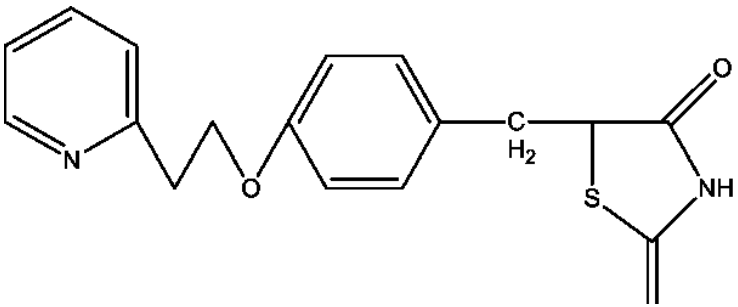
Since pioglitazone has a pyridyl ring at its left end, it is important to discuss compound 59 and related compounds described in Sohda II in some detail. To begin with, the term pyridine refers to a six-membered carbon-

containing ring with one carbon replaced by a nitrogen. A pyridyl ring is diagramed as follows:

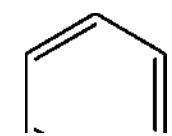


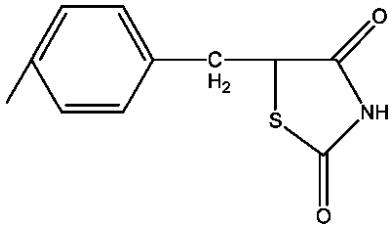
The numbering on a ring begins with the highest atomic weight atom in the ring, which in this case is nitrogen. The numbering moves in a counterclockwise fashion. As noted, compound 59 was a 3-pyridyl ring, which means that the ring is attached at the third position to the rest of the molecule.

The article disclosed two 2-pyridyl compounds: compound 57, the unsubstituted 2-pyridyl, and compound 58, the 6-methyl substituted 2-pyridyl. The term unsubstituted indicates that the pyridyl ring does not have any substituents (such as a methyl or ethyl group) linked to it, while the term 6-methyl indicates that a methyl is linked to the ring at the 6 position, using the numbering system described above. Diagrams of the two compounds are presented below:



Compound 3894





Compound 3959
Compound (b)

Compound 57 from Sohda II was designated by Takeda as Compound 3894 ("Compound 3894"), and compound 58 was designated Compound 3959 ("Compound 3959") and identified in the '777 Patent as compound (b). The defendants' challenges to the '777 Patent largely hinge on assertions concerning these two compounds, and they will generally be referred to as compounds 3894 and (b) in the course of this Opinion.[11]

The 101 compounds described by Sohda II were organized into seven groups. The article commented on characteristics associated with compounds in each of the seven groups. When discussing the group into which compounds 57 and 58 fell, it noted that "[a]lthough compounds 56, 57, 58, 59 and 63...showed potent activities, they, especially 57 and 58, caused considerable increases in body weight and brown fat weight," in the rodents in which they were tested. (Emphasis supplied.)

In the 1980's, scientists believed, as they do today, that increases in body weight are not desirable for diabetics. There was disagreement, however, about the implications of an increase in brown fat in rodents for humans treated with the same compound. Adult humans have relatively little brown (as opposed to white) fat, while rodents carry a significant amount of brown fat in the saddle between their scapulas. Brown fat has a thermogenetic effect, generating heat to keep them warm. At the time that Sohda II was written, overall weight and fat gain caused by pharmaceuticals were thought to correlate in mammals, including rodents and humans.

[11] As already noted, compound (b) had previously been disclosed by Takeda as compound 42 in the '200 Patent, and was also one of the twelve compounds later listed in the Fujita declaration that accompanied an amendment to the application for the '605 Patent.

G. The Third Divisional Patent: The '779 Patent

On March 15, 1983, Takeda filed a third divisional patent to the '200 Patent. The application sought to expand the grouping of compounds originally covered by the '605 Patent, by adding compounds where "the pyridyl or thiazolyl groups may be substituted."[12] A preliminary amendment also noted that compounds in which "hetrocyclic rings are substituted have become particularly important, especially Compound 42 in example 9." Compound 42 was the compound destined to be used as a comparator in the '777 Patent, where it is listed as compound (b).

Because the application only sought to expand the groups covered by the '605 Patent but not to introduce a substantively different claim, Takeda filed a terminal disclaimer, noting that the "inventive entity" covered by the '605 Patent and the application were the same, and thereby disclaiming any protection of the compounds in this application beyond the expiration of the '605 Patent. The application was approved by the PTO and issued on April 24, 1984, as U.S. Patent No. 4,444,779 ("'779 Patent").

H. The '902 Patent

Takeda's patent prosecutions were not limited to the divisionals of the '200 Patent. On December 29, 1982, Takeda filed an application covering TZD derivatives with a cyclohexane ring on the left end.[13] The patent issued on July 24, 1984 as U.S. Patent 4,461,902 ("'902 Patent").

I. The Failure of Ciglitazone

After Takeda's TZD development program attracted the interest of Upjohn, Takeda and Upjohn worked together on the development of ciglitazone from 1981 to 1983. Both companies analyzed the compound's anti-diabetic properties and toxicity, and based on those studies, began Phase I safety studies with human volunteers in both the U.S. and Japan.

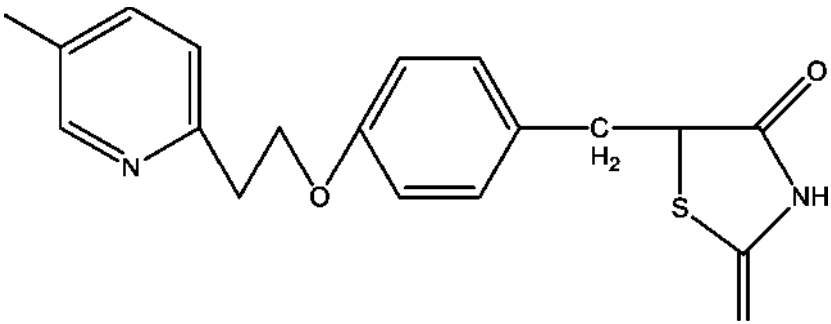
[12] A thiazolyl is a five member heterocycle, with a nitrogen and sulfur at positions 1 and 3, respectively.

[13] A cyclohexane ring is a saturated ring of six carbons. Ciglitazone's left moiety contains a cyclohexane ring.

As work on the development of ciglitazone progressed it became evident that the compound could not be successful as a commercial anti-diabetic. In November 1982, it was determined that ciglitazone caused cataracts in rats that were being treated with the compound as part of a ninety-day toxicology study. Upjohn believed that the FDA would block a compound that caused cataracts from the U.S. market. Second, a clinical trial in Japan suggested that ciglitazone might not be effective for a Type 2 diabetic patient unless the dose was above 500 milligrams per day, a dosage which was impractical. By 1983, Takeda and Upjohn renewed their search for a more potent, non-toxic compound.

J. Initial Development of Pioglitazone

Meanwhile, Fujita was working with Dr. Kanji Meguro ("Meguro"), the Chief Scientist of the Chemical Research Laboratory at Takeda, to develop ideas for new compounds to be synthesized and tested. On September 7, 1982, pioglitazone was synthesized. It terminates at its left end in a 2-pyridyl ring with an ethyl at the 5 position on that ring.[14] It was given the internal Takeda compound number 4833.



Pioglitazone Compound 4833

[14] An ethyl group is C2H5. Ethyl groups differs from methyl groups, CH3, by a single CH2 group. Ethyl and methyl are both lower alkyls.

The first screening of pioglitazone for efficacy in November 1982 noted its promise:

> Initial Screening
>
> 10 Samples were tested in KKAy mice. 2 samples were significant in lowering blood glucose. The effect of AD-4833 was relatively strong, 0.005% food admixture 4-day administration resulted in reducing blood glucose, plasma TG and NEFA by 46%, 31% and 30% respectively. No significant increase in body weight was observed. The effect was weaker than that of ADD-3959 [identified as compound (b) in the '777 Patent].[15]

Takeda scientists also conducted preliminary toxicity tests on compounds that showed promise. Pioglitazone was the least toxic of all the TZD compounds evaluated in 1983 and 1984.

Following the failure of ciglitazone, Upjohn and Takeda renewed their collaborative research. In their search for a new compound they focused on the 130 TZD derivatives that had been tested during the ciglitazone selection process, but also synthesized some new compounds.

The decision by Takeda and Upjohn to continue to research TZD derivatives went against some of the thinking in the industry. Other leaders in the diabetes field believed that better avenues for research included developing insulin secretagogues (compounds which combat insulin resistance by causing the pancreas to create more insulin) and treatments for late-stage consequences of Type 2 diabetes, such as neuropathy, nephropathy, and retinpathy.

One of the compounds that was retested during this period was compound (b). Compound (b) had shown strong blood glucose lowering activity in mice and triglyceride lowering activity in both mice and rats. Despite its efficacy, compound (b) was dropped from consideration when testing

[15] Takeda seems to have used both AD- and ADD- as prefixes when designating compounds during their research. No explanation has been given for any difference between the two prefixes. This Opinion does not use either designation.

revealed significant toxicity to the liver and heart as well as a decrease in the number of erythrocytes, a sign of potential toxicity to bone marrow. Compound (b) also failed the cataract screening test conducted by Upjohn.

Based on the experiences with ciglitazone and compound (b), Takeda made identifying a compound without toxic effects its highest priority. It was Upjohn's view that any compound that failed the in vitro chick lens assay test for cataractogenesis had to be ruled out from consideration for development. K.Takeda's Testing Methods Takeda conducted many efficacy tests on numerous compounds, including pioglitazone, throughout 1983 and 1984. In order to screen for efficacy, KKAy mice or rats were treated with different dosage levels of a compound for four days. Initial tests usually involved just two doses of the compound to determine roughly if the compound was active. The dosage levels were calculated as milligrams of compound per kilogram of body weight of the treated animal per day (mg/kg/day). The researchers typically matched the animals to be tested by age, sex and body weight. From the pools of animals, groups of five animals were randomly chosen for each dosage level in the test and a separate group of five was chosen to serve as a control. On the fifth day of the screening, the blood glucose and triglyceride levels of the test animals were measured and were compared to blood taken from untreated control animals.

For many compounds Takeda also conducted three dose efficacy tests, to assist researchers in determining the dosage of a compound necessary to reduce an animal's blood glucose level or trigylceride level by 25%. The effective dose required to reduce the levels by 25% is called the "ED25."

Takeda's experiments were performed by technicians. At the end of a three dose efficacy test, the technician would perform regression calculations to plot the best straight line between the three data points. The results would then be reviewed by a trained scientist or by Fujita in order to determine whether the points plotted or the line determined by the regression equation actually corresponded as well as it should to a true dose response curve.

The relationships between two variables in biological systems, such as the changes in blood glucose concentrations with a change in a dosage of a drug, are usually not linear but rather exponential. Plotting the change of

the one variable against the other will often result in a curve which is made linear through the application of a process called linear regression. There are limitations, however, on the reliability of a linear regression. A linear regression is more reliable if the interval between the data points is limited. It is significantly less reliable when the administered dosages do not fall within the effective dosage range of the compound being tested since including even one data point that is outside of the linear response region can significantly change the relationship between the three points plotted in a three-dose test. Extending a line beyond a data point to reach an ED25 value that was not within the tested range also runs a considerable risk that the projected results will be unreliable.

Takeda was testing new compounds whose properties were unknown and it had to guess what the best dosage range for testing might be. Not infrequently, it chose dosages that were above or below the effective dosage range. This meant that Takeda often had to conduct several experiments to improve its understanding of the effective dosage range of a compound. In addition to the challenges of making an accurate determination of the ED25 values, Takeda scientists also had to monitor the experiments for other possible factors that might make a particular experiment's results unreliable.

L. Report A-15-13

On February 8, 1984, Takeda forwarded a copy of Fujita's report A-15-13 ("Report A-15-13") to Upjohn. The report, which was titled "Preliminary Studies on Toxicological Effects of Ciglitazone-Related Compounds in the Rats," disclosed the results of preliminary toxicity studies conducted on fourteen compounds that Takeda had considered as candidates for development. The report detailed the method of testing that had been employed: oral doses of 100mg/kg/day of the test compound for two weeks given to five to six week old male and female Wistar rats. At the end of the testing period the rats were sacrificed, body weights and organ weights were analyzed, as were blood chemistry and hematology. The report contained the organ weight expressed as normalized weight (calculated by dividing the organ's weight by the weight of the rat and expressing the weight as a percentage) in order to compensate for the fact

that animals differ in size. Pioglitazone was one of the compounds presented in Report A-15-13 and showed no statistically significant toxicity.

In addition to pioglitazone, several other compounds of interest to this Opinion were among the fourteen, including the unsubstituted 2-pyridyl (compound 3894) and the 5-methyl 2-pyridyl (compound (c) as designated in the '777 Patent). The introduction to the report noted that each of these three compounds was less toxic "in regard to reduction of blood red (sic) cells and hypertrophy of liver and heart which were common toxic effects in ciglitazone-related compounds." It added, "[c]onsidering the fact" that compound 3894, pioglitazone and compound (c) "are five times as potent as ciglitazone in the pharmacological activities, they appear to be much easier to continue further studies including clinical trials." In point of fact, however, the report found that compound 3894 produced a statistically significant negative effect on the heart of male rats and that compound (c) had such an impact on platelets. Two other compounds that were used as comparators in the '777 Patent also demonstrated toxicity. Compound (b) was toxic to the liver, heart and erythrocytes, among others things, while compound (d) was toxic to the liver and heart.

M. March 1984 Plan

After two days of meetings between Takeda and Upjohn in March 1984, at Upjohn's headquarters in Kalamazoo, Michigan, the participants agreed that Takeda would select fifty TZD compounds based on hypoglycemic activity in both the KKAy mouse and the Wistar-fatty rat. Upjohn was to test the leads identified by Takeda in the in vitro chick lens assay for cataractogenic activity, and Takeda was responsible for other toxicity testing.[16] Takeda had already provided Upjohn with KKAy mice so that Upjohn could replicate Takeda's efficacy testing. It also gave Upjohn the fifty compounds that it had synthesized and selected for this intensive review.

The minutes of the March meeting reflect that it was "desirable that leads selected for further development are clean" in the chick lens assay. Based on a combination of the chick lens assay and the toxicity studies, nine to ten

[16] Takeda was to carrying out two-week toxicity studies for the leads in Wistar rats at 100 mg/kg/day.

leads were expected to emerge and be subject to further testing by Takeda and Upjohn. It was anticipated that four to five leads would emerge from that further testing and proceed to ninety-day toxicity studies in both rats and dogs. Compounds which emerged as "clean" through all of the stages of testing would be "considered for further development with a goal of IND filing for the best compound as a drug candidate."[17] The minutes established a time line for each stage in the process. The next meeting, for selection of the nine to ten leads was scheduled for August 1984.

In selecting the fifty compounds, Takeda was also to consider the "uniqueness of chemical structure." The emphasis on the uniqueness of the chemical structure as a criterion for selecting the initial fifty compounds arose from a Takeda policy that candidate compounds should be reasonably unique from each other in their chemical structures because toxicological problems and adverse reactions are often caused by discrete chemical structures. By emphasizing variety in the chemical structures to be studied, Takeda hoped to avoid losing entire ranges of candidates due to a particular structure's toxicity.[18] Based on those same concerns, Upjohn researchers endorsed the decision to make chemical uniqueness a selection criterion.

The fifty compounds chosen by Takeda were a mix of those that had already been tested in earlier research and those that Takeda had recently synthesized. Among the recently synthesized compounds were three that appeared as comparators in the '777 Patent: compounds (c), (d), and (e), which were first synthesized on July 21, May 4, and August 4, 1983, respectively. Because Takeda had observed that pioglitazone was comparatively potent and exhibited no toxicity it synthesized compounds that were structurally related so that it could compare the results.

[17] An Investigational New Drug Application ("IND") is an application filed with the FDA to conduct clinical trials (i.e. tests on humans). Merck KGaA v. Integra Life Sciences I, Ltd., 125 S.Ct. 2372, 2377 (2005).

[18] While Mylan argued that Takeda and Upjohn were concerned in 1984 not with identifying the best anti-diabetic treatment but with the patentability of a compound, the Takeda and Upjohn witnesses presented entirely credible testimony that they were driven by concerns about efficacy and safety. After all, a patent on a useless compound is useless.

Takeda's benchmark for efficacy was the ED25 of ciglitazone. The candidate compounds were continually evaluated from July through October of 1984 in order to find what Takeda scientists considered the most reliable ED25 values.

N. October 30, 1984 Meeting and Report A-15-34

Obtaining the efficacy and toxicity data for the candidate compounds turned out to be much more complicated and time consuming than expected. The meeting with Upjohn originally planned for August 1984 did not take place until the end of October. At the meeting Takeda presented Fujita's report A-15-34, which was titled "Pharmacological and Toxicological Studies of Ciglitazone and its Analogues" ("Report A-15-34"). This report is of critical importance to the issues of inequitable conduct raised by defendant Mylan.

Report A-15-34 lists fifty compounds in Table 1. The report gives the chemical structure of each compound as well as efficacy and toxicity data. In generating the report, Fujita examined all of the test results to locate the most reliable ED25 numbers for each compound. In addition to listing the ED25 score which he considered to be the most reliable for each compound, Fujita also indicated in a parenthetical the relative efficacy of each compound to that of ciglitazone. For instance, the benchmark for all testing, ciglitazone, was listed first with an ED25 for glucose lowering in KKAy mice of "40 (1)." Pioglitazone was listed about one-third of the way down the table with an ED25 of "6 (6.7)," indicating that a dose of 6mg (per kg per day) of pioglitazone achieved an ED25, rendering it about 6.7 times more potent than ciglitazone, which required a dose of 40mg to achieve that result. The parenthetical sometimes indicated the range of the test results obtained by Takeda.

Table 1 also indicated the results of the in vitro chick lens assays conducted by Upjohn. A compound failed the chick lens assay if it caused a change in pH or a cloudy appearance at a lower concentration than did ciglitazone.

Finally, the report provided summary data for hepatomegaly (liver toxicity), cardiomegaly (heart toxicity) and anemia (erythrocyte depletion) from two-week toxicology studies in male and female Wistar rats. The data were

presented using a rating system based on the degree of toxicity. For liver and heart, toxicity was evaluated by a percentage gain in weight; for anemia, toxicity was evaluated by a percentage decrease of erythrocytes. Rather than give precise toxicity numbers, the report listed three ranges of toxicity in terms of growth or decline: 8-20%, 21-25%, and 26% and above.

Fujita selected twelve of the fifty compounds as compounds on which the meeting participants should particularly focus their attention, and presented the data for these twelve on Table 2 in the report. In selecting the twelve, Fujita considered the potency of a compound in comparison to its performance in toxicity testing, including the chick lens assay tests, as well as the structural diversity of the compounds. Fujita selected only two compounds whose left end was a pyridyl ring. One of those two was pioglitazone. Pioglitazone was the only compound among the twelve that showed no toxicity, although many of the others listed on Table 2 were far more potent. None of the comparator compounds from the '777 Patent appear on Table 2, although all of them appear on Table 1 of Report A-15-34.

During the meeting, the scientists from Takeda and Upjohn reviewed the data for all the compounds presented in Table 1, giving particular attention to the twelve compounds on Table 2. The discussion was an open one and Upjohn was free to suggest that any compound from Table 1 be considered for selection as a lead.

At the meeting, Upjohn conveyed its view that low toxicity was far more important than extreme potency. Upjohn urged that the most important criterion for selection was the therapeutic ratio, that is, the difference between the effectiveness of the drug and the appearance of side effects. Due to its lack of toxicity, Upjohn pressed for the selection of pioglitazone over far more potent compounds.

In the end, Takeda and Upjohn selected five compounds from Table 2 for further testing. Pioglitazone was among the five. None of the other four ended in a pyridyl ring, and none of the others emerged as a viable candidate for commercial development from the additional testing which followed.

The decisions reached at the October meeting were vitally important to both Takeda and Upjohn. Each company intended to spend millions of dollars and valuable research resources on the selected compounds. In addition, their scientists would be spending several years of their professional lives developing the chosen compound. Having experienced a significant set back with the failure of ciglitazone, Upjohn and Takeda were looking for a compound that would validate both their focus on TZDs and their use of the KKAy mouse as an effective way to test the efficacy of compounds intended to treat diabetes. Development of a safe and efficacious molecule that could be successfully developed as a pharmaceutical would validate the years Takeda and Upjohn had invested in research.

O. Final Selection of Pioglitazone

Takeda and Upjohn continued their evaluation of the candidate compounds in late 1985 and early 1986. After more extensive toxicity studies, pioglitazone was chosen as the primary candidate for commercial development at a meeting between Upjohn and Takeda in Osaka on March 7, 1986. Pioglitazone met the important toxicity criteria: it was clean at 100 mg/kg/day in heart, liver and erythrocyte toxicity screening, as well as in the in vitro chick lens assay. Upjohn repeatedly confirmed pioglitazone's ED25 score.

Upjohn's decision to develop pioglitazone was not based on Takeda's data alone. Upjohn, under Colca's supervision, had conducted confirmatory efficacy and toxicity tests on over fifty of the TZD derivatives for which it received data from Takeda, including ciglitazone and pioglitazone, following experimental protocols identical to those described by Takeda in Report A-15-34. Upjohn's tests did not produce any results that were materially inconsistent with those reported to it by Takeda.

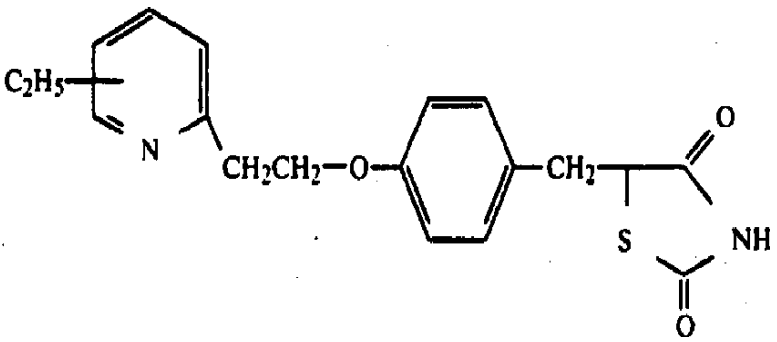
P. Prosecution History of the '777 Patent

In December 1984, Meguro submitted a request to file a patent application to Takeda's Central Research Library. The request, dated December 17, 1984, names Meguro and Fujita as joint inventors and identifies the structure of pioglitazone.

The internal patent request only claims pioglitazone; there is no request to claim an ethyl substituent at any other position on the pyridyl ring.

On January 19, 1985, Takeda filed a Japanese priority patent application covering pioglitazone, and containing the efficacy and toxicity data presented in Table 1 of the '777 Patent. On January 17, 1986, Takeda filed the U.S. patent application covering pioglitazone. The substance of the application was virtually identical to the Japanese priority patent application. The patent application included an Information Disclosure Statement ("IDS") which identified relevant prior art references as including the '200 Patent and Sohda II.

Takeda made six claims in its application. Claim 1 was for a compound of the formula:



or a pharmacologically acceptable salt thereof.

The right end of the molecule is the defining TZD structure. For our purposes, the critical part of the formula was the left-hand portion, which was the pyridyl ring with a C2H5 (or ethyl group) connected to the pyridyl ring by a line leading into the middle of the ring. Drawing a line into the center of the ring means that the ethyl group can be located on any open position on the pyridyl ring.

Claims 2, 3 and 4 are dependent claims which refer back to claim 1.[19] Claim 2 is for the compound in claim 1 with the ethyl group in the 5 position, that is, pioglitazone. Claim 3 is for the sodium salt of pioglitazone. Claim 4 is for

[19] The application also included two claims that were later withdrawn.

the compound in claim 1 with the ethyl group in the 6 position. This compound has never been developed by Takeda.

Takeda's application states that the purpose of its invention "is to provide compounds which can be practically used as anti-diabetic agents having a broad safety margin between pharmacological effect and toxicity or unfavorable side reactions." In support of its statement, Takeda provided efficacy and toxicity data on six compounds. The toxicity data are identical to the data presented in Report A-15-13. The efficacy data are identical to that contained in Report A-15-34.

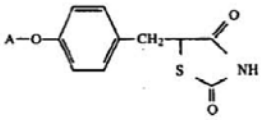
The six compounds listed in the table are identified as (I), (a), (b), (c), (d), and (e). Compound (I) is pioglitazone. Compound (a) is ciglitazone, which has a different left end moeity than that in the other five compounds identified in the table. Ciglitazone has a methylcyclohexyl ring instead of a 2-pyridyl ring. Ciglitazone was disclosed in the prior art, having been specifically identified in both the '200 Patent and Sohda II.

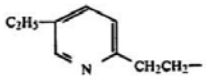
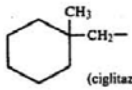
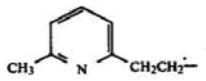
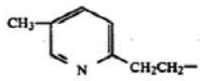
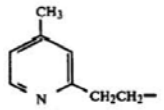
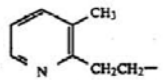
Compounds (b), (c), (d), and (e) and pioglitazone each have a 2-pyridyl ring at the left end. Compounds (b), (c), (d), and (e) have a methyl at the 6, 5, 4, and 3 positions, respectively, on the 2-pyridyl ring. Pioglitazone has an ethyl at the 5 position. Compound (b) was also specifically identified in both the '200 Patent and Sohda II.[20] Compound (c), which has the methyl in the 6 position, is the homolog of pioglitazone.[21] Table 1 of the '777 Patent is reproduced below:

[20] As has been noted previously, compound (b) was compound 42 from the '200 Patent and compound 58 from Sohda II.

[21] The term homolog describes the relationship between two compounds that differ by the addition of a repeating group, usually a single CH2 group. An ethyl group, C2H5, differs from a methyl, CH3, by a single CH2 group.

TABLE 1



Compound A	Blood Glucose (ED_{25}) mouse	TG(ED_{25}) mouse	TG(ED_{25}) rat	Two-weeks toxicity (rat, %) Liver weight ♂	Liver weight ♀	Heart weight ♂	Heart weight ♀	number of erythrocyte ♂	number of erythrocyte ♀
(I) 	6	6	3	−0.7	−3.5	+0.9	−3.9	−3.4	−0.7
(a)  (ciglitazone)	40	40	70	+6.6*	+10.8*	+13.4*	+4.0	+3.5	−0.2
(b) 	4	3	5	+3.8	+10.7**	+19.9**	+17.8**	−2.9	−8.8**
(c) 	20	20	—	+1.3	−1.2	+7.2	+3.0	−4.2	−6.0
(d) 	20	20	—	+8.8*	+8.4**	+3.3	+7.3*	−3.7	−2.5
(e) 	20	20	—	−2.3	+6.6**	+10.9	+9.8*	−8.7*	−7.0**

t-test: *P < 0.05; **P < 0.01

Comparative data on compound (b) were included in Table 1 of the patent application because it is the closest prior art. Data on ciglitazone were included, despite its clinical failures, because it was the first TZD evaluated by Takeda to show potential for use as an anti-diabetic compound and had served as an index against which to compare new compounds. The application included data on the 3, 4 and 5-methyl variants of compound (b) because the compounds were structurally close to both pioglitazone and compound (b). They were also included to emphasize that the results for pioglitazone reported in Table 1 were "quite unexpected" even when compared to its homolog, compound (c).

Two errors were made in the section which describes the method by which Takeda tested for toxicity in rats. First, the application indicates that data on

toxicity were obtained using Sprague-Dawley rats, when in fact the data were obtained from Wistar rats. Both are normal strains of rats and the same methods are used to test for toxicity in either strain. The error had no implications for the validity of the test results. In previous toxicology screens, the results of studies with the two species had been comparable.

The second error involved the age of the rats used in the testing. In the patent application, the age of the rats is listed as 5 weeks old when it should have been listed as 5-6 weeks old. In the two-week toxicity tests reported in Table 1 of the '777 Patent, the results for pioglitazone were obtained from rats that were six weeks old at the beginning of the two week test; the results for the other compounds were obtained from rats that were five weeks old at the beginning of the two-week experiments. The data for all the compounds were normalized to body weight to account for variation in the size of the animals, and in each test the age of rats in the control group was the same as in the group receiving the compound. The one week age difference between the five and six week old rats did not affect the validity of the comparison.

On July 1, 1986, the examiner in charge of Takeda's U.S. patent application issued an office action ("Office Action") requesting an explanation of how to interpret the data presented in Table 1, particularly how to "balance the need for effective ED25 versus the need for lower toxicity." He rejected claims 1-5 under 35 U.S.C. §112, quoting the section as follows:

> The specification shall contain a written description of the invention and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The Office Action also noted that Table 1 failed "to provide values for the control group." As a result of the lack of guidance on how to read the table, the Office Action pointed out that "one of ordinary skill is not taught how to interpret the data and distinguish over the prior art." The Office Action requested guidance on whether there was a "therapeutic ratio" that could be

used to compare the compounds and whether there was a threshold of "maximum toxicity." The Office Action concluded by asking "at what point is increased potency not desirable over increased toxicity? From the data provided one cannot conclude that [pioglitazone] is unexpectedly different from the rest."[22]

In response to the Office Action, Takeda submitted an amendment ("Amendment") and a declaration from Fujita ("Declaration"). The Amendment explained how to read Table 1, noting that the compounds (c), (d), and (e) were not disclosed in the prior art, but were tested because their chemical structure is similar to pioglitazone's. The Amendment explained how the ED25 values were calculated and the significance of the two-week toxicity testing in rats. It noted that only pioglitazone and compound (c) did not show any toxicity at a dose of 100 mg/kg/day for two weeks.[23] The Amendment calculated a "safety margin" for the different compounds, dividing the lowest toxic dose by the minimum effective dose. Noting that a compound with a higher safety margin is preferable, it argued that the test results showed that pioglitazone was "the most advantageous." The Amendment also explained why it was "meaningless to show the values of the control" if one is skilled in the art.

In order to complete the safety margin calculations, Fujita's Declaration added calculations for rat triglyceride ED25 values for three compounds. These values were the only omissions in the columns of data presented in Table 1. Fujita asked his researchers to perform the experiments to generate the missing triglyceride ED25 data for compounds (c), (d), and (e). The report from the researchers who conducted the experiments showed ED25 data for two of the compounds but reported that compound (d) showed no effect. Fujita chose to take the ED25 rat triglyceride data for the third compound from Report A-15-34.

[22] The file history for the '777 Patent reflects that three examiners, each of whom was trained in chemistry, were involved in the prosecution. Their annotations to Sohda II and Table 1 show particular attention to prior art compound (b).

[23] As previously noted, pioglitazone and compound (c) are the only compounds in Table 1 with substituents at position 5 on the 2-pyridyl ring.

The experiments for rat triglyceride values for compounds (c) and (e) were performed by an experienced technician and supervised by an experienced researcher. During the experiment, the supervisor decided to exclude a control rat from consideration. It was common at Takeda to give researchers discretion not to use data from a single outlier animal.

Takeda filed its Amendment and the accompanying Declaration from Fujita with the PTO in November 1986. The PTO issued a Notice of Allowability on January 6, 1987. The patent issued on August 18, 1987. The '777 Patent was originally set to expire on January 17, 2006. The patent term was extended by five years to January 17, 2011, pursuant to a petition filed by Takeda under the Hatch-Waxman Act.

Q. Upjohn Abandons Pioglitazone

Upjohn ended its collaboration with Takeda in September of 1993. In doing so, Upjohn considered an upcoming "milestone" payment due to Takeda, its desire to leave the diabetes market, and its concern about litigation risks associated with launching a new drug. Upjohn management also had concerns about some of the results from longer term toxicity studies on pioglitazone. The Upjohn scientists most directly involved in supervising the development of pioglitazone disagreed with the decision and were deeply disappointed by it. Upjohn's decision contributed to the long delay between the '777 Patent issuing and the FDA approving ACTOS®, a delay which resulted in pioglitazone being the third TZD, instead of the first, to reach the U.S. market.

R. Combination Uses

Takeda has received seven patents for pioglitazone to be used in combination with other drugs ("Combination Use Patents"). All but one of the Combination Use Patents expire on June 16, 2016; one expires on August 9, 2016. As already noted, it is common for diabetics to be treated with several drugs at the same time, each targeting a different body mechanism associated with the disease.

S. Marketing ACTOS®

The FDA approved ACTOS® in July 1999. Before May 1998, Takeda had no wholly owned United States sales entity. Takeda North America was created in May 1998 to market ACTOS® in the United States. In preparation for the launch of ACTOS®, Takeda Pharmaceuticals America, Inc. ("TPA"), the predecessor to Takeda North America, entered into a license agreement with Takeda which would allow Takeda North America to sell and market ACTOS® in the United States. TPA also entered into an agreement on December 14, 1998 with Eli Lilly and Company, which required Eli Lilly to co-promote ACTOS® with Takeda North America.

T. Hatch-Waxman Act [24]

The introduction of new drugs in the U.S. market is governed by the Federal Food, Drug and Cosmetic Act, which prohibits the introduction into interstate commerce of "any new drug, unless an approval of an application filed pursuant to subsection (b)" of 21 U.S.C. §355 "is effective with respect to such drug." 21 U.S.C. §355(a). Subsection (b) describes the process of filing a New Drug Application ("NDA") with the FDA. The process of filing an NDA is typically costly and time-consuming. In the case of pioglitazone, for example, it took almost 12 years from the issuance of the '777 Patent until pioglitazone (in the form of pioglitazone hydrochloride) was approved by the FDA for the treatment of Type 2 diabetes on July 15, 1999.

In 1984, in order to accelerate the approval process for low-cost generic versions of established drugs, Congress enacted the Hatch-Waxman Act. Among other things, the Hatch-Waxman Act added subsection (j) to Section 355. Hatch-Waxman Act §101. Subsection (j) provides for the filing of an Abbreviated New Drug Application ("ANDA") with the FDA for the bioequivalent form of a drug already approved for safety and effectiveness. 21 U.S.C. §355(j) (1), (j) (2) (A), (j) (7) (A). Subsection (j) (7) (A) further provides that the Secretary of the FDA will create and maintain a list of such approved drugs. Id. §355(j) (7) (A). This list, Approved Drug Products

[24] This treatment of the Hatch Waxman Act draws significantly from the description in In re Tamoxifen Citrate Antitrust Litig., 429 F.3d 370, 374-77 (2d Cir. 2005).

with Therapeutic Equivalent Evaluations, is commonly known as the "Orange Book." *See* id.; www. fda.gov/cder/ob/default.htm.

When filing an ANDA, the filer must also include, with the application, "the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug...." 21 U.S.C. §355(b) (1). An ANDA filer must certify, with respect to each patent that claims the listed drug, either that no patent was filed for the listed drug (a "paragraph I" certification), that the patent has expired (a "paragraph II" certification), that the patent will expire on a specified date and the ANDA filer will not market the drug until that date (a "paragraph III" certification), or that the patent is invalid or would not be infringed by the manufacture, use, or sale of the new drug (a "paragraph IV" certification). 21 U.S.C. §355(j) (2) (A) (vii).

An ANDA filer that elects a paragraph IV certification must notify each affected patent owner of the certification. Id. §355(j) (2) (B) (I). The patent owner then has forty-five days after the date it receives such notice to bring suit against the ANDA filer for patent infringement. Id. §355(j) (5) (B) (iii). If no patent owner brings such a lawsuit during this period, the FDA may immediately approve the ANDA. Id. If, however, the patent owner brings suit during this period, the FDA's final approval of the ANDA is stayed for thirty months after the date the patent owner received the requisite notice,[25] or until a district court returns a decision as to the validity of the patent or its infringement if it does so before the thirty-month period expires. Id.

ANDA applicants may also satisfy their obligation to address all relevant patents by filing a statement under 21 U.S.C. 355(j) (2) (viii) ("Section viii Statement"). By filing a Section viii Statement the applicant acknowledges that the drug sought to be manufactured is protected by a method of use patent, but claims that the applicant is not seeking approval for the patented use. An ANDA filer can submit either a Section viii Statement or a paragraph IV certification for each listed patent, but not both. *See* Purepac Pharm. Co. v. Thompson, 354 F.3d 877, 880 (D.C. Cir. 2004).

[25] The notices of paragraph IV certification that Takeda received from Mylan and Alphapharm are dated September 8, 2003, and January 29, 2004, respectively. Thus, the 30 month periods will run on March 8 and July 29, 2006.

Any approval letter sent by the FDA before the expiration of the prescribed stay and before a court ruling of patent invalidity or non-infringement is tentative. *See* 21 C.F.R. §314.105(d). If before the thirty months expire a court rules that the patent is either invalid or not infringed, the tentative approval of the ANDA is made effective as of the date of judgment. 21 U.S.C. §355(j) (5) (B) (iii) (I). If after thirty months there has been no ruling on patent validity or infringement and the stay expires, the ANDA filer can distribute and market the drug but, depending on the court's later patent ruling, an ANDA filer that chooses to follow this course may thereafter become liable for damages if infringement is found. In re Tamoxifen, 429 F.3d at 376.

As an incentive for generic manufacturers to choose the paragraph IV certification route, and thereby to challenge weak patents, the Hatch-Waxman Act offers under certain conditions, the first ANDA filer with a paragraph IV certification the opportunity to market its generic drug exclusively for 180 days. To this end, the FDA may not approve the ANDA of a subsequent filer until 180 days after the earlier of the date 1) the first ANDA filer commercially markets the generic drug, or 2) a court of competent jurisdiction concludes that the patent in question is invalid or not infringed. 21 U.S.C. §355(j) (5) (B) (iv) (I) (II).[26]

Alphapharm was the first to file an ANDA. Its submission to the FDA was ultimately rejected because it could not make a pill that was a bioequivalent to ACTOS®.[27] As a result, the second filer, Mylan, will enjoy the six month exclusivity period if the '777 Patent is invalidated.

[26] Until 1998, the 180 day exclusivity period was available to the first ANDA filer to elect a paragraph IV certification only if it successfully defended a lawsuit for infringement of the relevant patent. *See* 21 C.F.R. §314.107(c) (1) (1995). This "successful defense" rule was challenged and rejected by circuit courts in two separate lawsuits. *See*, *e.g.*, Mova Pharm. Corp. v. Shalala, 140 F.3d 1060, 1076 (D.C. Cir. 1998). The FDA formally revoked the "successful defense" requirement in 1998. *See* Effective Date of Approval of an Abbreviated New Drug Application, 63 Fed. Reg. 59,710, 59,710 (Nov. 5, 1998), 21 C.F.R. §314.107 (1999).

[27] It appears that the FDA rejected Alphapharm's ANDA at some point between its initial filing in July 2003, and its filing of a Section 355 Statement in January 2004.

U. The Defendants' ANDA Filings

On July 15, 2003, Watson Pharmaceuticals, Inc., Watson Laboratories, Inc., and Danbury Pharmacal, Inc. ("Watson"), Alphapharm, Ranbaxy Laboratories, Ltd., and Ranbaxy Pharmaceuticals, Inc. ("Ranbaxy"), and Mylan all filed ANDAs seeking approval to market 15 mg, 30 mg, and 45 mg pioglitazone hydrochloride tablets. Ranbaxy and Watson filed paragraph III certifications with respect to the '777 Patent; they did not challenge its validity, representing instead that they will not make, use, sell, or offer for sale their products until the expiration of the '777 Patent. Both Ranbaxy and Watson also filed paragraph IV certifications relating to the composition claims in the Combination Use Patents.[28]

Alphapharm filed a paragraph IV certification claiming that the '777 Patent is invalid. Alphapharm filed a Section viii Statement with the FDA with respect to the Combination Use Patents, asserting that it does not seek approval for any of the uses covered by those patents.

Mylan filed a paragraph IV certification with respect to the '777 Patent, claiming that it is invalid. With respect to the Combination Use Patents, Mylan filed a paragraph IV certification addressing the pharmaceutical composition claims of one of the patents and a Section viii Statement regarding the method claims.

V. The Alphapharm and Mylan Statements of Obviousness

In their paragraph IV certifications, both Alphapharm and Mylan claimed that the '777 Patent was invalid due to obviousness. Alphapharm and Mylan were required to send a notice of paragraph IV certification that included detailed statements of the legal basis of their positions that the '777 Patent was invalid ("Section 355 Statement"). *See* 21 U.S.C. §355(j) (2) (b) (ii). By the time of trial, each defendant had radically altered the approach to the invalidity issue expressed in its statement. Mylan abandoned its articulated theory of obviousness in its entirety, and pursued an inequitable conduct claim at trial. Alphapharm altered its obviousness argument in several

[28] Ranbaxy also included, with its Paragraph IV certification, Section viii Statements with respect to the method claims contained in the Combination Use Patents.

substantial ways. The following describes the parties' Section 355 Statements and compares them to the positions they took at trial.

Alphapharm's Section 355 Statement, dated January 29, 2004, recognized that it had the burden to prove by clear and convincing evidence that the prior art must provide some reason or motivation for a person of ordinary skill to make pioglitazone. It identified only two sources of prior art: the '200 Patent and Sohda II. As its position at trial evolved, it also argued that the divisional patents to the '200 Patent and a few articles in scientific journals were also prior art.

Insofar as the '200 Patent was concerned, Alphapharm argued in the Statement that the patent generically disclosed pioglitazone, and identified three compounds related to pioglitazone: compounds 16, 40, 42.[29] It noted that compound 42 is the methyl homolog of the ethyl compounds covered by Claim 1 of the '777 Patent, and argued that an exchange of an ethyl group for a methyl group would have been obvious.

Next, relying on the fact that two compounds discussed in Sohda II, compounds 11 and 14, are revealed in that article to have identical efficacy and yet differ only in that one has an ethyl substituent and another has a methyl substituent, Alphapharm contended that one of ordinary skill would conclude that the methyl and ethyl are "equivalent with respect to biological activity on a closely related analog of pioglitazone." In making this assertion, Alphapharm identified each compound as attached to a pyridyl ring. Neither compound has a pyridyl ring as its left end moeity and Alphapharm does not argue at trial that they do.[30]

At trial, Alphapharm concentrated on an entirely different compound described in Sohda II. It argued that the discussion in Sohda II of compound 58 (which had a higher combined efficacy score than either compound 11 or 14) would have led one of ordinary skill in the art to

[29] Compound 16 has an ethyl substituent on a phenyl ring. Compound 40 is the unsubstituted pyridyl ring known as compound 3894. Compound 42 has a 6-methyl substituent on a pyridyl ring; it is compound (b).

[30] A benzene ring is at the left end of each compound.

choose compound 58 as the lead compound for further development. That argument is not to be found in Alphapharm's Section 355 Statement.

Alphapharm also argued in its Section 355 Statement that both the '200 Patent and Sohda II identify ciglitazone as having low toxicity, and that Takeda did not demonstrate that pioglitazone was surprisingly superior to ciglitazone.

Similarly, it contended that the '777 Patent alleges an entirely different activity for ciglitazone than was disclosed in Sohda II. Alphapharm did not pursue either theory concerning ciglitazone at trial.

Next, Alphapharm's Section 355 Statement argued that Table 1 in the '777 Patent does not support the superiority of pioglitazone, and that the testing methodology described in the patent is flawed. Specifically, Alphapharm argued that "many" of the toxicity values on Table 1 were not "statistically significant." Alphapharm did not make this argument at trial.

Alphapharm argued in its Section 355 Statement that the experiments underlying the testing of a compound's toxicity to the heart were "inherently flawed" since Table 1 in the '777 Patent indicated that pioglitazone did not cause heart enlargement with a dose of 100 mg/kg, while the prescribing information for ACTOS® advises that heart enlargement was observed at 4 mg/kg in rats. The screening tests that produced the Table 1 data were, as described in the Patent's Application, two-week tests. The tests to which the ACTOS® disclosure refers were long-term tests conducted by Upjohn in 1992. Alphapharm tried to use this flawed post-hoc reasoning at trial, and that effort was rejected.

In its Section 355 Statement, Alphapharm next argued that the examiner should not have found that Takeda presented sufficiently compelling evidence to overcome the prima facie obviousness of pioglitazone. It pointed to the efficacy data for the rats, which showed that the ED25 values for all of the pyridyl ring compounds were comparable and that all have strong pharmacological activity. In a related argument, Alphapharm contended in its Section 355 Statement that Takeda did not present any data to the examiner to establish that the other three ethyl 2-pyridyl compounds covered by Claim 1 had surprising or unexpected results. At

trial, the thrust of Alphapharm's evidence concerned compound (b), which Table 1 revealed was potent in both mice and rats, but highly toxic. Alphapharm did, however, particularly in its summation, try to fashion an argument about the ethyl compounds other than pioglitazone that are covered by the patent.

Mylan's Section 355 Statement, dated September 8, 2003, was far more straightforward. It also identified only two relevant pieces of prior art, the '200 Patent and Sohda II. It argued simply that one compound described in both, which had a benzene ring at the left end instead of a pyridyl ring, and which was identified in Sohda II as having high efficacy,[31] made the invention of pioglitazone obvious. According to Mylan, the two compounds are "bioisosteres," and their structural similarity made it obvious to replace a benzene ring with a pyridine ring.

Mylan incorrectly described the benzene compound both in terms of its structural relationship to pioglitazone and in terms of its efficacy.[32] In any event, Mylan completely abandoned this theory of obviousness during the discovery period. It proceeded to trial on an inequitable conduct claim.

W. Procedural History

On September 16, 2003, Takeda sued Mylan, Watson and Ranbaxy. Takeda sued Alphapharm on March 12, 2004. Takeda alleged direct infringement of the claims of the '777 Patent against Mylan and Alphapharm, and sought a declaratory judgment of induced infringement of the claims of the Combination Use Patents against all four defendants. Takeda's action against Alphapharm was accepted as a related to the other three actions on March 18, 2004. In their answers, Mylan and Alphapharm both asserted that the '777 Patent was invalid on the ground of obviousness. Defendant Watson moved to dismiss as non-justiciable those claims in Takeda's complaint that alleged induced infringement of the Combination Use Patents. Watson's motion was denied because Takeda alleged "a

[31] The benzene compound is compound 16 in the '200 Patent and compound 14 in Sohda II.

[32] The compound had a combined efficacy score of 5; many compounds had higher scores.

controversy of sufficient immediacy." Takeda Chem. Indus., Ltd. v. Watson Pharm., Inc., 329 F. Supp. 2d 394, 403 (S.D.N.Y. 2004). A July 20, 2004 Order set May 27, 2005 as the date by which fact discovery would end, and set January 16, 2006 as the trial date.[33]

Alphapharm moved to dismiss nine of Takeda's claims relating to the Combination Use Patents on May 21, 2004. On the same day, Takeda moved to dismiss Alphapharm's affirmative defense and counterclaim for "patent misuse." Alphapharm's motion was denied by Order dated August 13, 2004. Takeda's motion to dismiss was granted in an Opinion that noted that Alphapharm had failed "to meet even the minimal requirements of notice pleading." Takeda Chem. Indus., Ltd. v. Alphapharm Pty. Ltd., 04 Civ. 1966 (DLC), 2004 WL 1872707 (S.D.N.Y. Aug. 19, 2004).

Mylan's substitution of an inequitable conduct claim for its obviousness theory occurred in 2005. By letter dated March 15, 2005, Mylan noted that it could not locate experiments in Takeda's laboratory notebooks to support all the data submitted to the PTO and raised for the first time an argument that Takeda may have procured the '777 Patent "through inequitable conduct." On April 25, in response to a contention interrogatory from Takeda, Mylan formally contended for the first time that the '777 Patent was unenforceable on the basis that Takeda had committed inequitable conduct in its prosecution of the '777 Patent.[34] On June 6, after the close of fact discovery, Mylan served supplemental responses to Takeda's interrogatories, in which it expressed the view that the '777 Patent was invalid on the basis of obviousness over compound 57 from Sohda II,[35] a different compound from the one identified in Mylan's Section 355 Statement. Mylan's effort to substitute a new theory of obviousness was rejected in an Order of June 15. Takeda Chem. Indus., Ltd. v. Mylan Labs., Inc., 03 Civ. 8253 (DLC), 2005 WL 1457696, at *2 (S.D.N.Y. June 15, 2005). *See also* Takeda Chem. Indus., Ltd. v. Mylan Labs., Inc., 03 Civ.

[33] The trial date was later moved to January 17, 2006, due to a federal holiday.

[34] Despite this notice, in early June, Mylan's counsel refused to let the company's Rule 30(b) (6) witness explain the bases for Mylan's contention that the '777 Patent is invalid on grounds other than those disclosed in the Mylan's Section 355 Statement.

[35] Compound 57 is Takeda compound 3894, the unsubstituted 2-pyridyl.

8253 (DLC), 2005 WL 2092920, at *1 (S.D.N.Y. Aug. 31, 2005). Meanwhile, on June 15, Mylan was given leave to amend its answer to add a claim for inequitable conduct, essentially because of the "desire that issues, if at all possible, be addressed on the merits in litigation." Takeda Chem. Indus., Ltd. v. Mylan Labs., Inc., 03 Civ. 8253 (DLC), 2006 WL 44053, at *1 n.2 (S.D.N.Y. Jan. 9, 2006). Given its late notice of this new claim, Mylan was required to present all bases for the claim in its expert reports.

All four actions were consolidated for trial by Order dated October 13, 2005, although the '777 Patent issues were to be tried before the issues relating to the Combination Use Patents. By Order of December 30, 2005, the trial on the Combination Use Patents was severed.

Takeda, Alphapharm and Mylan moved in limine to strike testimony by or to preclude certain witnesses. Takeda moved against Mylan experts Hendry, Nusbaum, and Ronis. Alphapharm moved against Takeda experts Hendrickson, Inzucchi, Kettyle, Koller and Stoner. Mylan moved against Stoner and to exclude a supplemental declaration from Landau. Mylan also moved to preclude Takeda from offering evidence of any missing laboratory notebooks.

Ronis' testimony was stricken to the extent it was not contained in his expert report. Id. at *2. Hendry's testimony was stricken to the extent it covered areas in which he had denied having expertise. Id. at *2-3. The motions addressed to testimony by Nusbaum and Stoner were granted to the extent they offered legal argument or opinions that went beyond their expertise. Id. at *3; Takeda Chem. Indus., Ltd. v. Mylan Labs., Inc., 03 Civ. 8253 (DLC), 2006 WL 137374, at *2 (S.D.N.Y. Jan. 9, 2006). Landau's supplemental declaration was stricken. Takeda, 2006 WL 444053, at *3. Mylan's motion to exclude evidence of any missing notebooks was denied. Takeda Chem. Indus., Ltd. v. Mylan Labs., Inc., 03 Civ. 8253 (DLC), 2006 WL 83112 (S.D.N.Y. Jan. 12, 2006).

Hendrickson's testimony was stricken to the extent he opined on the selection of lead compound. Takeda, 2006 WL 137374. The motions concerning Koller, id. at *2, and Inzucchi and Kettyle were denied, Takeda Chem. Indus., Ltd. v. Mylan Labs., Inc., 03 Civ. 8253, 2006 WL 66480 (S.D.N.Y. Jan. 12, 2006).

At trial Mylan offered into evidence the unredacted declarations from Hendry and Ronis that it had served with the Joint Pretrial Order. The unredacted Ronis declaration was submitted as an Offer of Proof pursuant to Rule 103 of the Federal Rules of Evidence. In making its Offer of Proof, Mylan emphasized that it was not seeking to make a motion for reconsideration of the Court's decision to strike parts of Ronis' testimony, Takeda, 2006 WL 44053, and it is not being treated as such.[36]

Discussion

Alphapharm asserts that pioglitazone is obvious in light of the prior art. Mylan contends that Takeda engaged in inequitable conduct. For the following reasons, each of these arguments is rejected.

I. Obviousness

Inherent in the Constitution's grant of patent power to Congress is the requirement that a patent monopoly be conveyed only where there is "[i]nnovation, advancement, and things which add to the sum of useful knowledge." Graham v. John Deere Co., 383 U.S. 1, 6 (1966). Through the 1952 Patent Act, Congress codified three conditions for patentability: novelty, utility, and non-obviousness. Id. at 17; 35 U.S.C. §101-103. It is the last of these three conditions on which Alphapharm rests its challenge to Takeda's '777 Patent.

A patent may not be obtained if "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. §103 (a) (emphasis supplied). Section 103 emanates from the Supreme Court's nineteenth century decision in Hotchkiss v. Greenwood, 52 U.S. 248 (1850), and its progeny, which took a functional

[36] At trial, Takeda presented its evidence first. At the close of Takeda's case on January 25, both Takeda and Alphapharm moved for judgment as a matter of law under Rule 52 (c). Fed. R. Civ. P. 52(c). Alphapharm had not carried its burden of showing obviousness at that point, and did not do so either through its later presentation of its own evidence. Since the burden rested on Alphapharm, it was not appropriate to grant Takeda's motion until Alphapharm had had an opportunity to present its case.

approach to patent analysis and eschewed labels. Graham, 383 U.S. at 12, 17. The talismanic statement of the obviousness inquiry appears in Graham, which identifies four factual underpinnings to a determination of obviousness: (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the differences between the prior art and the claimed invention, and (4) objective indicia of non-obviousness. Id. at 17-18; *see* Merck & Co., Inc. v. Teva Pharm. USA, Inc., 395 F.3d 1364, 1372-73 (Fed. Cir. 2005). The issue of obviousness is a question of law. Richardson-Vicks Inc. v. Upjohn Co., 122 F.3d 1476, 1479 (Fed. Cir. 1997).

The scope and content of the prior art includes art that is "reasonably pertinent to the particular problem with which the invention was involved." Ruiz v. A.B. Chance Co., 234 F.3d 654, 664 (Fed. Cir. 2000) (citation omitted). Prior art must be available before the date of invention. 35 U.S.C. §103(a), *see* Richardson-Vicks Inc., 122 F.3d at 1480. Prior art teaches away from an invention "when it suggests that the developments flowing from its disclosures are unlikely to produce the objective of the applicant's invention." Syntex (U.S.A.) LLC v. Apotex, Inc., 407 F.3d 1371, 1380 (Fed. Cir. 2005).

Whether the claimed invention is obvious must be evaluated from the perspective of a hypothetical person of ordinary skill in the art. Ruiz, 234 F.3d at 666. In determining what constitutes ordinary skill in the art, a court may consider "1) the types of problems encountered in the art; 2) the prior art solutions to those problems; 3) the rapidity with which innovations are made; 4) the sophistication of the technology; and 5) the educational level of active workers in the field." Id. at 666-67.

Secondary considerations or the objective indicia of non-obviousness include "commercial success, long-felt but unresolved need, failure of others, copying, and unexpected results." Id. at 662-63. These considerations are probative to the extent they "give light to the circumstances surrounding the origin of the subject matter sought to be patented." Graham, 383 U.S. at 17-18. The "nexus" or causal relationship between the secondary consideration and the claimed invention should shed light on whether the invention was obvious or not. *See* Merck, 395 F.3d at 1376. A presumption that a patented invention is commercially successful arises when a patentee can demonstrate "significant sales in a

relevant market, and that the successful product is the invention disclosed and claimed in the patent." Ecolochem, Inc. v. Southern California Edison Co., 227 F.3d 1361, 1377 (Fed. Cir. 2000) (citation omitted).

Patents are presumed to be valid. 35 U.S.C. §282. A party challenging a patent can establish a prima facie case of invalidity by showing that the invention is obvious under an analysis of the first three Graham factors. Winner Intern. Royalty Corp. v. Wang, 202 F.3d 1340, 1350 (Fed. Cir. 2000). If a prima facie case of obviousness is established, the burden of production shifts to the party defending the patent to demonstrate non-obviousness under the fourth Graham factor. Id. The burden of persuasion, by clear and convincing evidence, always remains with the party asserting the invalidity of the patent. Beckson Marine, Inc. v. NFM, Inc., 292 F.3d 718, 725 (Fed. Cir. 2002). The burden is "especially difficult" if the challenger relies on prior art "that was before the patent examiner during prosecution." Glaxo Group Ltd. v. Apotex, Inc., 376 F.3d 1339, 1348 (Fed. Cir. 2004) (citation omitted). This added burden stems from the "deference that is due to a qualified government agency presumed to have properly done its job." Ultra-Tex Surfaces, Inc. v. Hill Brothers Chem. Co., 204 F.3d 1360, 1367 (Fed. Cir. 2000) (citation omitted).

A strand of the law of obviousness addresses patents protecting chemical compounds. In the case of a chemical compound, a prima facie case of obviousness exists where there is a "structural similarity between claimed and prior art subject matter" and "the prior art gives reason or motivation to make the claimed compositions." Yamanouchi Pharm. Co., Ltd. v. Danbury Phamacal, Inc., 231 F.3d 1339, 1343 (Fed. Cir. 2000) (citation omitted). "[O]bviousness may render a claimed invention invalid where the record contains a suggestion or motivation to modify the prior art teaching to obtain the claimed invention." Beckson, 292 F.3d at 727. Thus, an invention is prima facie obvious where the prior art would imbue one of ordinary skill in the art with a "reasonable expectation of success" in achieving the goals that the inventor sought to accomplish by transforming a compound in the prior art into the structurally similar claimed invention. Yamanouchi, 231 F.3d at 1343 (citation omitted). While a reasonable expectation of success must be shown, in order to show prima facie obviousness it is not necessary to show that success was absolutely predictable. Id.

Where the creation of a chemical compound requires the chemist to pursue several steps in manipulating a compound revealed in the prior art, the patent challenger must show that one of ordinary skill in the art would have had sufficient motivation to take each of those steps. Id. at 1344-45. Similarly, if the prior art "offers no suggestion to pursue the particular order" of manipulations that led to an invention, and where a deviation in the order would have taught away from the invention, then the challenger must show what would have led any ordinary artisan in the field "to follow the precise steps that produced a remarkable invention." Id. at 1345.

A prima facie case of obviousness may be rebutted by "showing that the claimed compositions possess unexpectedly improved properties or properties that the prior art does not have." Dillon, 919 F.2d at 692-93. When rebuttal evidence is submitted, "all the evidence must be considered anew." In re Eli Lilly and Co., 902 F.2d 943, 945 (Fed. Cir. 1990); *see also* Glaxo Group Ltd., 376 F.3d at 1349; Richardson-Vicks, 122 F.3d at 1482-83.

Alphapharm contends that pioglitazone is prima facie obvious over the prior art compound (b) from Table 1 of the '777 Patent, which had been identified in both the '200 Patent and Sohda II.

Alphapharm argues that the prior art clearly identified compound (b) as a lead compound warranting further investigation, and that the application of a few, obvious chemical processes would have produced pioglitazone. Turning to objective evidence of pioglitazone's obviousness, Alphapharm contends that pioglitazone's lack of toxicity is not unexpected because variability among compounds is "inherent." As for its commercial success, Alphapharm argues that the success of ACTOS® must be discounted because inter alia pioglitazone was not the first TZD on the market and is not the only successful TZD still on the market. These and Alphapharm's other arguments are described in detail below.[37]

[37] It has been challenging to capture Alphapharm's arguments because it has presented a constantly shifting set of arguments, abandoning some, inventing others, and even contradicting itself as the trial progressed. Nonetheless, every effort has been made to address each of the principal arguments raised during the trial by Alphapharm.

Alphapharm's arguments fall woefully short of the mark. The prior art did not disclose or suggest either the pioglitazone molecule itself or how to make it. Alphapharm has not shown by any persuasive evidence, much less by clear and convincing evidence, that one with ordinary skill in the art would have had any reasonable expectation based on the prior art that synthesizing pioglitazone would result in the discovery of a non-toxic, effective treatment for diabetes, and therefore would not have had any motivation to do so. To begin with, the evidence is overwhelming that one skilled in the art would not have, based on the prior art, chosen compound (b) as a lead compound. Beyond that, Alphapharm has not shown that the ordinary artisan would have had sufficient motivation to take each of the several conceptual and experimental steps that were necessary to move beyond compound (b) and create the pioglitazone molecule.

Even if Alphapharm had been able to show a prima facie case of obviousness, there is compelling and conclusive evidence that pioglitazone's non-toxicity was unexpected. Alphapharm is unable to overcome the extreme differences in the toxicity profiles between pioglitazone and prior art compound (b), whose modification it contends would have led to the discovery of pioglitazone. Confronted with overwhelming evidence that the non-toxicity of pioglitazone was entirely unexpected given the high toxicity of compound (b), including the admission of Alphapharm's own expert that there was no reasonable basis to expect that pioglitazone would be non-toxic, Alphapharm ignores the relevant legal standard and argues simply that there is so much variability in the pharmacological effects of compounds, even compounds that share similar structures, that a compound's non-toxicity is "not surprising." This does not carry Alphapharm's burden of showing obviousness. The discussion that follows examines each of the Graham factors, paying particular attention to the identification of a lead compound, the motivation to alter that compound, and unexpected results.

A. Qualifications of a Person of Ordinary Skill in the Art

The parties agree that a person with ordinary skill in the art would have a graduate degree in chemistry or a relevant branch of chemistry and practical experience applying that education by working at or consulting with a pharmaceutical company in the development of pharmaceutical

compounds.[38] It is unnecessary to refine further the minimum qualifications of a person with ordinary skill in the art, since nothing that follows in this analysis turns on the presence of a more precisely drawn definition.

Alphapharm has argued that one of Takeda's experts, Danishefsky, is not qualified to opine about what one with ordinary skill in the art of medicinal chemistry would understand or do since he is a synthetic organic chemist. Danishefsky is a renowned synthetic organic chemist who has devoted his entire career to exploring the issues of medicinal chemistry.[39] He supervises the training of medicinal chemists, has recently been nominated to receive a lifetime achievement award in chemistry from a major pharmaceutical company,[40] and regularly consults with major hospitals and pharmaceutical companies on issues of medicinal chemistry. He is superbly qualified to opine in the field of medicinal chemistry.

B. Relevant Prior Art

As noted above, Takeda applied in Japan for what became known as the '777 Patent in January 1985, and in the United States in January 1986; the '777 Patent issued on August 18, 1987. It is undisputed that the relevant prior art for the '777 Patent includes the '200 Patent, issued in 1981; and Sohda II, published in 1982, both of which were identified by Takeda in its application for the '777 Patent. The '200 Patent first disclosed the

[38] Alphapharm defines someone of ordinary skill in the art as a person who would have secured a Ph.D. in medicinal chemistry or a related field, done postdoctoral work for two to three years and thereafter worked for a pharmaceutical company for two to three years. Takeda defines the person as someone with a Master's Degree in chemistry or chemical engineering with four years experience in the research and development of pharmaceuticals or medical organic compounds, or someone with a Ph.D. in chemistry or chemical engineering with two years of experience in the research and development of pharmaceuticals or medicinal organic compounds.

[39] Takeda brought to this trial experts of extraordinary accomplishment and distinction. Many of them, including Danishefsky, were preeminent in their field of endeavor. These were scientists whose knowledge and opinions were uniformly helpful to the Court in understanding the science at issue here.

[40] Danishefsky will receive a lifetime achievement award from Bristol-Myers Squibb in May 2006 and the National Academy of Science's medal in chemical sciences in April 2006.

compound on which Alphapharm relies for its obviousness argument, compound (b).[41] Alphapharm's expert identifies Sohda II as the "key" piece of prior art on which the skilled artisan would have relied to identify compound (b) as the lead compound for further investigation.[42]

Although Alphapharm's Rule 30(b) (6) witness testified that Alphapharm was not aware of any prior art that Takeda failed to put before the examiner, at trial Alphapharm identified two additional patents and one other article as prior art. It asserts that two divisional patents for the '200 Patent, the '605 and '779 Patents, issued on July 20, 1982, and April 24, 1984, respectively, and their prosecution histories, should also be considered relevant prior art.[43] In particular, it asserts that the prosecution history of the '779 Patent, which was available to the public through examination in Washington, D.C. when the '779 patent was issued, would have assisted those with ordinary skill in the art in selecting compound (b) as a lead compound for further investigation. Finally, Alphapharm identifies an article in a peer reviewed scientific journal: Nohara, A. et al., "Studies of Antianaphylactic Agents. 6.1 Synthesis of Some Metabolites of 6-Ethyl-3(1H-tetrazol-5-yl)chromone and their Analogues," Journal of Medicinal Chemistry, 22:3, 290-295 (1979) ("Nohara Article").[44] Mosberg gleaned from the Nohara Article that persons of ordinary skill in the art, including Takeda, practiced the synthesis of routine homologs to improve promising drug compounds as of 1979.

[41] Compound (b) from Table 1 is a 6-methyl, which was identified in the '200 Patent as compound 42.

[42] While Alphapharm began the trial by identifying Sohda II as the critical writing which would have led one skilled in the art to identify compound (b) as a lead compound, in the face of overwhelming evidence to the contrary, by the end of the trial it had virtually abandoned reliance on Sohda II.

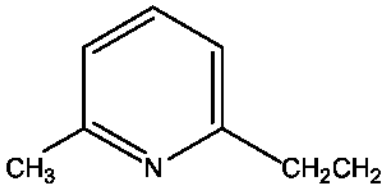
[43] Takeda disputes that these patents can properly be considered prior art.

[44] Alphapharm has abandoned its contention that a second article, Cunningham, S. et al., "The Characterization and Energetic Potential of Brown Adipose Tissue on Man," Clinical Science 69, 343-348 (1985) ("Cunningham Article"), was prior art. Alphapharm's expert used the Cunningham Article to educate himself about how persons of ordinary skill viewed the issue of brown fat in the 1980's. Compound (b) was identified in Sohda II as increasing brown fat.

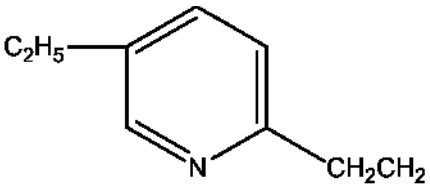
C. Differences Between the Prior Art and Pioglitazone

Alphapharm's assertion of obviousness rests on two claims: that it would have been obvious to select a single compound from the prior art -- a 6-methyl on a pyridyl ring, which is compound (b) on Table 1 of the '777 Patent—as the "lead compound" for development, and that it would have been obvious to create and test the compounds that lie between the 6-methyl and pioglitazone, which is a 5-ethyl on a pyridyl ring.[45] The program would have entailed synthesizing compounds in which a methyl appears at each of the open positions on the pyridyl ring, a process that Alphapharm terms "walking the ring," and also synthesizing compounds in which the substituent on the pyridyl ring at each of these positions is an ethyl instead of a methyl, a process referred to as "homologation."

The following diagrams of the left end of compound (b) and pioglitazone illustrate the changes in the molecular structure that were necessary to make the transformation.



Compound (b)



Pioglitazone

[45] As already noted, a methyl group contains one carbon, while an ethyl group contains two carbons.

Both of these structures are on a pyridyl ring.[46] Compound (b) has a substituent added at the 6th position on the ring; pioglitazone's substituent is added at the 5th position, counting counter-clockwise from the nitrogen atom on the ring.

1) Identification of a Lead Compound

Alphapharm's obviousness argument relies in the first instance on its contention that one skilled in the art would have recognized compound (b) as the lead compound for further development.[47] Alphapharm's expert has rested his identification of compound (b) as a lead compound on his reading of the '200 Patent and Sohda II.

As described above, the '200 Patent provided protection for TZD derivatives. The molecular structure of compound (b) was illustrated in the patent as one of fifty-four examples of TZD compounds with a certain structure that had been synthesized through steps described in the patent. Examples of still more TZD compounds synthesized through other procedures were also illustrated. The prosecution history of the '200 Patent includes some test results for nine compounds that were presented to the PTO as "typical" of compounds covered by the disclosed invention in order to demonstrate that TZD compounds covered by the invention were "far superior" in their blood glucose and plasma triglyceride lowering effects than compounds in the prior art. Compound (b) was one of the nine whose test results were charted, and it was one of three such compounds charted in the '200 Patent that had the best disclosed performance.[48]

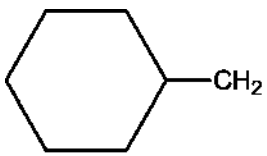
[46] For ease of reference, certain explanations are repeated here. Pyridyl denotes a six-membered ring of five carbon atoms and one nitrogen atom. The numbering on a ring begins with the highest atomic weight atom in the ring, which in this case is nitrogen. The numbering moves in a counterclockwise fashion.

[47] Alphapharm's Section 355 Statement did not explain why compound (b) would be chosen as a lead compound over others described in either the '200 Patent or Sohda II. Alphapharm has abandoned its assertion in its Section 355 Statement that pioglitazone was obvious based on an analysis of compounds 11 and 14 in Sohda II.

[48] Of the nine, three compounds, including compound (b), had a combined score of 7; five had a score of 6; one had a score of 2.

Since Takeda only presented test results for nine of the hundreds of millions of TZD compounds covered by the patent application, one with ordinary skill in the art would have had no reasonable basis to conclude that these nine were the best performing of all of the compounds tested by Takeda, and thus that one of these nine should be selected as the lead compound for further development. Even if one could make that leap, however, the prosecution history for the '200 Patent disclosed two other compounds, in addition to compound (b), that appeared to have superior performance among the nine that were tested. And, the next year, when Sohda II was published, compound (b) was not singled out as one of the best performing compounds.

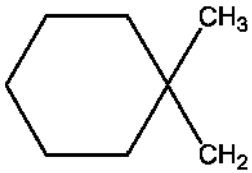
Sohda II, which has also been described above, reported test results on 101 TZD compounds, and identified three that "exhibited the most favorable properties in terms of activity and toxicity." Each of these three compounds had a different left moeity, and therefore, provided different starting points from which one of ordinary skill in the art could make changes in the hope of identifying successful compounds. Compound 47 terminated with an unsubstituted cyclohexane ring[49] and is connected to the rest of the compound by a CH2. Compound 49, which is ciglitazone, has a similar structure to compound 47, however, there is methyl substituent at the point of attachment to the rest of the compound. Compound 59 is the only one of the three with a pyridyl ring at the left end moeity, however, it is a 3-pyridyl ring. (Pioglitazone's pyridyl ring is a 2-pyridyl ring.[50]) The following diagrams illustrate the differences in the left end of these structures more effectively than a narrative description.



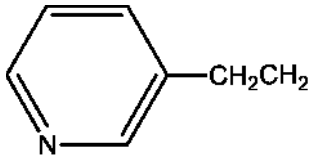
Compound 47

[49] A cyclohexane ring is a saturated ring of six carbons.

[50] The 2-pyridyl is attached to the remainder of the TZD molecule at the second position on the pyridyl ring; the 3-pyridyl, at the third position.



Compound 49



Compound 59

Compound (b) was among the 101 whose test results were reported in Sohda II, but it was not one of the three compounds identified by the authors as having the most favorable performance.

Sohda II gave detailed efficacy data, but did not set out the toxicity test results in comparable chart form. It did discuss in its narrative sections, however, various toxicity and side effect issues which eliminated some of the compounds with strong efficacy ratings from being singled out for their overall performance. For example, seven compounds had the highest combined efficacy score, which was a rating of 7. Sohda II identified problems with toxicity or side effects for six of the seven compounds.[51] Compound (b) was one of the seven, but was described as causing "considerable increases in body weight and brown fat weight."[52] The three compounds that were identified as having the most favorable performance each had a combined efficacy score of only 5.[53]

[51] The one compound that scored 7 and yet had no identified problems was compound 99. Its structure at the left end moiety differs significantly from the pyridyl.

[52] Compound 3894, which had a combined potency score of five, was described as having the same problematic side effects as compound (b).

[53] Of the 101 compounds in Sohda II, 39 had a combined score of 5 or higher. Twenty-nine of the thirty-nine had been described in the '200 Patent.

A person with ordinary skill in the art would had concluded from an examination of the '200 Patent, including its file wrapper, and of Sohda II, that the three compounds identified in Sohda II as promising should be the starting point for further investigation. There were literally thousands of different substituents that one of ordinary skill in the art could consider in modifying those three compounds. Such a person would certainly not have concluded that compound (b) should be chosen as a lead compound over the many other more obvious or at the very least similarly interesting choices presented by that prior art. Indeed, Sohda II teaches away from compound (b) when it specifically comments on its negative effects on body weight and brown fat. Type 2 diabetes is a chronic disease. Any effective drug will be given over a long period of time, and therefore, those of ordinary skill in the art would have been especially sensitive to toxicity and side-effects.

History confirms this analysis. Takeda and another pharmaceutical company worked extensively to develop one of the three compounds identified by Sohda II as particularly promising, before abandoning it because of its toxicity. Ciglitazone was Sohda II's compound 49, and was withdrawn by Takeda from further development during human testing both because it failed the chick lens assay test and due to efficacy concerns.

In fact, because of concerns over toxicity in treating a chronic disease like diabetes, one skilled in the art would have been more likely to choose as a starting point for further research one of the many compounds in Sohda II, and there were over ninety, where the authors did not disclose the existence of toxicity or side effects, and to engage in research to increase the efficacy and confirm the absence of toxicity of those compounds, than to choose as a starting point a compound with identified adverse effects. If for some yet unexplained reason one chose to start with a compound that had identified problems, one skilled in the art would be motivated to make fairly radical changes to it in order to try to overcome the problems.

Admissions from an Alphapharm scientist confirm that there was no basis to select compound (b) (that is compound 58 from Sohda II) as a lead compound other than hindsight. At his deposition, Rosenberg, who is the head of Alphapharm's intellectual property department and who was also the scientist who formulated its Section 355 Statement, admitted that there

was "nothing to recommend" compound (b) over any of the other compounds that had a combined score of 7, and that he only chose compound (b) from Sohda II "because it was similar to pioglitazone."

During his cross-examination, Alphapharm's expert Mosberg presented a new and remarkable explanation for why compound (b) would have been selected as the lead compound by one of ordinary skill in the art over the other six compounds with a rating of 7 and over the three compounds singled out for favorable mention in Sohda II. He argued that it appeared from Sohda II that each of these other compounds, and the molecules closely related to them, were being pursued actively by Takeda and that it would be impractical to compete with Takeda, given its head start, and to invest precious research resources into the compounds Takeda was investigating. This argument was not presented by Mosberg in his direct testimony, where he essentially ignored the existence of the other compounds that scored 7 and the three compounds given prominence in Sohda II. It also directly contradicts his direct testimony, where he asserted that compound (b) would have been selected as a lead compound by one skilled in the art because of the evidence that Takeda was "zeroing in on substituted pyridyl rings."[54]

In any event, there are a myriad of problems with Mosberg's recently invented analysis. First, it is not supported by any intellectually rigorous analysis. Second, the test is not whether a compound seems an unpopular candidate for development among competitors but rather whether one of ordinary skill in the art would have been motivated to choose it as a lead compound in an effort to develop a safe and effective drug to treat diabetes. Third, Mosberg's analysis completely undercuts Alphapharm's contention that compound (b) was the obvious lead compound for investigation. Surely, under Mosberg's revisionist reading of Sohda II, the compounds in which Takeda seemed to be expressing an interest were the more appropriate choices for one skilled in the art who was seeking to find a successful anti-diabetic agent, instead of compound (b), which he believes Takeda had abandoned.

[54] Mosberg's trial testimony also directly contradicts Alphapharm's proposed findings of fact submitted before trial, which indicate that it hoped to establish that one skilled in the art would have understood that Takeda was focusing its attention on compound (b).

Mosberg also tries to transform its identified problems of an increase in body weight and brown fat into an advantage for compound (b). He argues, with some creativity but little persuasion, that these identified problems would only "motivate one of skill in the art to make changes" in the compound.[55] Such a response does not explain, however, why compound (b), with its associated problems, should be chosen as the lead compound for further investigation.

Mosberg makes two other arguments in an effort to explain why compound (b) would be selected as a lead compound. First, Mosberg argues that further support for focusing on compound (b) comes from the '779 Patent, which specifically claims over sixty compounds including compound (b). Alphapharm's Section 355 Statement did not identify the '779 Patent as relevant prior art.

As already described, it was the PTO's initial rejection of the '200 Patent that led Takeda subsequently to file the '605, '779, and '141 divisional patents. Because they are divisional patents, the text of each of the divisional patents is identical to the text of the '200 Patent. The '200 Patent discloses hundreds of millions of TZD compounds. The divisional patents are directed to subsets of those compounds covered by the generic disclosure in the '200 Patent. The '779 Patent, which was filed after the '605 Patent, actually claims a larger class of compounds than the '605 Patent. The '605 Patent claims 1080 compounds, while the '779 Patent claims over one million compounds.[56] These patents claimed not only pyridyl derivatives but also thiazolyl derivatives.
Takeda filed the application for what became the '779 Patent on March 15, 1983, identifying through supporting diagrams over 60 compounds that were TZD derivatives. Essentially, the claims were directed to a structure

[55] It is undisputed that weight management is an important element in the treatment of Type 2 diabetes and that this was understood in the 1980s. Takeda's expert opines persuasively that the Cunningham Article, which warned that "considerable caution" should used in extrapolating animal studies' brown fat findings to humans, would not have diminished the negative impact of the statements about weight gain in Sohda II on a scientist evaluating compound (b) for exploration. Mylan's Rule 30(b) (6) witness opined that one of ordinary skill in the art would rule out compound (b) as a compound of interest because of its negative profile disclosed in Sohda II.

[56] These numbers do not include the salts and stereoisomers covered by the patents.

with a pyridyl or a thiazolyl group at the left end of the TZD molecule, with one to three substituents on those rings, the substituents being selected from lower alkyls, halogens and hydroxyl. Two compounds were specifically claimed, compound (b) and a thiazolyl.[57] Compound (b) was also diagramed as compound 42 on the application. In a preliminary amendment of the same date, Takeda stated, "the compounds in which these heterocyclic rings are substituted have become important, especially Compound 42."

There are several problems with Alphapharm's reliance on the '779 Patent.[58] Takeda's expert has given compelling evidence that medicinal chemists do not consider arguments made by patent counsel, particularly when there is contrary information in peer-reviewed literature (such as Sohda II), and that he has never known anyone in his over forty years of work in the field of medicinal chemistry to establish research priorities in this way. Alphapharm's expert essentially agreed, and Alphapharm has presented no evidence to the contrary.[59]

Moreover, if Alphapharm wishes now to rely on a divisional patent as prior art to explain why one skilled in the art would select compound (b) as a lead compound, then it is necessary to consider what one skilled in the art would have concluded by an examination of each of the Takeda TZD patents that had issued by this time. Taken together, they show that Takeda was actively conducting research in many directions, and had not narrowed its focus to compound (b).

[57] The thiazolyl was a 4-methyl 5-thiazolyl.

[58] Alphapharm may also be attempting to make an inequitable conduct argument concerning the presentation of the toxicity data for compound (b) in the '777 Patent by comparing it to general statements in the '779 Patent about toxicity levels in TZD derivatives. The comparison is spurious and does not require further discussion.

[59] In addition, the file wrapper for the '779 Patent was simply not accessible to one of ordinary skill in the art. As of 1983, patent applications were not prosecuted publicly and the application would not have been available to the public until the patent had issued on April 24, 1984. At that time, the file history would have had to be specially obtained at the patent office.

Finally, in support of Alphapharm's argument that compound (b) would have been selected as the lead compound from the prior art, in particular from Sohda II, Mosberg contends that one of ordinary skill in the art would have observed that the four compounds revealed in Sohda II with a pyridyl ring on the left hand side of the structure, display high potency and that of those compounds the compound with the methyl substituent, that is compound (b) or 58, had the highest potency. He points with emphasis to the fact that the substituted pyridyl has a higher combined efficacy score than the unsubstituted pyridyl.[60] From that, Mosberg suggests that one of ordinary skill in the art would have concluded that the methyl substituent was responsible for increasing potency and thus would have been strongly motivated to attempt further substituent replacement to reduce the unwanted side effects of the 6-methyl, while maintaining its potency.

This argument benefits entirely from hindsight. Sohda II describes several clusters of efficacious compounds, including the cluster into which compounds 47 and 49 fall, compounds 47 and 49 being two of the three compounds given particular attention by the authors. In any event, of the cluster into which compound (b) falls, the most obvious candidate for a lead compound is the one identified by the article for further investigation, that is compound 59, since the article reported no toxicity or harmful side effects for that compound. Exploration of that compound, which has a 3-pyridyl ring at its left end rather than the 2-pyridyl ring shared by pioglitazone and compound (b), would of course have led in a different direction.[61]

In sum, Alphapharm has failed to show that compound (b) would have been understood by one skilled in the art as a lead compound. There is no support for such a finding based on the prior art that Alphapharm identified in its Section 355 Statement: the '200 Patent and Sohda II. Thus, it now turns to a statement about compound (b) in application for the '779 Patent. One skilled in the art would not have relied on that reference to identify

[60] The unsubstituted 2-pyridyl (compound 57) had a combined score of 5, while the 2-pyridyl with a methyl at the 6 position (compound 58) had a combined score of 7.

[61] At his deposition Mosberg admitted that one skilled in the art would have been led to investigate all of the compounds based on the 2-, 3-, and 4-pyridyl ring, with less emphasis on the 4-pyridyl compounds.

compound (b) as a lead compound given the more exhaustive and reliable scientific analysis presented by Sohda II, which taught away from compound (b), and the evidence from all of the TZD patents that Takeda filed contemporaneously with the '779 Patent showing that there were many promising, broad avenues for further research.

2) Motivation to Create Pioglitazone

Assuming that compound (b) would have been identified by one skilled in the art as a lead compound, Alphapharm has not shown that such a person would have been motivated to synthesize the compounds that had to be created to find pioglitazone. First, one skilled in the art would have done an initial screening of compound (b) for toxicity and concluded that its toxicity made it an extremely poor candidate for modification.[62] The likely course of action at that point, would have been to return to the compounds actually identified in Sohda II as worthy of further research.[63] Second, Alphapharm has failed to point to anything in the prior art that would have presented one skilled in the art with a reasonable expectation of success in creating the compound that became pioglitazone.

Before addressing Alphapharm's specific arguments, it is useful to describe briefly some of the pertinent chemistry and research issues that one skilled in the art would have faced in the 1980s. Many of the tools that assist today in the process of chemical synthesis were not available in the 1980s. At that time, the process of discovering new compounds for pharmaceutical development involved the screening of sample collections, usually those already in the libraries of the pharmaceutical company, or those created by the chemistry laboratories of the company. When a lead compound was identified, a lead compound being one that contains suggestive properties that are indicative of possibilities for progress, the scientist would modify the lead compound to achieve the right balance of potency and non-toxicity. The

[62] As indicated on Table 1 to the '777 Patent, compound (b) was extremely toxic to the liver, heart, and blood.

[63] There is no contention that the investigation of the three compounds identified in Sohda II as worthy of further investigation would have led with sufficient directness to pioglitazone. As already noted, among other things, two did not have a pyridyl ring on the left moiety, and the left moiety in the third was a 3-pyridyl ring rather than the 2-pyridyl ring in the pioglitazone molecule, meaning that its attachment to the remainder of the TZD molecule was from a different point on the pyridine ring.

modification process was not routine. The chemistry laboratories of the company needed to create, through chemical synthesis, each new compound that needed its potency and toxicity tested. The conceptual acts of moving a methyl substituent to another position on a ring and of replacing it with an ethyl substituent require different starting materials and different chemical processes. While it may be easy to describe in English, the science is time-consuming.

The left-hand end of the TZD molecule is known as a terminating region, and is a so-called hot spot, where small changes can have dramatic repercussions in performance. It would have been a significant research project to understand the consequences of even small modifications to this region of the molecule, and one skilled in the art would not have had any reasonable basis to expect that even small changes in this area would result in an increase as opposed to a decrease in either the efficacy or toxicity of the molecule in any particular organ or body system much less in the body as a whole. There was absolutely no basis whatsoever to form a belief that any particular modification would change a toxic molecule into a non-toxic compound. There was simply no scientific literature which explained how the particular changes to a molecule that are at issue here would lead to a drug with particular effects, whether for better or worse, in the body. As of the 1980s, and even today, the actual mechanism through which a TZD molecule interacts with the body's processes is not understood. In the 1980s, for instance, scientists did not know the shape of the insulin receptor or the specific molecular target for the TZD compound.

Predicting toxicity based on the structure of a compound is particularly difficult. And, in selecting a lead compound for development of a drug to treat a chronic disease, one skilled in the art would have been particularly sensitive to issues of toxicity. As a result of all of these challenges, it is not uncommon to synthesize thousands of compounds before arriving at a new drug that survives all review and enters the pharmaceutical market in the United States. Alphapharm's expert estimates that, even when one has identified a lead compound, success is achieved in at most 1% of research projects.

Alphapharm's expert, Mosberg, argues that the twin steps of "walking the methyl around the ring" and "homologation" to create an ethyl from a methyl are routine steps in the drug optimization process that would have been performed by one of ordinary skill in the art and would have led quite

directly to the discovery of pioglitazone from the investigation of compound (b). Mosberg's opinion was completely undermined by the other evidence presented at trial, including the far more credible testimony from Takeda's experts. It was also contradicted by Alphapharm's in-house medicinal chemist whose deposition testimony was partially adopted as Rule 30(b) (6) testimony for Alphapharm.[64] Rosenberg testified that in making changes to the pyridyl ring on the left end of the TZD molecule, one would look at a host of substituents, such as chlorides, halides and others, not just methyls. He did not even mention ethyls.

a) Walking the Ring

Nothing in the prior art teaches that changing the position of the methyl substituent on the pyridyl ring could be expected to have a beneficial effect. Indeed, the prior art teaches that the results of a modification like walking a substituent around a ring were highly unpredictable.

Sohda II has only one pyridyl with a methyl substituent, compound 58. There is nothing in Sohda II from which one skilled in the art would conclude that a methyl in a different position on the pyridyl ring would improve efficacy or avoid or reduce compound 58's identified negative side effects.

Mosberg opines that the '200 Patent teaches that walking a substituent around the ring was a process "known" to Takeda.

Many common (as well as sophisticated) chemical processes were no doubt known to Takeda; that is beside the point. The issue is whether there was any ground for a reasonable expectation of success that can be located in the prior art by a person of ordinary skill to choose a particular process to achieve the desired goal.

[64] Alphapharm had identified Rosenberg as one of its trial experts, and had served his expert report. After he was deposed, however, Alphapharm withdrew its offer of Rosenberg as an expert at trial. Before making that decision, Alphapharm had adopted portions of Rosenberg's deposition testimony as evidence given by Alphapharm pursuant to Rule 30(b) (6), Fed. R. Civ. P.

Mosberg gives three sets of examples[65] from the illustrations in the '200 Patent that show either a methoxy (CH3O) or a chloro (CI) being "walked around" a different ring, a benzene ring.[66] He does not assert, however, that any of the disclosed results from that process taught that such a process would be likely to lead to any success, or that any particular position on a ring was likely to more efficacious or less toxic than any other. None of the three examples includes a substituent at the 5th position on the ring, where pioglitazone's substituent is located.

An examination of the efficacy data from Sohda II for the phenyl compounds to which Mosberg points suggests that substituents in a lower ring position may be more potent, principally by comparing the efficacy scores for substituents in the 4th position with those in the 2nd position.[67] Alphapharm has not shown, however, that one skilled in the art would have understood that these results were transferable from a phenyl to a pyridyl compound, that they would pertain to a comparison between a substituent in the 6th and 5th positions, or that they would eliminate toxicity.

Mosberg argues that Takeda's historical experience confirms his opinion that it was expected that one would simply walk the methyl around the ring. This is, of course, an improper use of hindsight. Nonetheless, Takeda's historical experience is directly to the contrary. Compounds (c), (d) and (e) were each first synthesized in 1983; pioglitazone was first synthesized in 1982. Takeda clearly did not move from compound (b), which had been synthesized in 1978, to pioglitazone by "walking the ring."

Even if Takeda had moved away from compound (b) by "walking the ring," it would have discovered significant toxicity problems as soon as it synthesized and then tested each of the other methyl substituents on the 2-pyridyl ring. As illustrated in Table 1, compounds (d) and (e) each have significant toxicity. Compound (c) failed the chick lens assay screening. In sum, Alphapharm has not shown that one skilled in the art would have been motivated to move to pioglitazone by "walking the ring."

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[65] Mosberg discusses compounds 1 and 2; compounds 18 and 19; and compounds 31, 32 and 33 from the '200 Patent. In Sohda II, these are compounds 32 and 31; compounds 13 and 12; and compounds 5, 4, and 3, respectively.

[66] A benzene ring, in contrast to a pyridyl ring, does not have a nitrogen atom. A compound with a benzene ring is referred to as a phenyl.

[67] Alphapharm did not make this comparison or argument at trial.

b) Homologation

Alphapharm has no more success with its argument that one skilled in the art would have been led to create a homolog of a methyl substituent on the 2-pyridyl ring,[68] than it did with its ring-walking argument. Alphapharm has failed to show that the prior art would have invested in a person with ordinary skill in the art a reasonable expectation that the substitution of an ethyl for an methyl would lead to beneficial results.

Sohda II describes over a score of compounds with a methyl substituent and eight compounds with an ethyl substituent. There is no discernable pattern of biological activity associated in a comparison of the two substituents in the prior art. Nothing in the prior art suggests that the process of substituting an ethyl for a methyl would be of any more assistance than using any other of the many possible substituents or changing course entirely and adopting a base structure other than the 2-pyridyl ring.

Indeed, Alphapharm has not identified any basis to find that even those with great skill understood in the 1980's (or even today) that the substitution of an ethyl group for a methyl group is likely to have a beneficial effect on biological processes. Our understanding of the biological properties of compounds is too rudimentary even today to allow us to form reasonable expectations regarding such a result.

In particular, Alphapharm is confronted again with the significant hurdle placed by the toxicity found in compound (b). Having found such high levels of toxicity to the heart, liver, and blood cells in compound (b), it has not pointed to anything in the prior art that would suggest that creating a homolog of the compound would be likely to reduce much less eliminate toxicity, either in any particular body system or as a whole.[69]

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[68] As noted earlier in this Opinion, a homolog is a chemical structure that differs from the parent compound by a single, constant increment of one carbon (and associated hydrogen atoms), such as adding a methyl group.

[69] If one of ordinary skill in the art were confronted with toxicity issues, she would be "well-advised," according to Danishefsky, to try substituents that would change significantly the dipole moment of the molecule, that is the electron density of the compound. Examples of such substituents do not include an ethyl, and do include methoxies, alcohols, and halides, among many others.

Ignoring entirely the substantial issue of compound (b)'s toxicity, Mosberg asserts that Sohda II teaches that the substitution of a methyl increases potency, and specifically that a comparison of Compounds 57 and 58 in Sohda II demonstrates that homologation increased the efficacy of pyridine compounds. Compound 57 is the unsubstituted pyridine ring; compound 58 is compound (b) (the 6-methyl on the pyridine ring).[70]

A more straightforward reading of Sohda II indicates that its authors understood that homologation does not ameliorate toxicity. The Sohda II authors point out that "[a]lthough compounds 56, 57, 58, 59 and 63 in Table IV showed potent activities, they, especially 57 and 58, caused considerable increases in body weight and brown fat weight." (Emphasis added.) One of ordinary skill in the art would therefore have been more likely to conclude from Sohda II that homologation had no tendency to decrease unwanted side effects and to focus research efforts elsewhere. There were other compounds described in Sohda II as efficacious as compound 58, including one with no identified side effects or toxicity. And, as already noted, the authors of Sohda II recommended investigation of three other compounds, not compound 58.

Mosberg argues that the '200 and '779 Patents teach that Takeda "may" prefer to use the lower alkyls[71] and in particular a methyl (CH3) or an ethyl (C2H5) as substituents, and therefore it would not be surprising if Takeda used an ethyl substituent on a pyridyl ring. He relies on the Nohara Article and Sohda II as evidence that homologation was routine at Takeda. The test, of course, is not what Takeda might have tried, but whether one skilled in the art would have a reasonable expectation of success from synthesizing the homolog.

In any event, nothing in the '200 and the '779 Patents, or in any other publication from Takeda, would have given one skilled in the art an expectation of success from the substitution of an ethyl for a methyl. In its patents, Takeda specifically claims a variety of substituents on identified systems. For example, the '779 Patent includes substituents on a pyridyl or thiazolyl group, noting that "[a] s examples of such substituents may be

[70] Compounds 57 and 58 were reported in Sohda II to have the same effect on hypoglycemic activity (a score of 3), while compound 57 scored 2 and compound 58 scored 4 with respect to plasma triglyceride-lowering activity.

[71] Alkyls are linear chains of carbon atoms singly bonded to other carbon atoms or hydrogen atoms.

mentioned lower alkyls (e.g., methyl, ethyl, etc.), lower alkoxy groups (e.g., methoxy, ethoxy, etc.), halogens (e.g., chlorine, bromine, etc.) and hydroxyl."

Finally, Mosberg points to specific illustrations in the '200 Patent that demonstrate to him that Takeda was aware that the substitution of a methyl with an ethyl "should be carried out to test for useful compounds." Again, this is not an opinion that there was any reasonable basis for an expectation of success. In any event, when the specific illustrations selected by Mosberg are actually examined, using the efficacy data on those same compounds as provided by Sohda II,[72] it is immediately apparent that the prior art did not teach that the substitution of an ethyl for a methyl was likely to be beneficial. Sohda II shows a higher combined efficacy score for the methyl over the ethyl for one set, and an identical combined score for the methyl and the ethyl in the second set. The third set in the '200 Patent includes five compounds, but only three of the five are discussed in Sohda II. This set is a homologous series, with a CH2 component repeatedly added. The Sohda II efficacy scores show no pattern, however, from the addition of the carbon atom.[73]

The position taken by Alphapharm's expert is perhaps best captured by his annotations to the expert report of Takeda's expert Danishefsky. On that report, he wrote in the margin that he agreed that a review of the biological effects of various substituents, as disclosed in the Sohda II article, made it clear that biological activity is "unpredictable." He added, "but this does not in [any] way make the choice of such analogs less obvious to try."[74] The test, of course, is not whether it is "obvious to try" the synthesis of a particular compound, *see*, *e.g.*, In re O'Farrell, 853 F.2d 894, 902 (Fed. Cir. 1988), but

[72] Mosberg cites to three sets of examples in the '200 Patent: compounds 3 and 4; compounds 5 through 9; and compounds 15 and 16. In Sohda II, these are compounds 36 and 37; 38 to 40 (only three of the five are reported in Sohda II); and 11 and 14.

[73] The compound in the middle of the series has the highest score.

[74] Additional annotations by Mosberg indicate that he did not believe that there was any reasonable expectation of success from any particular modification of the molecule. He agreed that "there is no data or information to even suggest that substitution of an ethyl for a methyl substituent would lead to predictable improvements in blood glucose or triglyceride lowering activity." Mosberg added in the margin, "there is no predictability only logical choice of analogs to try." As a final example, Mosberg notes in another annotation, that an effect on toxicity from small structural changes "can be neither expected nor unexpected. It would not be surprising."

whether one skilled in the art would have a reasonable expectation of success from doing so. At trial, the best the expert for Alphapharm could offer is that essentially anything can happen when one modifies a compound, so a change for the better might happen, and if it did, it would not be surprising. This does not come any closer to articulating a reasonable expectation of success.

In summation, Alphapharm's counsel tried with no success to limit the damage done by its expert's testimony. Admitting that there is inherent variability in the biological effects produced from even small changes in the structure of chemical compounds, he argued that a variation in the degree of an effect is entirely expected and is not surprising. He suggested that what would be surprising was to find an effect from the small change in the composition of a molecule in an entirely different body organ or system. Again, the issue is not whether something would be surprising, although the discovery that pioglitazone was non-toxic certainly qualifies as a surprising and unexpected event, but whether one could reasonably expect success.

In sum, even if compound (b) could have been identified by one skilled in the art as a lead compound worthy of further investigation, Alphapharm has failed to show that such a person would have had a reasonable expectation of success in synthesizing the pioglitazone molecule. Alphapharm has not shown that pioglitazone was prime facie obvious.

D. Objective Indicia of Non-Obviousness

1) Unexpected Results

Given Alphapharm's failure to show prima facie obviousness, there is no need for an extended discussion of the objective factors used to evaluate obviousness. For reasons already described, pioglitazone's non-toxicity was entirely unexpected. Compound (b) was a highly toxic compound, and nothing in the prior art would have led one skilled in the art to expect that the 5-ethyl on a 2-pyridyl ring would be non-toxic. As Alphapharm's Rosenberg admitted at his deposition, pioglitazone is "clearly superior" to compound (b) because of its non-toxicity.

There is one evidentiary issue that arose in connection with the issue of unexpected results that requires some discussion. Alphapharm offered evidence at trial that a long-term study of the effect of pioglitazone in dogs, conducted by Upjohn after Takeda had applied for what became the '777

Patent, suggested that pioglitazone may lead to an increase in heart size, and thus has some toxicity. An Upjohn scientist who testified at trial discounted that interpretation of the test results. It is unnecessary to make any findings regarding this evidence, however, since it is entirely irrelevant to the issue of whether pioglitazone's non-toxicity, as disclosed in the '777 Patent, was an unexpected result.

Pioglitazone has, of course, been approved by the FDA and the defendants challenge Takeda's patent because they believe it is an effective and non-toxic drug that will be profitable for them to sell. As significantly, while it may be appropriate to use later-acquired evidence to bolster a finding of unexpected results,[75] to illustrate for instance that an invention is even more beneficial to mankind than was originally understood, *see* Knoll Pharm. Co. v. Teva Pharm. Co., 367 F.3d 1381, 1385 (Fed. Cir. 2004), it is another thing altogether to suggest that after-acquired evidence should be used to undercut what appeared at the time of the patent application to be unexpected results. For instance, it would be entirely unfair to the patent applicant to discount what appeared at the time of an application to be unexpected results because our advancing and improved scientific knowledge allows us to understand why such results are to be expected. Therefore, as with all objective factors used to analyze the obviousness issue, after-acquired evidence of unexpected results should not be used to undermine a patent without a careful analysis of relevance. Here, the Upjohn tests, conducted long after the application for the '777 Patent, are irrelevant.

2) Additional Secondary Considerations

Evidence concerning other objective factors also shows that pioglitazone was a non-obvious invention. First of all, it is a huge commercial success. ACTOS® was launched in 1999, and by 2003 held 47% of the TZD market, as well as 9.9% of the total OAD market. In 2003, the gross sales of ACTOS® exceeded $1.7 billion. ACTOS® is the embodiment of pioglitazone, the invention disclosed in the '777 Patent, and therefore this commercial success can presumptively be attributed to the invention itself.
Pioglitazone also responds to a long felt but unmet need in the market of pharmaceutical treatments of diabetes. The introduction of TZDs, led by

[75] There is, for example, strong evidence that the scientific community has come to understand that pioglitazone has a measurable and unexpected advantage over the other TZD on the U.S. market.

Rezulin® in 1997, revolutionized the care of diabetes. Rezulin®, however, has been removed from the U.S. market due to issues associated with liver toxicity, and today, only ACTOS® and Avandia® are available. Out of the millions of TZDs, only these two have been found to be safe and effective to treat insulin resistance in the muscle.

Alphapharm presents several arguments in a futile effort to undermine Takeda's compelling objective evidence of non-obviousness, particularly its evidence of commercial success. While Alphapharm concedes that there is evidence both of commercial success and that the successful product is claimed in the patent, it argues that other factors serve to undercut "the prima facie case of nexus" between the commercial success and the claimed invention.

Alphapharm argues that much of the commercial success of ACTOS® is due to events that were unforeseen at the time that the '777 Patent issued, such as the withdrawal of Rezulin® from the market, and an unexpected rise in obesity with an accompanying increase in the incidence of diabetes.[76] These arguments miss the mark. There is no requirement that the invention be the only successful product in its market niche or the most successful. Moreover, ACTOS® would have been an important and successful invention by any reasonable measure even if the incidence of diabetes had remained unchanged since the time of the invention.

Alphapharm also argues that Takeda's success is more attributable to its marketing efforts, particularly its partnership with Eli Lilly, than the inherent value of the invention. This argument flies in the face of the strong evidence from medical practitioners about the benefits and the perceived benefits of ACTOS®. In any event, Takeda and GlaxoSmithKline invest roughly the same amount of money in their efforts to market their two TZD products, and both drugs have found success.

Finally, Alphapharm argues that Takeda's prior art patents, particularly the '200 and '605 Patents, undermine the nexus between ACTOS®' commercial success and the non-obviousness of the '777 Patent. The suggestion is that because Takeda had the right to exclude others from making the closest prior

[76] There is no need to explore the extent to which the perceived rise in obesity and diabetes is due to a redefinition of obesity in 1998, and a change in the diagnostics for diabetes in 1997.

art compounds, the ability of other companies to enter the TZD market was stifled.[77] The argument is completely specious. Alphapharm has not shown that any of the compounds disclosed by Takeda in its patents were viable candidates for commercial development. Takeda's competitors had every opportunity to develop new compounds that were improvements over the compounds Takeda disclosed. This is exactly what Sankyo did in developing troglitazone, the active ingredient in Rezulin®. The patent that protects troglitazone lists the '605 and '902 Patents as prior art. The fact that only one other company has a TZD in the market today, despite the commercial opportunities available for an effective insulin sensitizer, is strong secondary evidence of pioglitazone's non-obviousness.

In sum, Alphapharm has not carried its burden of showing that the invention of pioglitazone was obvious. It has searched for a theory of obviousness, and its efforts have proven futile with each iteration of a theory.[78] Alphapharm's Section 355 Statement did not articulate a successful theory of obviousness, and its efforts to create one through the direct testimony of its expert, and yet another one as the trial unfolded all failed. Nothing in the prior art would have given one skilled in the art any reasonable expectation that the creation of pioglitazone would result in the discovery of an anti-diabetic treatment that was efficacious and non-toxic.

II. Inequitable Conduct

Mylan contends that the '777 Patent is invalid because Takeda engaged in inequitable conduct. Applicants for patents are bound by a duty of "candor and good faith" to the PTO. Purdue Pharma L.P. v. Endo Pharm. Inc., 04-1189, 04-1347, 04 1357, 2006 WL 231480, at *4 (Fed. Cir. Feb. 1, 2006).[79]

[77] In making this argument, Alphapharm relies on Merck, 395 F.3d at 1377, but in doing so, reads the case far too broadly. In Merck the patent at issue was a method claim for the use of a particular compound, which was protected by a patent owned by Merck. Id. at 1366. Because Merck owned the underlying patent, and thus could prevent others from commercially developing the method of use at issue, the court found that the "chain of inferences fails on these facts." Id. at 1377. The case does not establish that commercial success is not probative simply because a patent holder also holds a prior art patent.

[78] It is telling that two of the defendants never sought to attack the '777 Patent on the ground that it was obvious, and a third defendant abandoned the theory of obviousness it had articulated in its own Section 355 Statement.

Included in the duty is the obligation of applicants to disclose information of which they are aware that is "material to the examination of the application." 37 C.F.R. §1.56(a) (1985).

The duty encompasses an "affirmative misrepresentation of a material fact, failure to disclose material information, or submission of false material information." Purdue Pharma, 2006 WL 231480, at *4. Materiality and intent "must be shown by clear and convincing evidence." Id. The burden of proof required to prove inequitable conduct has been described as a "heavy burden." Hoffman-La Roche, Inc. v. Promega Corporation, 323 F.3d 1354, 1359 (Fed. Cir. 2003)

For patents prosecuted before 1992, "information is material where there is a substantial likelihood that a reasonable examiner would consider it important in deciding whether to allow the application as a patent." 37

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[79] The conduct of applicants while applying for patents is governed by 37 C.F.R. §1.56 ("Rule 56"), which is promulgated by the PTO pursuant to 35 U.S.C. §§6 and 131. *See* Molins PLC v. Textron, Inc., 48 F.3d 1172, 1179 n.8 (Fed. Cir. 1995). The governing standard for evaluating defendant Mylan's claims of inequitable conduct is the regulation as it stood in 1986, when Takeda pursued its application for the invention covered by the '777 Patent. *See* id. In 1986, the regulation read in relevant part:

(a) A duty of candor and good faith toward the Patent and Trademark Office rests on the inventor, on each attorney or agent who prepares or prosecutes the application and on every other individual who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee or with anyone to whom there is an obligation to assign the application. All such individuals have a duty to disclose to the Office information they are aware of which is material to the examination of the application. Such information is material where there is a substantial likelihood that a reasonable examiner would consider it important in deciding whether to allow the application to issue as a patent. The duty is commensurate with the degree of involvement in the preparation or prosecution of the application.

(b) No patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or gross negligence. The claims in an application shall be rejected if upon examination pursuant to 35 U.S.C. 131 and 132 [sic], it is established by clear and convincing evidence (1) that any fraud was practiced or attempted on the Office in connection with the application, or in connection with any previous application upon which the application relies, or (2) that there was any violation of the duty of disclosure through bad faith or gross negligence in connection with the application, or in connection with any previous application upon which the application relies.

37 C.F.R. §1.56 (a), (d) (1985).

C.F.R. §1.56 (a); *see* Dayco Products, Inc. v. Total Containment, Inc., 329 F.3d 1358, 1365 (Fed. Cir. 2003). Materiality is not limited to matters reflected in the claims of the patent, PerSeptive Biosystems, Inc. v. Pharmacia Biotech, Inc., 225 F.3d 1315, 1322 (Fed. Cir. 2000), but embraces "any information that a reasonable examiner would substantially likely [sic] consider important in deciding whether to allow an application to issue as a patent." Dayco Products, 329 F.3d at 1368 (citation omitted); *see* Akron Polymer Container Corp. v. Exxel Container, Inc., 148 F.3d 1380, 1382 (Fed. Cir. 1998). The standard for materiality is not a "but for" standard. Merck & Co. v. Danbury Pharmacal, Inc., 873 F.2d 1418, 1421 (Fed. Cir. 1989); *see also* Digital Control Inc. v. Charles Mach. Works, 05-1128, 2006 WL 288075, at *7 (Fed. Cir. Feb. 8, 2006). It is not necessary to find that an examiner relied on the misrepresentation or omission at issue, only that it would have been "within a reasonable examiner's realm of consideration." Hoffman-La Roche, Inc., 323 F.3d at 1368 (citing Merck & Co., 873 F.2d at 1421). Affidavits submitted to the PTO may be "inherently material." Digital Control, 2006 WL 288075, at *8; *see also*, Refac Intern., Ltd. v. Lotus Development Corp., 81 F.3d 1576, 1583 (Fed. Cir. 1996).

Direct evidence of intent to deceive is "rarely available," but intent "may be inferred from clear and convincing evidence of the surrounding circumstances." Purdue Pharma, 2006 WL 231480, at *9 (citation omitted); *see also* Ferring B.V. v. Barr Labs., Inc., 05-1284, 2006 WL 335601, at *8 (Fed. Cir. Feb. 15, 2006). While a "court must weigh all evidence, including evidence of good faith" in determining intent, "a patentee facing a high level of materiality and clear proof that it knew or should have known of that materiality, can expect to find it difficult to establish 'subjective good faith' sufficient to prevent the drawing of an inference of intent to mislead." Purdue Pharma, 2006 WL 231480, at *9 (citation omitted).

If the duty is breached in a way that is both material and intentional, then the patent will be invalidated if "the equities warrant a conclusion that inequitable conduct occurred." Id. at *4. The material misrepresentations or omissions must be "sufficiently serious in light of the evidence of intent to deceive, under all the circumstances, to warrant the severe sanction of holding the patent unenforceable." Hoffman-La Roche, 323 F.3d at 1372.

Mylan has failed to carry its heavy burden of showing that Takeda engaged in inequitable conduct. Mylan principally claims that Takeda intentionally made material misrepresentations in its presentation of the comparative test results for the six compounds listed in Table 1 of the '777 Patent, and that Takeda should have added information concerning a seventh compound to the table.

There are many indicia of Takeda's good faith in its application to the PTO in 1986. First, with the exception of two test results it obtained in response to the Office Action, the test results Takeda presented to the PTO in Table 1 were drawn from reports that Takeda and its research partner Upjohn had used in 1984 to select five compounds, including pioglitazone, for further research and potential development as a pharmaceutical. Takeda had every incentive to reflect in those reports its best judgment about what the test results showed so that the companies' money and the scientists' energies would be spent as productively as possible. There is simply no basis to find that there was any misrepresentation in the 1984 reports, much less any incentive to misrepresent test data.

Second, Takeda identified the relevant prior art to the PTO. Both Sohda II and the '200 Patent were described. In addition, the chemical structure for the closest prior art–-compound (b) on Table 1, which is compound 58 in Sohda II—is set out in a diagram so that it can be easily compared to the chemical structure for pioglitazone and other compounds listed in Table 1.

Third, Takeda did not manipulate the data presented in Table 1 to make pioglitazone appear better than its internal data reflected. For example, Table 1 shows that compound (b) is superior to pioglitazone in the reduction of both blood glucose and triglycerides. Even when the Office Action required Takeda to fill in three more data points in Table 1 –- the triglyceride data for rats for compounds (c), (d) and (e) –- Takeda gave the PTO figures that were comparable to or superior to the figures for pioglitazone in Table 1.[80]

[80] Pioglitazone ED25 value for lowering rat triglyceride levels was shown as 3; the comparable values for compounds (c), (d) and (e) were reported as 6, 4 and 2, respectively.

Fourth, Takeda had powerful additional evidence of the superiority of pioglitazone over the prior art which it did not present to the PTO. Report A-15-34 reflects the results of the in vitro chick lens assay[81] for many compounds, including those in Table 1. Only pioglitazone and compound (e) of the six compounds listed in Table 1 showed no evidence of toxicity in this test. This was additional evidence of the superiority of pioglitazone over the compound in the prior art to which it was most structurally similar, compound (b), which Takeda had at hand to share with the PTO if necessary.

Fifth, there is no dispute about the superiority of pioglitazone over compound (b), the only prior art compound in Table 1. Mylan cannot explain how Takeda could have anticipated in 1984, when it created Reports A-15-13 and A-15-34, that information about compounds (c), (d) or (e) would be included in the PTO application or what additional explanations the examiner would seek in an Office Action.

Ignoring this powerful evidence that Takeda acted in good faith in its presentation to the PTO, Mylan has cobbled together a series of arguments in an effort to show inequitable conduct. As noted, its arguments relate to the presentation of data in Table 1. It emphasizes data concerning two compounds: compound (c), which is the 5-methyl homolog of pioglitazone, and compound 3894, which is the unsubstituted pyridyl ring. With respect to compound (c), Mylan contends that Takeda misrepresented the data regarding compound (c)'s potency to make it appear weaker than pioglitazone. It points out that compound (c) had no toxicity indicated on Table 1, and therefore, pioglitazone would not have appeared superior to compound (c) if their efficacy numbers were presented as comparable.[82] With respect to compound 3894, Mylan argues that Takeda had a duty to report the comparative test results for this compound on Table 1, but did not. Compound 3894 had comparable if not better efficacy than pioglitazone, but was rejected for development by Takeda due to its toxicity

[81] It was this test which had resulted in the abandonment of ciglitazone as a marketable pharmaceutical.

[82] Compound (c) failed the chick lens assay test, but those data were not presented to the PTO.

to the heart. In addition, as described below, Mylan raises a few other issues to attack Taeda's honesty in its presentation of Table 1 data.

Before addressing Mylan's categories of alleged misrepresentations, a few observations are in order. Many of Mylan's examples of the misrepresentation or omission of data rest on testing data it culled from surviving Takeda notebooks that were produced in discovery in 2004 and 2005. The screening tests were conducted approximately 20 years earlier, and not all of Takeda's laboratory notebooks have survived. Thus, Mylan's analysis rests on the fallacy that it has a complete set of the testing data from which to judge the completeness and fairness of the presentation of the testing results to the PTO.

There is a second flaw in Mylan's contention that Takeda should have used the experimental data lifted directly from the notebooks rather than the data in the reports on which Takeda and Upjohn relied to make their research decisions. Presenting raw, unanalyzed data from notebooks would have been both incomprehensible to an examiner and misleading. Indeed, the notebooks contain some test results for pioglitazone that are more favorable than those listed on Table 1 and test results for some of the other compounds that are less favorable than the descriptions of those compounds on Table 1.

Fujita analyzed all of the test results in 1984, and chose to include in Report A-15-34 those that he considered the most reliable. Takeda and Upjohn relied upon the data in that report in making critical business decisions, and it was entirely appropriate for Takeda to rely on that same data in preparing Table 1 for the PTO.

With two exceptions, which are discussed below and concern the strain and age of rats, Mylan has failed to show that there was any misrepresentation or material omission in Takeda's presentation of data. With respect to the two errors, Mylan has failed to show that the errors were either material or the result of any intentional misconduct by Takeda.

A discussion of Mylan's specific contentions follows.

Its contentions are organized according to the column in Table 1 to which they relate. Its arguments concerning compound 3894 –-the compound not included on Table 1—are addressed last.

A. Misrepresentations

1) Mouse ED25 values

Mylan argues that most of the ED25 values for the lowering of blood glucose and plasma triglycerides in mice that were reported in Table 1 were false and misleading, and that the actual test results obtained by Takeda were not reported to the PTO. In particular, Mylan stresses data obtained in a single 1983 experiment in which pioglitazone and compound (c) were tested together or head to head,[83] and shown to have roughly the same ED25 values, while Table 1 reflects pioglitazone significantly outperforming compound (c) in these measures.[84]

As already noted, the ED25 mouse data in Table 1 is identical to that contained in Report A-15-34. Mylan's assertion that there was a misrepresentation is based exclusively on the results of a handful of experiments Mylan located in surviving Takeda notebooks. There were many more experiments conducted by Takeda than are reflected in the surviving notebooks. Indeed, as has been explained previously, because there were so many screening tests performed, for many compounds Report A-15-34 presents a range of test results for the efficacy testing. It first lists the figure which Fujita selected as the most reliable, and then in parentheticals gives a range of test results.[85]

[83] Mylan makes a similar argument for compound (e), claiming that data from a single experiment in a Takeda notebook shows that compound (e) outperformed pioglitazone. For the reasons discussed in the analysis of the argument concerning compound (c), Mylan has not shown that a misrepresentation occurred in the presentation of the ED25 mice data on Table 1.

[84] Table 1 showed ED25 blood glucose and triglyceride lowering scores of 6 and 6 for pioglitazone, but 20 and 20 for compound (c). In the single experiment to which Mylan points, the comparable pioglitazone values were 5.2 and 14, but 6.4 and 18 for compound (c).

[85] For instance, the ED25 blood glucose data for compound (c) were reflected in Report A-15-34 as: "20 (2-5)." The data in the parenthetical represent the relative potency of

It was entirely appropriate, and indeed necessary, for Fujita to apply his professional judgment to the mass of test results and select the test results on which he felt that Takeda and Upjohn could best rely in the Fall of 1984. Not all tests yield similarly reliable data. Some of the test results from the Takeda notebooks on which Mylan has relied are preliminary two dose tests, which would not yield reliable ED25 data. In other tests it appears that the effective dose is beyond the administered doses, and again would not be a reliable basis for determining the effective dose. In other surviving tests, where there does not appear to be any particular defect in the test, Mylan still has not shown that those data should have been used in Table 1 instead of the data Takeda chose to present there.[86] Without having all of the underlying test results from which Fujita selected the most reliable tests to calculate the ED25 values contained in Report A-15-34, it is simply impossible today to reconstruct why any single test was or was not chosen as the most reliable. What can be established today with confidence, however, is that Fujita had every motive to use his best judgment in 1984 in compiling the data for Report A-15-34, and it was those data which were presented to the PTO in 1986.

In this connection it is important to note that Takeda had given over fifty compounds to Upjohn, as well as KKAy mice, so that Upjohn could replicate the efficacy testing that Takeda was doing in its own laboratories. Two scientists who were deeply involved in the 1984 diabetes drug program at Upjohn testified at trial and confirmed that Upjohn not only did its own efficacy testing but also that all of the results it obtained were consistent with the results that Takeda reported. These two scientists, neither of whom has any stake in this litigation, spoke highly of the competence and integrity of the Takeda scientists and its testing program. The existence of Upjohn's parallel testing program is yet another reason to find that Fujita used his best

compound (c) to ciglitazone, ciglitazone being accorded a rating of one. Fujita chose the test reflecting an ED25 value of 20 as the most reliable test, but by including the data in the parenthetical, reflected that the test results ranged from values between 8 and 20. Ciglitazone had an ED25 value of 40 in Report A-15-34.

[86] Using the notebook data to create ED25 values, and after eliminating tests where only two doses were administered or where the dose response curve was flat (indicating that the ED25 value was beyond the range of doses tested), the data currently available results in an identical ranking of pioglitazone, and compounds (a) and (c) to that presented to the PTO: pioglitazone was superior to compound (c); compound (a) had the poorest performance. There was insufficient surviving data for the other compounds to do a meaningful comparison.

judgment in choosing the efficacy numbers (and other data) for Report A-15-34. Upjohn's scientists were in a position to disagree with his presentation of the data, and Fujita knew that.[87]

There are two additional arguments that Mylan makes about the presentation of the efficacy scores in Table 1 for mice. It points to comparisons with ciglitazone that were contained in monthly internal reports at Takeda in early 1984, and Report A-15-13, circulated in February 1984. These comparisons listed compounds that screening tests had determined were "five times as potent as ciglitazone." Pioglitazone and compound (c) were among the compounds found as having such a superior performance. Mylan argues that it is inconsistent to identify compound (c) as five times more potent than ciglitazone in these internal documents, and yet to list it on Table 1 as only two times as potent.[88]

Takeda's early screening tests were part of a program to find more potent and less toxic compounds than ciglitazone. They created new compounds, including compounds (c), (d) and (e) in mid-1983, and subjected them initially to two-dose tests, and those that survived that screening, to three-dose tests. During 1984, Takeda continued to test compounds. For the reasons already explained, there is no reason to doubt that Takeda used its best judgment in selecting the most reliable potency values for Report A-15-34 from among the universe of available test results,[89] and those same numbers appear in Table 1. Mylan has not shown that Takeda engaged in inequitable conduct by failing to give the PTO data reflecting the best

[87] In a chapter of a book published in 1990, the Upjohn scientists who testified at trial described research into ciglitazone, pioglitazone and other TZDs. They reported that Takeda discovered through its research that replacing the left hand moeity of ciglitazone with a 2-pyridinylethoxy produced compounds "approximately 5-10 times more potent than ciglitazone." They added that further testing of the compounds for efficacy and safety resulted in the selection of pioglitazone for development. Despite Mylan's arguments to the contrary, nothing in this general description of the Takeda screening program undermines the reliability of Report A-15-34, a report on which these same Upjohn scientists relied to make research decisions.

[88] On Table 1, ciglitazone's ED25 values for lowering blood glucose and triglyceride levels in mice are both 40, while compound (c)'s are listed as 20.

[89] As already noted, Report A-15-34 did include a range of potency, comparing each compound's potency to ciglitazone, and compound (c)'s range of potency was listed in Report A-15-34 as "2-5" or two to five times as potent as ciglitazone.

performance by a compound, instead of the performance judged by extremely well qualified scientists as the most reliable performance.[90]

Finally, Mylan finds in another section of Report A-15-34 support for its argument that Table 1 was misleading. In Figures 5 and 6 of Report A-15-34, pioglitazone is shown as somewhat more potent in mice, and as creating less "brown fat" in rats, than compound (c).[91] Pioglitazone is not shown in these figures, as it is in Table 1 of Report A-15-34 (and in Table 1 of the patent), as over three times more potent than compound (c). Takeda apparently chose to use some of the test results for compound (c) in these figures that were different from the values it chose as the most reliable when it created Table 1 of Report A-15-34.

Mylan has not shown that Takeda should have presented the data used to create the two figures in Report A-15-34 instead of the Table 1 data to the PTO. The two figures do not even have numbers associated with a particular compound; the figures are simply graphs composed of points entered on a logarithmic scale. One can only estimate, and very roughly at that, what the underlying values are. The only reliable numbers in Report A-15-34 are those that were reported to the PTO.

Takeda's testing, which was extensive, was nonetheless preliminary, screening testing, used to identify a small group of compounds, ultimately five, for more intensive testing and potential development. Takeda was under no obligation to conduct more extensive testing before applying for a patent; its only obligation was to present its results as of that time honestly. Mylan has not shown that Takeda violated that obligation in connection with the mouse efficacy data.

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[90] Mylan has argued that Takeda should have given the PTO the range of test results reflected in the parentheticals in Report A-15-34. Mylan has not shown that the range of results would have been material to the examiner or anything other than an additional layer of detail that was unnecessary for the examiner to perform his function. Giving the PTO the most reliable test data, as opposed to a summary of all test results was sufficient to meet Takeda's obligations to the PTO.

[91] Takeda created a graph of the data using these two parameters and from that graph formed the hypothesis that the increase in the brown adipose tissue ("brown fat") in the rats may be partially due to the pharmacological potency of a compound.

2) Rat ED25 values

Mylan argues that some of the ED25 values for plasma triglyceride lowering that Takeda obtained from testing rats were not obtained in the manner Takeda described to the PTO in the '777 Patent application and the Amendment, and that Takeda concealed some of the results it did obtain from its testing.[92] Mylan makes three separate arguments, but has not shown in connection with any of them that Takeda engaged in inequitable conduct.

a) ED25 value for pioglitazone

Relying again on surviving notebook data, Mylan argues that Takeda misrepresented the ED25 in rats for pioglitazone. Table 1 reported the value as 3 for pioglitazone, but Mylan points to data from tests reflected in surviving notebooks that show different values, one of them lower than a 3.[93] For the reasons already discussed, Mylan has not shown that there was any misrepresentation by Takeda. Takeda took the figure for pioglitazone from Report A-15-34, and that was a reliable source of data to present to the PTO.

b) Exclusion of a control animal

Mylan argues that Takeda misrepresented its testing protocol to the PTO when it indicated that there were five rats in each testing group, including the group of animals used as a control. Mylan argues that Takeda should have advised the PTO that in one test it had omitted test data obtained from one control animal.[94]

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[92] In its summation, Mylan only mentioned one of these three issues: the failure to tell the PTO that a control animal had been excluded from an experiment.

[93] The ED25 values identified by Mylan for pioglitazone are 17.9, 7.8 and 2.3.

[94] Mylan initially argued that Takeda should not have eliminated the control animal from its calculations since the censoring of the animal dramatically altered the test results. It appears to have abandoned this argument. As explained above, the censoring was entirely appropriate.

In responding to the Office Action, Takeda conducted experiments to obtain ED25 values for plasma triglyceride lowering in rats for compounds (c), (d) and (e). One of the five animals in the control group gained comparatively little weight during the test period and had anomalous readings for other pertinent characteristics.[95] In averaging the data obtained from the control group in this test, a Takeda researcher chose to eliminate the readings from this one animal.

The "censoring" of animals in biological testing is encouraged where results are not representative and where inclusion would be misleading. The exclusion of one control animal was entirely appropriate here and reflects the exercise of sound scientific judgment. Scientific publications do not always report the exclusion of one laboratory animal in their description of test results, and there is no basis to find that it should have been reported to the PTO or that the test results should have included the readings obtained from this single animal.

Mylan also argues that Takeda's statement in the Amendment about control group values was misleading because it did not explain that an animal had been censored in one experiment. In the Office Action, the examiner expressed uncertainty about how to interpret the Table 1 data, noting inter alia that the disclosure failed to provide "values for the control group." In response, Takeda explained that

> Each control value of blood glucose and TG is determined to be 100% and that of "liver weight," "heart weight" and "number of erythrocyte" is estimated to be zero % from the above numerical expressions. Therefore it is meaningless to show the values of the control. The disclosure of the table...is sufficient for those skilled in the art to interpret the data. (Emphasis supplied).

Takeda's response to the examiner's inquiry was entirely accurate. It explained why one skilled in the art would understand all control values to

[95] The control animal had an elevated NEFA level (nonesterified fatty acids), which indicated that it was either not sufficiently eating or assimilating its food.

be 100%, and the performance of a compound to be measured against that assumed control value. This explanation helped the examiner to read Table 1; it did not concern the particular experiment in which an animal was censored or even the circumstances more generally in which one animal would be censored in order to obtain a reliable test result. Mylan has not shown that there was any misrepresentation or material omission.

c) ED25 data for compound (d)

As noted, the Office Action requested that Takeda provide triglyceride effectiveness data for compounds (c), (d), and (e). These were the only three fields of data not completed in Table 1 as it was originally presented to the PTO. When the supplemental testing done to respond to the Office Action demonstrated no triglyceride-lowering activity in compound (d), Fujita lifted the results from Report A-15-34 and reported a "4" as the ED25 value, a number close to the value of "3" reported for pioglitazone. Ciglitazone's value was "70."

Mylan has not shown that there was any effort to mislead the PTO by reporting a "4" for compound (d). If Takeda had reported that compound (d) had no potency, rather than fairly strong potency, then Mylan may have had grounds to complain. As it was, what Takeda did was utterly inconsistent with any effort to place pioglitazone in a more favorable light than it deserved.

3) Toxicity in Rats

Mylan has argued that Takeda misled the PTO by falsely describing the strain and age of rats that it used to obtain toxicity data.[96] It has failed to show inequitable conduct in either instance.

a) Strains of rats

The studies measuring the potency of compounds were performed in Sprague-Dawley rats, while the toxicology tests were performed in Wistar rats. Takeda represented to the PTO that all of the testing had been

[96] It is not entirely clear if Mylan continues to press these arguments. Mylan did not mention either of these issues in its summation.

performed in Sprague-Dawley rats.[97] Mylan has not shown that this error was material.

Two of the most common strains[98] of laboratory rat used in toxicology studies are Wistar and Sprague-Dawley. Both strains are of healthy animals, and toxicology assays are almost always performed in healthy animals in order to rule out other causes of abnormalities.[99] The Sprague-Dawley strain originated from crosses with Wistar females and remains genetically similar to the Wistar today. Indeed, there are still no genetic markers to differentiate the two strains. Credible expert testimony established at trial that the use of Wistar rats instead of Sprague-Dawley rats did not change the reliability of the conclusions that were presented to the PTO since the same strain was used across the toxicology experiments.[100] There is simply no basis to find that the error was material or made as a result of an intent to mislead.

b) Safety margin analysis

Mylan argues that the value of the safety margin analysis that Takeda developed in response to the Office Action is undercut by the fact that Takeda used Sprague-Dawley rats for its efficacy data, but Wistar rats for

[97] The '777 Patent described the experimental process for obtaining data regarding lipid lowering activity and toxicity in rats. The patent represented that the former tests had been conducted with "[m]ale Sprague-Dawley rats" and the latter with "[m]ale and female Sprague-Dawley rats."

[98] A strain is a group of individuals who share a presumed common ancestry and have clear-cut physiological, but not usually morphological, distinctions. Wistar and Sprague-Dawley rats are both outbred strains, meaning that they are maintained as colonies of animals of unidentified genotype. Individual animals from an outbred stock may differ markedly in their genetic characteristics. In contrast, due to cross-breeding of brother-sister pairs in inbred strains over many generations, individuals within an inbred strain are treated as genetic clones.

[99] Three dose effectiveness tests were done in normal Sprague-Dawley rats to obtain plasma triglyceride levels. If the levels of treated animals were reduced, that was an indicator of the compound's antidiabetic activity.

[100] For example, when two-week toxicity studies were done in both Wistar and Sprague-Dawley rats for pioglitazone, the results were essentially equivalent.

the toxicity testing. This argument reflects a fundamental misunderstanding of the testing process. Since the same strain of rat was used as both the control animal and the animal receiving the compound in any given experiment, the efficacy data and the toxicity data were each derived from a scientifically sound experiment. Scientists commonly derive safety margin data using two different animal models. Again, Mylan has not shown that there was any failure to provide the PTO with information material to the examiner.

c) Age of rats

The '777 Patent and the Declaration both explain that the toxicity studies in rats were two-week tests done in rats that were "5 weeks old." In one of the two-week toxicology studies, however, the one in which pioglitazone itself was tested, at the initiation of the study the rats were six weeks of age.[101] Since the results were based on normalized weight calculations and a comparison to control groups of the same age as the test groups, the error in describing the age of the rats was immaterial.

Mylan argued at trial that testing pioglitazone in animals that are one week older gave it an advantage because rats at that age are going through puberty and as more mature and bigger animals will be less susceptible to the toxic effects of the compounds. The credible scientific evidence at trial established that this small difference in age at the point in which the tests began had no effect on the validity of the test results.[102]

Puberty is a process and individual rats generally enter this process at any time between thirty-five to sixty days, that is, between five to eight and a half weeks. Tests conducted on rats that are from five to seven weeks old and from six to eight weeks old are thus each conducted on rats presumptively undergoing puberty. Using control animals of the same age and normalizing

[101] Pioglitazone and compound 3894 were tested in rats at least six weeks old. The compounds listed on Table 1 other than pioglitazone were tested in rats five weeks old.

[102] Even though Alphapharm purported to be pursuing an obviousness claim, it chose to cross-examine Takeda's expert on the issue of the age of the rats, using a series of graphs it prepared based on data drawn from Takeda's test results. Correctly interpreted, the graphs in fact underscored the expert's opinion that the one week age difference had no impact whatsoever on the test results.

organ weights to body weight, which Takeda did for each test, are sufficient to eliminate any variations of significance among the tests.

B. Omission: Compound 3894

Mylan argues that Takeda had an obligation to disclose to the PTO activity and toxicity data regarding compound 3894, a compound revealed in the prior art, specifically in Sohda II. Compound 3894 is a TZD molecule with a 2-pyridyl ring at the left end, but no substituents on that ring. It is the parent structure for the left hand moeity of the pioglitazone molecule. Mylan argues that if Takeda had revealed that compound 3894 had a comparable activity and toxicity performance to pioglitazone then the PTO "may" have concluded that pioglitazone was not patentable over prior art. Put another way, Mylan argues that Takeda falsely asserted to the PTO that the introduction of an ethyl group to the 2-pyridyl ring produced unexpected results because it knew that pioglitazone is not superior to compound 3894.

In the '777 Patent Takeda made the following statement:

> As is apparent from the experimental results given in Table 1, Compound (I) of this invention is superior to the compounds (a), (c), (d) and (e) and comparable to the compound (b) in hypoglycemic and hypolipidemic activities, while showing extremely low toxicity as compared with the compounds (a), (b), (d) and (e). Such an effect as above caused by the introduction of an ethyl group is quite unexpected. (Emphasis supplied.)

Compound 3894 is toxic. As reflected in Reports A-15-13 and A-15-34, two-week toxicity tests performed in rats demonstrated a statistically significant toxicity to the heart known as cardiomeglia or enlargement of the heart. Mylan has not shown either that Takeda should not have relied on the results reflected in Report A-15-34 in making judgments about the unexpected results achieved through the introduction of an ethyl group, or that the underlying test results on the toxicity of compound 3894 were unreliable.[103]

[103] Mylan first suggested that the statistical significance of the toxicity finding needed to be confirmed through an analysis of variance or ANOVA, with a Dunnett's post-test. Mylan, however, did not perform that test, and when Takeda's expert did, the testing

Mylan points to Takeda documents in which the effects on the heart by compound 3894 were described as "weak" or "mild," as well as Report A-15-13 from February 2004, where this compound was described as one of four compounds that appeared less toxic than the others that had been tested as of that time, and which because of their potency, appeared "much easier to continue further studies including clinical trials." These preliminary views are insufficient to overcome the compelling evidence that as of the Fall 2004, when Report A-15-34 was prepared and Takeda and Upjohn made their judgments about what toxicity levels would be disqualifying and which compounds warranted further testing, compound 3894 was disqualified because of its toxicity.

As already discussed in connection with the discussion of the issue of obviousness, the closest prior art to pioglitazone was compound (b), not compound 3894.[104] Moreover, it was important to compare pioglitazone to ciglitazone, which had advanced as far as human trials before it had to be abandoned because of toxicity. It was unnecessary for Takeda to present testing data for compound 3894 as well. By presenting the comparison with compound (c), Takeda was presenting data with its methyl-substituted homolog, which was more closely related to pioglitazone in its chemical structure than the unsubstituted compound 3894.

One Mylan expert had asserted without any analysis that compound 3894 was the closest prior art, but admitted on cross examination to each of the facts on which Takeda's far more impressive and careful expert relied in forming his conclusion that a substituted pyridyl, such as compound (b), is closer structurally to pioglitazone than an unsubstituted pyridyl. To give but one example, the introduction of an alykyl substituent changes the shape of

confirmed Takeda's finding of statistical significance. Mylan's expert then speculated that the testing results might be an "artifact." He suggested that the results be confirmed through retesting, but Mylan undertook no such testing.

[104] By the time of its summation, Mylan had abandoned any claim that compound 3894 was the closest prior art. It argued that In re Johnson, 747 F.2d 1456 (Fed. Cir. 1984), requires an applicant for a patent to present information about any relevant prior art, even if it is not the closest prior art. Johnson reaffirms that an applicant must compare the invention to the closest prior art. Id. at 1461. That was done here. Johnson also addresses the duty of comparison where there are two equally close references. Id. That is not an issue presented here.

the TZD molecule dramatically, which can have profound effects on the interface between the TZD and the PPAR-gamma molecules.

C. Intent

It is undisputed that Takeda made two misstatements of fact to the PTO. Takeda erred in describing the strain and age of rats used in the toxicity testing. Neither of these errors was material. Mylan has failed to show that Takeda made any other misstatements or failed to provide the PTO with material information. In any event, Mylan has utterly failed to show that Takeda ever acted in bad faith in the prosecution of the '777 Patent.

The evidence of Takeda's good faith is abundant. Takeda's lead scientist for this project was Fujita. As the Chief Scientist of the Biology Research Laboratory, he had ultimate responsibility for the conduct of the screening tests run in 1983 and 1984; he chose the efficacy values for Report A-15-34; and he recommended pioglitazone as one of the twelve compounds from which Takeda and Upjohn should select their candidates in October 1984 for more intensive studies and possible development as a pharmaceutical. He did not include either compound 3894 or any other Table 1 compound among that group of twelve. Fujita has long since retired from Takeda, but he testified at trial. He was an entirely credible witness. Despite extensive cross-examination, he remained a patient, careful witness who worked hard to give precise, accurate answers to every question that he was asked. Although he had no current recollection of many of the details of events from the mid-1980s, his testimony established beyond peradventure that he had used his best scientific judgment and considerable expertise at that time. He is, in short, an honorable man and distinguished scientist.

There is absolutely no evidence that he ever acted with intent to deceive either other scientists at Takeda or Upjohn in preparing Report A-15-34 or the PTO.

Fundamentally, Mylan has never been able to overcome the hurdle presented by the fact that Takeda's work was undertaken in collaboration with Upjohn, and that the Table 1 data were taken directly from Report A-15-34. Even if his character would have permitted him to act other than with complete scientific integrity, Fujita had no motive to use anything

other than his best judgment in creating Report A-15-34. He had no way to know what results Upjohn had obtained in testing these same compounds and whether its judgments would agree with his own, and he certainly had no ability to anticipate what data might be important in any future PTO proceedings. As significantly, he had no motive to fabricate data for compounds such as compound (c) that were not even in the prior art.[105] Fujita's only identifiable motive was to choose as wisely as he could the most promising compounds into which Takeda and Upjohn would invest significant resources to determine if they had successfully identified an efficacious, safe compound for use as a pharmaceutical. To place Mylan's argument in stark relief, Mylan would have vehemently complained if Takeda had presented to the PTO any toxicity or efficacy numbers other than those in Reports A-15-13 and A-15-34.

Many of the arguments pressed by Mylan (and Alphapharm) at trial flow from a convoluted theory of a conspiracy by Takeda to obtain patent protection for the 6-ethyl.[106] The 6-ethyl is a homolog of compound (b), which is a prior art compound. This theory suffers from several flaws, including most prominently the fact that when Fujita's department applied internally within Takeda to begin the process of applying for the patent that became the '777 Patent, it sought patent protection for the pioglitazone molecule alone and no other compound. In addition, of course, Takeda has never developed a 6-ethyl compound.

In sum, Mylan has failed to carry its burden of showing either a material misstatement or omission. It has also failed to present any evidence of intent to deceive the PTO.

[105] If, for instance, compound (c) had been a better choice for pharmaceutical development than pioglitazone, then Takeda would have had no reason not to select compound (c) for development. It certainly would have been able to show the PTO its unexpected superiority over prior art compound (b) easily, given compound (b)'s extreme toxicity.

[106] The '777 Patent claims include not just the pioglitazone molecule, but also each of the ethyls on the 2-pyridine moeity. The ethyl in the sixth position is referred to as the 6-ethyl.

Conclusion

Each defendant having failed to carry its burden at trial, the challenges to the '777 Patent by Alphapharm on the ground of obviousness and by Mylan on the ground of inequitable conduct are denied. Takeda shall submit a proposed judgment.

SO ORDERED:

Dated: New York, New York
February 21, 2006

DENISE COTE
United States District Judge

Courtesy of Patrick H. Higgins, Buchanan Ingersoll & Rooney PC

APPENDIX C

EDWARD H. PHILLIPS V. AWH CORPORATION, HOPEMAN BROTHERS INC., AND LOFTON CORPORATION

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

03-1269-1286

EDWARD H. PHILLIPS,
Plaintiff-Appellant
v.
AWH CORPORATION,
HOPEMAN BROTHERS, INC., and LOFTON CORPORATION,
Defendants-Cross Appellants

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Appealed from: United States District Court for the District of Colorado Judge Marcia S. Krieger.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

03-1269-1286

EDWARD H. PHILLIPS,
Plaintiff-Appellant
v.
AWH CORPORATION,
HOPEMAN BROTHERS, INC., and LOFTON CORPORATION,
Defendants-Cross Appellants

DECIDED: July 12, 2005

Before MICHEL, Chief Judge, NEWMAN, MAYER, LOURIE, CLEVENGER, RADER, SCHALL, BRYSON, GAJARSA, LINN, DYK, and PROST, Circuit Judges.

Opinion for the court filed by Circuit Judge BRYSON, in which Chief Judge MICHEL and Circuit Judges CLEVENGER, RADER, SCHALL, GAJARSA, LINN, DYK, and PROST join; and in which Circuit Judge LOURIE joins with respect to parts I, II, III, V, and VI; and in which Circuit Judge NEWMAN joins with respect to parts I, II, III, and V. Opinion concurring in part and dissenting in part filed by Circuit Judge LOURIE, in which Circuit Judge NEWMAN joins. Dissenting opinion filed by Circuit Judge MAYER, in which Circuit Judge NEWMAN joins.

BRYSON, Circuit Judge.

Edward H. Phillips invented modular, steel-shell panels that can be welded together to form vandalism-resistant walls. The panels are especially useful in building prisons because they are load-bearing and impact-resistant, while also insulating against fire and noise. Mr. Phillips obtained a patent on the invention, U.S. Patent No. 4,677,798 ("the '798 patent"), and he subsequently entered into an arrangement with AWH Corporation, Hopeman Brothers, Inc., and Lofton Corporation (collectively "AWH") to market and sell the panels. That arrangement ended in 1990. In 1991, however, Mr. Phillips received a sales brochure from AWH that suggested

to him that AWH was continuing to use his trade secrets and patented technology without his consent. In a series of letters in 1991 and 1992, Mr. Phillips accused AWH of patent infringement and trade secret misappropriation. Correspondence between the parties regarding the matter ceased after that time.

In February 1997, Mr. Phillips brought suit in the United States District Court for the District of Colorado charging AWH with misappropriation of trade secrets and infringement of claims 1, 21, 22, 24, 25, and 26 of the '798 patent. Phillips v. AWH Corp., No. 97-N-212 (D. Colo.). The district court dismissed the trade secret misappropriation claim as barred by Colorado's three-year statute of limitations.

With regard to the patent infringement issue, the district court focused on the language of claim 1, which recites "further means disposed inside the shell for increasing its load bearing capacity comprising internal steel baffles extending inwardly from the steel shell walls." The court interpreted that language as "a means…for performing a specified function," subject to 35 U.S.C. §112, paragraph 6, which provides that such a claim "shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof." Looking to the specification of the '798 patent, the court noted that "every textual reference in the Specification and its diagrams show baffle deployment at an angle other than 90° to the wall faces" and that "placement of the baffles at such angles creates an intermediate interlocking, but not solid, internal barrier." The district court therefore ruled that, for purposes of the '798 patent, a baffle must "extend inward from the steel shell walls at an oblique or acute angle to the wall face" and must form part of an interlocking barrier in the interior of the wall module. Because Mr. Phillips could not prove infringement under that claim construction, the district court granted summary judgment of non-infringement.

Mr. Phillips appealed with respect to both the trade secret and patent infringement claims. A panel of this court affirmed on both issues. Phillips v. AWH Corp., 363 F.3d 1207 (Fed. Cir. 2004). As to the trade secret claim, the panel unanimously upheld the district court's ruling that the claim was barred by the applicable statute of limitations. Id. at 1215. As to the patent infringement claims, the panel was divided. The majority sustained the

district court's summary judgment of non-infringement, although on different grounds. The dissenting judge would have reversed the summary judgment of non-infringement.

The panel first determined that because the asserted claims of the '798 patent contain a sufficient recitation of structure, the district court erred by construing the term "baffles" to invoke the "means-plus-function" claim format authorized by section 112, paragraph 6. Id. at 1212. Nonetheless, the panel concluded that the patent uses the term "baffles" in a restrictive manner. Based on the patent's written description, the panel held that the claim term "baffles" excludes structures that extend at a 90 degree angle from the walls. The panel noted that the specification repeatedly refers to the ability of the claimed baffles to deflect projectiles and that it describes the baffles as being "disposed at such angles that bullets which might penetrate the outer steel panels are deflected." '798 patent, col. 2, ll. 13-15; *see also* id. at col. 5, ll. 17-19 (baffles are "disposed at angles which tend to deflect the bullets"). In addition, the panel observed that nowhere in the patent is there any disclosure of a baffle projecting from the wall at a right angle and that baffles oriented at 90 degrees to the wall were found in the prior art. Based on "the specification's explicit descriptions," the panel concluded "that the patentee regarded his invention as panels providing impact or projectile resistance and that the baffles must be oriented at angles other than 90°." Phillips, 363 F.3d at 1213. The panel added that the patent specification "is intended to support and inform the claims, and here it makes it unmistakably clear that the invention involves baffles angled at other than 90°." Id. at 1214. The panel therefore upheld the district court's summary judgment of non-infringement.

The dissenting judge argued that the panel had improperly limited the claims to the particular embodiment of the invention disclosed in the specification, rather than adopting the "plain meaning" of the term "baffles." The dissenting judge noted that the parties had stipulated that "baffles" are a "means for obstructing, impeding, or checking the flow of something," and that the panel majority had agreed that the ordinary meaning of baffles is "something for deflecting, checking, or otherwise regulating flow." Phillips, 363 F.3d at 1216-17. In the dissent's view, nothing in the specification redefined the term "baffles" or constituted a disclaimer specifically limiting the term to less than the full scope of its

ordinary meaning. Instead, the dissenting judge contended, the specification "merely identifies impact resistance as one of several objectives of the invention." Id. at 1217. In sum, the dissent concluded that "there is no reason to supplement the plain meaning of the claim language with a limitation from the preferred embodiment." Id. at 1218. Consequently, the dissenting judge argued that the court should have adopted the general purpose dictionary definition of the term baffle, i.e., "something for deflecting, checking, or otherwise regulating flow," id., and therefore should have reversed the summary judgment of non-infringement.

This court agreed to rehear the appeal en banc and vacated the judgment of the panel. Phillips v. AWH Corp., 376 F.3d 1382 (Fed. Cir. 2004). We now affirm the portion of the district court's judgment addressed to the trade secret misappropriation claims. However, we reverse the portion of the court's judgment addressed to the issue of infringement.

I

Claim 1 of the '798 patent is representative of the asserted claims with respect to the use of the term "baffles." It recites:

> Building modules adapted to fit together for construction of fire, sound and impact resistant security barriers and rooms for use in securing records and persons, comprising in combination, an outer shell…, sealant means…and further means disposed inside the shell for increasing its load bearing capacity comprising internal steel baffles extending inwardly from the steel shell walls.

As a preliminary matter, we agree with the panel that the term "baffles" is not means-plus-function language that invokes 35 U.S.C. §112, paragraph 6. To be sure, the claim refers to "means disposed inside the shell for increasing its load bearing capacity," a formulation that would ordinarily be regarded as invoking the means-plus function claim format. However, the claim specifically identifies "internal steel baffles" as structure that performs the recited function of increasing the shell's load-bearing capacity. In contrast to the "load bearing means" limitation, the reference to "baffles" does not use the word "means," and we have held that the absence of that

term creates a rebuttable presumption that section 112, paragraph 6, does not apply. *See* Personalized Media Communications, LLC v. Int'l Trade Comm'n, 161 F.3d 696, 703-04 (Fed. Cir. 1998).

Means-plus-function claiming applies only to purely functional limitations that do not provide the structure that performs the recited function. *See* Watts v. XL Sys., Inc., 232 F.3d 877, 880-81 (Fed. Cir. 2000). While the baffles in the '798 patent are clearly intended to perform several functions, the term "baffles" is nonetheless structural; it is not a purely functional placeholder in which structure is filled in by the specification. *See* TurboCare Div. of Demag Delaval Turbomachinery Corp. v. Gen. Elec. Co., 264 F.3d 1111, 1121 (Fed. Cir. 2001) (reasoning that nothing in the specification or prosecution history suggests that the patentee used the term "compressed spring" to denote any structure that is capable of performing the specified function); Greenberg v. Ethicon Endo-Surgery, Inc., 91 F.3d 1580, 1583 (Fed. Cir. 1996) (construing the term "detent mechanism" to refer to particular structure, even though the term has functional connotations). The claims and the specification unmistakably establish that the "steel baffles" refer to particular physical apparatus. The claim characterizes the baffles as "extend[ing] inwardly" from the steel shell walls, which plainly implies that the baffles are structures. The specification likewise makes clear that the term "steel baffles" refers to particular internal wall structures and is not simply a general description of any structure that will perform a particular function. *See*, *e.g.*, '798 patent, col. 4, ll. 25-26 ("the load bearing baffles 16 are optionally used with longer panels"); id., col. 4, ll. 49-50 (opposing panels are "compressed between the flange 35 and the baffle 26"). Because the term "baffles" is not subject to section 112, paragraph 6, we agree with the panel that the district court erred by limiting the term to corresponding structures disclosed in the specification and their equivalents. Accordingly, we must determine the correct construction of the structural term "baffles," as used in the '798 patent.

II

The first paragraph of section 112 of the Patent Act, 35 U.S.C. §112, states that the specification

> shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person

> skilled in the art to which it pertains…to make and use the same…

The second paragraph of section 112 provides that the specification

> shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Those two paragraphs of section 112 frame the issue of claim interpretation for us. The second paragraph requires us to look to the language of the claims to determine what "the applicant regards as his invention." On the other hand, the first paragraph requires that the specification describe the invention set forth in the claims. The principal question that this case presents to us is the extent to which we should resort to and rely on a patent's specification in seeking to ascertain the proper scope of its claims.

This is hardly a new question. The role of the specification in claim construction has been an issue in patent law decisions in this country for nearly two centuries. We addressed the relationship between the specification and the claims at some length in our en banc opinion in Markman v. Westview Instruments, Inc., 52 F.3d 967, 979-81 (Fed. Cir. 1995) (en banc), aff'd, 517 U.S. 370 (1996). We again summarized the applicable principles in Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576 (Fed. Cir. 1996), and more recently in Innova/Pure Water, Inc. v. Safari Water Filtration Systems, Inc., 381 F.3d 1111 (Fed. Cir. 2004). What we said in those cases bears restating, for the basic principles of claim construction outlined there are still applicable, and we reaffirm them today. We have also previously considered the use of dictionaries in claim construction. What we have said in that regard requires clarification.

A

It is a "bedrock principle" of patent law that "the claims of a patent define the invention to which the patentee is entitled the right to exclude." Innova, 381 F.3d at 1115; *see also* Vitronics, 90 F.3d at 1582 ("we look to the words of the claims themselves…to define the scope of the patented invention"); Markman, 52 F.3d at 980 ("The written description part of the specification

itself does not delimit the right to exclude. That is the function and purpose of claims."). That principle has been recognized since at least 1836, when Congress first required that the specification include a portion in which the inventor "shall particularly specify and point out the part, improvement, or combination, which he claims as his own invention or discovery." Act of July 4, 1836, ch. 357, §6, 5 Stat. 117, 119. In the following years, the Supreme Court made clear that the claims are "of primary importance, in the effort to ascertain precisely what it is that is patented." Merrill v. Yeomans, 94 U.S. 568, 570 (1876). Because the patentee is required to "define precisely what his invention is," the Court explained, it is "unjust to the public, as well as an evasion of the law, to construe it in a manner different from the plain import of its terms." White v. Dunbar, 119 U.S. 47, 52 (1886); *see also* Cont'l Paper Bag Co. v. E. Paper Bag Co., 210 U.S. 405, 419 (1908) ("the claims measure the invention"); McCarty v. Lehigh Valley R.R. Co., 160 U.S. 110, 116 (1895) ("if we once begin to include elements not mentioned in the claim, in order to limit such claim…, we should never know where to stop"); Aro Mfg. Co. v. Convertible Top Replacement Co., 365 U.S. 336, 339 (1961) ("the claims made in the patent are the sole measure of the grant").

We have frequently stated that the words of a claim "are generally given their ordinary and customary meaning." Vitronics, 90 F.3d at 1582; *see also* Toro Co. v. White Consol. Indus., Inc., 199 F.3d 1295, 1299 (Fed. Cir. 1999); Renishaw PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1249 (Fed. Cir. 1998). We have made clear, moreover, that the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application. *See* Innova, 381 F.3d at 1116 ("A court construing a patent claim seeks to accord a claim the meaning it would have to a person of ordinary skill in the art at the time of the invention."); Home Diagnostics, Inc. v. LifeScan, Inc., 381 F.3d 1352, 1358 (Fed. Cir. 2004) ("customary meaning" refers to the "customary meaning in [the] art field"); Ferguson Beauregard/Logic Controls v. Mega Sys., LLC, 350 F.3d 1327, 1338 (Fed. Cir. 2003) (claim terms "are examined through the viewing glass of a person skilled in the art"); *see also* PC Connector Solutions LLC v. SmartDisk Corp., 406 F.3d 1359, 1363 (Fed. Cir. 2005) (meaning of claim "must be interpreted as of

[the] effective filing date" of the patent application); Schering Corp. v. Amgen Inc., 222 F.3d 1347, 1353 (Fed. Cir. 2000) (same).

The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation. *See* Innova, 381 F.3d at 1116. That starting point is based on the well-settled understanding that inventors are typically persons skilled in the field of the invention and that patents are addressed to and intended to be read by others of skill in the pertinent art. *See* Verve, LLC v. Crane Cams, Inc., 311 F.3d 1116, 1119 (Fed. Cir. 2002) (patent documents are meant to be "a concise statement for persons in the field"); In re Nelson, 280 F.2d 172, 181 (CCPA 1960) ("The descriptions in patents are not addressed to the public generally, to lawyers or to judges, but, as section 112 says, to those skilled in the art to which the invention pertains or with which it is most nearly connected.").

Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification. This court explained that point well in Multiform Desiccants, Inc. v. Medzam, Ltd., 133 F.3d 1473, 1477 (Fed. Cir. 1998):

> It is the person of ordinary skill in the field of the invention through whose eyes the claims are construed. Such person is deemed to read the words used in the patent documents with an understanding of their meaning in the field, and to have knowledge of any special meaning and usage in the field. The inventor's words that are used to describe the invention—the inventor's lexicography—must be understood and interpreted by the court as they would be understood and interpreted by a person in that field of technology. Thus the court starts the decision-making process by reviewing the same resources as would that person, viz., the patent specification and the prosecution history.

See also Medrad, Inc. v. MRI Devices Corp., 401 F.3d 1313, 1319 (Fed. Cir. 2005) ("We cannot look at the ordinary meaning of the term…in a vacuum.

Rather, we must look at the ordinary meaning in the context of the written description and the prosecution history."); V-Formation, Inc. v. Benetton Group SpA, 401 F.3d 1307, 1310 (Fed. Cir. 2005) (intrinsic record "usually provides the technological and temporal context to enable the court to ascertain the meaning of the claim to one of ordinary skill in the art at the time of the invention"); Unitherm Food Sys., Inc. v. Swift-Eckrich, Inc., 375 F.3d 1341, 1351 (Fed. Cir. 2004) (proper definition is the "definition that one of ordinary skill in the art could ascertain from the intrinsic evidence in the record").

B

In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words. *See* Brown v. 3M, 265 F.3d 1349, 1352 (Fed Cir. 2001) (holding that the claims did "not require elaborate interpretation"). In such circumstances, general purpose dictionaries may be helpful. In many cases that give rise to litigation, however, determining the ordinary and customary meaning of the claim requires examination of terms that have a particular meaning in a field of art. Because the meaning of a claim term as understood by persons of skill in the art is often not immediately apparent, and because patentees frequently use terms idiosyncratically, the court looks to "those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean." Innova, 381 F.3d at 1116. Those sources include "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." Id.; *see also* Gemstar-TV Guide Int'l, Inc. v. Int'l Trade Comm'n, 383 F.3d 1352, 1364 (Fed. Cir. 2004); Vitronics, 90 F.3d at 1582-83; Markman, 52 F.3d at 979-80.

1

Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of particular claim terms. *See* Vitronics, 90 F.3d at 1582; *see also* ACTV, Inc. v.

Walt Disney Co., 346 F.3d 1082, 1088 (Fed. Cir. 2003) ("the context of the surrounding words of the claim also must be considered in determining the ordinary and customary meaning of those terms").

To begin with, the context in which a term is used in the asserted claim can be highly instructive. To take a simple example, the claim in this case refers to "steel baffles," which strongly implies that the term "baffles" does not inherently mean objects made of steel. This court's cases provide numerous similar examples in which the use of a term within the claim provides a firm basis for construing the term. *See*, *e.g.*, Mars, Inc. v. H.J. Heinz Co., 377 F.3d 1369, 1374 (Fed. Cir. 2004) (claim term "ingredients" construed in light of the use of the term "mixture" in the same claim phrase); Process Control Corp. v. HydReclaim Corp., 190 F.3d 1350, 1356 (Fed. Cir. 1999) (claim term "discharge rate" construed in light of the use of the same term in another limitation of the same claim).

Other claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment as to the meaning of a claim term. Vitronics, 90 F.3d at 1582. Because claim terms are normally used consistently throughout the patent, the usage of a term in one claim can often illuminate the meaning of the same term in other claims. *See* Rexnord Corp. v. Laitram Corp., 274 F.3d 1336, 1342 (Fed. Cir. 2001); CVI/Beta Ventures, Inc. v. Tura LP, 112 F.3d 1146, 1159 (Fed. Cir. 1997). Differences among claims can also be a useful guide in understanding the meaning of particular claim terms. *See* Laitram Corp. v. Rexnord, Inc., 939 F.2d 1533, 1538 (Fed. Cir. 1991). For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim. *See* Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 910 (Fed. Cir. 2004).

2

The claims, of course, do not stand alone. Rather, they are part of "a fully integrated written instrument," Markman, 52 F.3d at 978, consisting principally of a specification that concludes with the claims. For that reason, claims "must be read in view of the specification, of which they are a part." Id. at 979. As we stated in Vitronics, the specification "is always highly

relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." 90 F.3d at 1582.

This court and its predecessors have long emphasized the importance of the specification in claim construction. In Autogiro Co. of America v. United States, 384 F.2d 391, 397-98 (Ct. Cl. 1967), the Court of Claims characterized the specification as "a concordance for the claims," based on the statutory requirement that the specification "describe the manner and process of making and using" the patented invention. The Court of Customs and Patent Appeals made a similar point. *See* In re Fout, 675 F.2d 297, 300 (CCPA 1982) ("Claims must always be read in light of the specification. Here, the specification makes plain what the appellants did and did not invent…").

Shortly after the creation of this court, Judge Rich wrote that "[t]he descriptive part of the specification aids in ascertaining the scope and meaning of the claims inasmuch as the words of the claims must be based on the description. The specification is, thus, the primary basis for construing the claims." Standard Oil Co. v. Am. Cyanamid Co., 774 F.2d 448, 452 (Fed. Cir. 1985). On numerous occasions since then, we have reaffirmed that point, stating that "[t]he best source for understanding a technical term is the specification from which it arose, informed, as needed, by the prosecution history." Multiform Dessicants, 133 F.3d at 1478; Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354, 1360 (Fed. Cir. 2004) ("In most cases, the best source for discerning the proper context of claim terms is the patent specification wherein the patent applicant describes the invention."); *see also*, *e.g.*, Kinik Co. v. Int'l Trade Comm'n, 362 F.3d 1359, 1365 (Fed. Cir. 2004) ("The words of patent claims have the meaning and scope with which they are used in the specification and the prosecution history."); Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1315 (Fed. Cir. 2003) ("[T]he best indicator of claim meaning is its usage in context as understood by one of skill in the art at the time of invention.").

That principle has a long pedigree in Supreme Court decisions as well. *See* Hogg v. Emerson, 47 U.S. (6 How.) 437, 482 (1848) (the specification is a "component part of the patent" and "is as much to be considered with the [letters patent] in construing them, as any paper referred to in a deed or

other contract"); Bates v. Coe, 98 U.S. 31, 38 (1878) ("in case of doubt or ambiguity it is proper in all cases to refer back to the descriptive portions of the specification to aid in solving the doubt or in ascertaining the true intent and meaning of the language employed in the claims"); White v. Dunbar, 119 U.S. 47, 51 (1886) (specification is appropriately resorted to "for the purpose of better understanding the meaning of the claim"); Schriber-Schroth Co. v. Cleveland Trust Co., 311 U.S. 211, 217 (1940) ("The claims of a patent are always to be read or interpreted in light of its specifications."); United States v. Adams, 383 U.S. 39, 49 (1966) ("[I]t is fundamental that claims are to be construed in the light of the specifications and both are to be read with a view to ascertaining the invention.").

The importance of the specification in claim construction derives from its statutory role. The close kinship between the written description and the claims is enforced by the statutory requirement that the specification describe the claimed invention in "full, clear, concise, and exact terms." 35 U.S.C. §112, para. 1; *see* Netword, LLC v. Centraal Corp., 242 F.3d 1347, 1352 (Fed. Cir. 2001) ("The claims are directed to the invention that is described in the specification; they do not have meaning removed from the context from which they arose."); *see also* Markman v. Westview Instruments, Inc., 517 U.S. 370, 389 (1996) ("[A claim] term can be defined only in a way that comports with the instrument as a whole."). In light of the statutory directive that the inventor provide a "full" and "exact" description of the claimed invention, the specification necessarily informs the proper construction of the claims. *See* Merck & Co. v. Teva Pharms. USA, Inc., 347 F.3d 1367, 1371 (Fed. Cir. 2003) ("A fundamental rule of claim construction is that terms in a patent document are construed with the meaning with which they are presented in the patent document. Thus claims must be construed so as to be consistent with the specification, of which they are a part.") (citations omitted). In Renishaw, this court summarized that point succinctly:

> Ultimately, the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim. The construction that stays true to the claim language and most naturally aligns with the patent's

> description of the invention will be, in the end, the correct construction.
>
> 158 F.3d at 1250 (citations omitted).

Consistent with that general principle, our cases recognize that the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs. *See* CCS Fitness, Inc. v. Brunswick Corp., 288 F.3d 1359, 1366 (Fed. Cir. 2002). In other cases, the specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor. In that instance as well, the inventor has dictated the correct claim scope, and the inventor's intention, as expressed in the specification, is regarded as dispositive. *See* SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc., 242 F.3d 1337, 1343-44 (Fed. Cir. 2001).

The pertinence of the specification to claim construction is reinforced by the manner in which a patent is issued. The Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." In re Am. Acad. of Sci. Tech. Ctr., 367 F.3d 1359, 1364 (Fed. Cir. 2004). Indeed, the rules of the PTO require that application claims must "conform to the invention as set forth in the remainder of the specification and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description." 37 C.F.R. §1.75(d)(1). It is therefore entirely appropriate for a court, when conducting claim construction, to rely heavily on the written description for guidance as to the meaning of the claims.

3

In addition to consulting the specification, we have held that a court "should also consider the patent's prosecution history, if it is in evidence." Markman, 52 F.3d at 980; *see also* Graham v. John Deere Co., 383 U.S. 1, 33 (1966) ("[A]n invention is construed not only in the light of the claims, but

also with reference to the file wrapper or prosecution history in the Patent Office."). The prosecution history, which we have designated as part of the "intrinsic evidence," consists of the complete record of the proceedings before the PTO and includes the prior art cited during the examination of the patent. Autogiro, 384 F.2d at 399. Like the specification, the prosecution history provides evidence of how the PTO and the inventor understood the patent. *See* Lemelson v. Gen. Mills, Inc., 968 F.2d 1202, 1206 (Fed. Cir. 1992). Furthermore, like the specification, the prosecution history was created by the patentee in attempting to explain and obtain the patent. Yet because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes. *See* Inverness Med. Switz. GmbH v. Warner Lambert Co., 309 F.3d 1373, 1380-82 (Fed. Cir. 2002) (the ambiguity of the prosecution history made it less relevant to claim construction); Athletic Alternatives, Inc. v. Prince Mfg., Inc., 73 F.3d 1573, 1580 (Fed. Cir. 1996) (the ambiguity of the prosecution history made it "unhelpful as an interpretive resource" for claim construction). Nonetheless, the prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be. Vitronics, 90 F.3d at 1582-83; *see also* Chimie v. PPG Indus., Inc., 402 F.3d 1371, 1384 (Fed. Cir. 2005) ("The purpose of consulting the prosecution history in construing a claim is to 'exclude any interpretation that was disclaimed during prosecution.'"), quoting ZMI Corp. v. Cardiac Resuscitator Corp., 844 F.2d 1576, 1580 (Fed. Cir. 1988); Southwall Techs., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1576 (Fed. Cir. 1995).

C

Although we have emphasized the importance of intrinsic evidence in claim construction, we have also authorized district courts to rely on extrinsic evidence, which "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." Markman, 52 F.3d at 980, citing Seymour v. Osborne, 78 U.S. (11 Wall.) 516, 546 (1870); *see also* Vitronics, 90 F.3d at 1583. However, while extrinsic evidence "can shed useful light on the

relevant art," we have explained that it is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" C.R. Bard, Inc. v. U.S. Surgical Corp., 388 F.3d 858, 862 (Fed. Cir. 2004), quoting Vanderlande Indus. Nederland BV v. Int'l Trade Comm'n, 366 F.3d 1311, 1318 (Fed. Cir. 2004); *see also* Astrazeneca AB v. Mutual Pharm. Co., 384 F.3d 1333, 1337 (Fed. Cir. 2004).

Within the class of extrinsic evidence, the court has observed that dictionaries and treatises can be useful in claim construction. *See* Renishaw, 158 F.3d at 1250; Rexnord, 274 F.3d at 1344. We have especially noted the help that technical dictionaries may provide to a court "to better understand the underlying technology" and the way in which one of skill in the art might use the claim terms. Vitronics, 90 F.3d at 1584 n.6. Because dictionaries, and especially technical dictionaries, endeavor to collect the accepted meanings of terms used in various fields of science and technology, those resources have been properly recognized as among the many tools that can assist the court in determining the meaning of particular terminology to those of skill in the art of the invention. *See* Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1325 (Fed. Cir. 2002). Such evidence, we have held, may be considered if the court deems it helpful in determining "the true meaning of language used in the patent claims." Markman, 52 F.3d at 980.

We have also held that extrinsic evidence in the form of expert testimony can be useful to a court for a variety of purposes, such as to provide background on the technology at issue, to explain how an invention works, to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field. *See* Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1308-09 (Fed. Cir. 1999); Key Pharms. v. Hercon Labs. Corp., 161 F.3d 709, 716 (Fed. Cir. 1998). However, conclusory, unsupported assertions by experts as to the definition of a claim term are not useful to a court. Similarly, a court should discount any expert testimony "that is clearly at odds with the claim construction mandated by the claims themselves, the written description, and the prosecution history, in other words, with the written record of the patent." Key Pharms., 161 F.3d at 716.

We have viewed extrinsic evidence in general as less reliable than the patent and its prosecution history in determining how to read claim terms, for several reasons.

First, extrinsic evidence by definition is not part of the patent and does not have the specification's virtue of being created at the time of patent prosecution for the purpose of explaining the patent's scope and meaning. Second, while claims are construed as they would be understood by a hypothetical person of skill in the art, extrinsic publications may not be written by or for skilled artisans and therefore may not reflect the understanding of a skilled artisan in the field of the patent. Third, extrinsic evidence consisting of expert reports and testimony is generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence. The effect of that bias can be exacerbated if the expert is not one of skill in the relevant art or if the expert's opinion is offered in a form that is not subject to cross-examination. *See* Senmed, Inc. v. Richard-Allan Med. Indus., Inc., 888 F.2d 815, 819 n.8 (Fed. Cir. 1989). Fourth, there is a virtually unbounded universe of potential extrinsic evidence of some marginal relevance that could be brought to bear on any claim construction question. In the course of litigation, each party will naturally choose the pieces of extrinsic evidence most favorable to its cause, leaving the court with the considerable task of filtering the useful extrinsic evidence from the fluff. *See* Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 595 (1993) ("Expert evidence can be both powerful and quite misleading because of the difficulty in evaluating it."). Finally, undue reliance on extrinsic evidence poses the risk that it will be used to change the meaning of claims in derogation of the "indisputable public records consisting of the claims, the specification and the prosecution history," thereby undermining the public notice function of patents. Southwall Techs., 54 F.3d at 1578.

In sum, extrinsic evidence may be useful to the court, but it is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence. Nonetheless, because extrinsic evidence can help educate the court regarding the field of the invention and can help the court determine what a person of ordinary skill in the art would understand claim terms to mean, it is permissible for the district court in its sound discretion to admit and use such evidence. In exercising

that discretion, and in weighing all the evidence bearing on claim construction, the court should keep in mind the flaws inherent in each type of evidence and assess that evidence accordingly.

III

Although the principles outlined above have been articulated on numerous occasions, some of this court's cases have suggested a somewhat different approach to claim construction, in which the court has given greater emphasis to dictionary definitions of claim terms and has assigned a less prominent role to the specification and the prosecution history. The leading case in this line is Texas Digital Systems, Inc. v. Telegenix, Inc., 308 F.3d 1193 (Fed. Cir. 2002).

A

In Texas Digital, the court noted that "dictionaries, encyclopedias and treatises are particularly useful resources to assist the court in determining the ordinary and customary meanings of claim terms." 308 F.3d at 1202. Those texts, the court explained, are "objective resources that serve as reliable sources of information on the established meanings that would have been attributed to the terms of the claims by those of skill in the art," and they "deserve no less fealty in the context of claim construction" than in any other area of law. Id. at 1203. The court added that because words often have multiple dictionary meanings, the intrinsic record must be consulted to determine which of the different possible dictionary meanings is most consistent with the use of the term in question by the inventor. If more than one dictionary definition is consistent with the use of the words in the intrinsic record, the court stated, "the claim terms may be construed to encompass all such consistent meanings." Id.

The Texas Digital court further explained that the patent's specification and prosecution history must be consulted to determine if the patentee has used "the words [of the claim] in a manner clearly inconsistent with the ordinary meaning reflected, for example, in a dictionary definition." 308 F.3d at 1204. The court identified two circumstances in which such an inconsistency may be found. First, the court stated, "the presumption in favor of a dictionary definition will be overcome where the patentee, acting

as his or her own lexicographer, has clearly set forth an explicit definition of the term different from its ordinary meaning." Id. Second, "the presumption also will be rebutted if the inventor has disavowed or disclaimed scope of coverage, by using words or expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." Id.

The Texas Digital court explained that it advanced the methodology set forth in that opinion in an effort to combat what this court has termed "one of the cardinal sins of patent law—reading a limitation from the written description into the claims," SciMed Life Sys., 242 F.3d at 1340. The court concluded that it is improper to consult "the written description and prosecution history as a threshold step in the claim construction process, before any effort is made to discern the ordinary and customary meanings attributed to the words themselves." Texas Digital, 308 F.3d at 1204. To do so, the court reasoned, "invites a violation of our precedent counseling against importing limitations into the claims." Id. Summarizing its analysis, the Texas Digital court stated:

> By examining relevant dictionaries, encyclopedias, and treatises to ascertain possible meanings that would have been attributed to the words of the claims by those skilled in the art, and by further utilizing the intrinsic record to select from those possible meanings the one or ones most consistent with the use of the words by the inventor, the full breadth of the limitations intended by the inventor will be more accurately determined and the improper importation of unintended limitations from the written description into the claims will be more easily avoided.
> Id. at 1205.

B

Although the concern expressed by the court in Texas Digital was valid, the methodology it adopted placed too much reliance on extrinsic sources such as dictionaries, treatises, and encyclopedias and too little on intrinsic sources, in particular the specification and prosecution history. While the court noted that the specification must be consulted in every case, it suggested a methodology for claim interpretation in which the specification

should be consulted only after a determination is made, whether based on a dictionary, treatise, or other source, as to the ordinary meaning or meanings of the claim term in dispute. Even then, recourse to the specification is limited to determining whether the specification excludes one of the meanings derived from the dictionary, whether the presumption in favor of the dictionary definition of the claim term has been overcome by "an explicit definition of the term different from its ordinary meaning," or whether the inventor "has disavowed or disclaimed scope of coverage, by using words or expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." 308 F.3d at 1204. In effect, the Texas Digital approach limits the role of the specification in claim construction to serving as a check on the dictionary meaning of a claim term if the specification requires the court to conclude that fewer than all the dictionary definitions apply, or if the specification contains a sufficiently specific alternative definition or disavowal. *See*, *e.g.*, Texas Digital, 308 F.3d at 1202 ("unless compelled otherwise, a court will give a claim term the full range of its ordinary meaning"); Nystrom v. TREX Co., 374 F.3d 1105, 1111-13 (Fed. Cir. 2004) (ascertaining the "full range" of the ordinary meaning of the term "board" through a collection of dictionary definitions, and stating that those candidate definitions should be removed from consideration only if they were "disclaimed" in the written description or prosecution history); Inverness Med. Switz., 309 F.3d at 1379 (claim should be construed to encompass multiple dictionary meanings unless "the specification or prosecution history clearly demonstrates that only one of the multiple meanings was intended"). That approach, in our view, improperly restricts the role of the specification in claim construction.

Assigning such a limited role to the specification, and in particular requiring that any definition of claim language in the specification be express, is inconsistent with our rulings that the specification is "the single best guide to the meaning of a disputed term," and that the specification "acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." Vitronics, 90 F.3d at 1582; Irdeto Access, Inc. v. Echostar Satellite Corp., 383 F.3d 1295, 1300 (Fed. Cir. 2004) ("Even when guidance is not provided in explicit definitional format, the specification may define claim terms by implication such that the meaning may be found in or ascertained by a reading of the patent documents.") (citations omitted); Novartis Pharms. Corp. v. Abbott Labs., 375 F.3d 1328,

1334-35 (Fed. Cir. 2004) (same); Bell Atl. Network Servs., Inc. v. Covad Communications Group, Inc., 262 F.3d 1258, 1268 (Fed. Cir. 2001) ("[A] claim term may be clearly redefined without an explicit statement of redefinition.").

The main problem with elevating the dictionary to such prominence is that it focuses the inquiry on the abstract meaning of words rather than on the meaning of claim terms within the context of the patent. Properly viewed, the "ordinary meaning" of a claim term is its meaning to the ordinary artisan after reading the entire patent. Yet heavy reliance on the dictionary divorced from the intrinsic evidence risks transforming the meaning of the claim term to the artisan into the meaning of the term in the abstract, out of its particular context, which is the specification. The patent system is based on the proposition that claims cover only the invented subject matter. As the Supreme Court has stated, "[i]t seems to us that nothing can be more just and fair, both to the patentee and the public, than that the former should understand, and correctly describe, just what he has invented, and for what he claims a patent." Merrill v. Yeomans, 94 U.S. at 573-74. The use of a dictionary definition can conflict with that directive because the patent applicant did not create the dictionary to describe the invention. Thus, there may be a disconnect between the patentee's responsibility to describe and claim his invention, and the dictionary editors' objective of aggregating all possible definitions for particular words.

Although the Texas Digital line of cases permit the dictionary definition to be narrowed in some circumstances even when there is not an explicit disclaimer or redefinition in the specification, too often that line of cases has been improperly relied upon to condone the adoption of a dictionary definition entirely divorced from the context of the written description. The problem is that if the district court starts with the broad dictionary definition in every case and fails to fully appreciate how the specification implicitly limits that definition, the error will systematically cause the construction of the claim to be unduly expansive. The risk of systematic overbreadth is greatly reduced if the court instead focuses at the outset on how the patentee used the claim term in the claims, specification, and prosecution history, rather than starting with a broad definition and whittling it down.

Dictionaries, by their nature, provide an expansive array of definitions. General dictionaries, in particular, strive to collect all uses of particular words, from the common to the obscure. By design, general dictionaries collect the definitions of a term as used not only in a particular art field, but in many different settings. In such circumstances, it is inevitable that the multiple dictionary definitions for a term will extend beyond the "construction of the patent [that] is confirmed by the avowed understanding of the patentee, expressed by him, or on his behalf, when his application for the original patent was pending." Goodyear Dental Vulcanite Co. v. Davis, 102 U.S. 222, 227 (1880). Thus, the use of the dictionary may extend patent protection beyond what should properly be afforded by the inventor's patent. *See* Smith v. Snow, 294 U.S. 1, 14 (1935) ("if the claim were fairly susceptible of two constructions, that should be adopted which will secure to the patentee his actual invention") (emphasis added). For that reason, we have stated that "a general-usage dictionary cannot overcome art-specific evidence of the meaning" of a claim term. Vanderlande Indus. Nederland, 366 F.3d at 1321; *see also* Renishaw, 158 F.3d at 1250, quoting Liebscher v. Boothroyd, 258 F.2d 948, 951 (CCPA 1958) ("Indiscriminate reliance on definitions found in dictionaries can often produce absurd results…One need not arbitrarily pick and choose from the various accepted definitions of a word to decide which meaning was intended as the word is used in a given claim. The subject matter, the context, etc., will more often than not lead to the correct conclusion.").

Even technical dictionaries or treatises, under certain circumstances, may suffer from some of these deficiencies. There is no guarantee that a term is used in the same way in a treatise as it would be by the patentee. In fact, discrepancies between the patent and treatises are apt to be common because the patent by its nature describes something novel. *See* Autogiro, 384 F.2d at 397 ("Often the invention is novel and words do not exist to describe it. The dictionary does not always keep abreast of the inventor. It cannot.").

Moreover, different dictionaries may contain somewhat different sets of definitions for the same words. A claim should not rise or fall based upon the preferences of a particular dictionary editor, or the court's independent decision, uninformed by the specification, to rely on one dictionary rather than another. Finally, the authors of dictionaries or treatises may simplify

ideas to communicate them most effectively to the public and may thus choose a meaning that is not pertinent to the understanding of particular claim language. *See* generally Ellen P. Aprill, The Law of the Word: Dictionary Shopping in the Supreme Court, 30 Ariz. St. L.J. 275, 293-314 (1998). The resulting definitions therefore do not necessarily reflect the inventor's goal of distinctly setting forth his invention as a person of ordinary skill in that particular art would understand it.

As we have noted above, however, we do not intend to preclude the appropriate use of dictionaries. Dictionaries or comparable sources are often useful to assist in understanding the commonly understood meaning of words and have been used both by our court and the Supreme Court in claim interpretation. *See* Exhibit Supply Co. v. Ace Patents Corp., 315 U.S. 126, 134 (1942) (relying on dictionaries to construe the claim term "embedded"); Weber Elec. Co. v. E.H. Freeman Elec. Co., 256 U.S. 668, 678 (1921) (approving circuit court's use of dictionary definitions to define claim terms); Renishaw, 158 F.3d at 1247-53 (approving the use of dictionaries with proper respect for the role of intrinsic evidence). A dictionary definition has the value of being an unbiased source "accessible to the public in advance of litigation." Vitronics, 90 F.3d at 1585. As we said in Vitronics, judges are free to consult dictionaries and technical treatises

> at any time in order to better understand the underlying technology and may also rely on dictionary definitions when construing claim terms, so long as the dictionary definition does contradict any definition found in or ascertained by a reading of the patent documents.
>
> Id. at 1584 n.6.

We also acknowledge that the purpose underlying the Texas Digital line of cases—to avoid the danger of reading limitations from the specification into the claim—is sound. Moreover, we recognize that the distinction between using the specification to interpret the meaning of a claim and importing limitations from the specification into the claim can be a difficult one to apply in practice. *See* Comark Communications, Inc. v. Harris Corp., 156 F.3d 1182, 1186-87 (Fed. Cir. 1998) ("there is sometimes a fine line

between reading a claim in light of the specification, and reading a limitation into the claim from the specification"). However, the line between construing terms and importing limitations can be discerned with reasonable certainty and predictability if the court's focus remains on understanding how a person of ordinary skill in the art would understand the claim terms. For instance, although the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments. *See*, *e.g.*, Nazomi Communications, Inc. v. ARM Holdings, PLC, 403 F.3d 1364, 1369 (Fed. Cir. 2005) (claims may embrace "different subject matter than is illustrated in the specific embodiments in the specification"); Liebel-Flarsheim, 358 F.3d at 906-08; Teleflex, 299 F.3d at 1327; SRI Int'l v. Matsushita Elec. Corp. of Am., 775 F.2d 1107, 1121 (Fed. Cir. 1985). In particular, we have expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment. Gemstar-TV Guide, 383 F.3d at 1366. That is not just because section 112 of the Patent Act requires that the claims themselves set forth the limits of the patent grant, but also because persons of ordinary skill in the art rarely would confine their definitions of terms to the exact representations depicted in the embodiments.

To avoid importing limitations from the specification into the claims, it is important to keep in mind that the purposes of the specification are to teach and enable those of skill in the art to make and use the invention and to provide a best mode for doing so. *See* Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1533 (Fed. Cir. 1987). One of the best ways to teach a person of ordinary skill in the art how to make and use the invention is to provide an example of how to practice the invention in a particular case. Much of the time, upon reading the specification in that context, it will become clear whether the patentee is setting out specific examples of the invention to accomplish those goals, or whether the patentee instead intends for the claims and the embodiments in the specification to be strictly coextensive. *See* SciMed Life Sys., 242 F.3d at 1341. The manner in which the patentee uses a term within the specification and claims usually will make the distinction apparent. *See* Snow v. Lake Shore & M.S. Ry. Co., 121 U.S. 617, 630 (1887) (it was clear from the specification that there was "nothing in the context to indicate that the patentee contemplated any alternative" embodiment to the one presented).

In the end, there will still remain some cases in which it will be hard to determine whether a person of skill in the art would understand the embodiments to define the outer limits of the claim term or merely to be exemplary in nature. While that task may present difficulties in some cases, we nonetheless believe that attempting to resolve that problem in the context of the particular patent is likely to capture the scope of the actual invention more accurately than either strictly limiting the scope of the claims to the embodiments disclosed in the specification or divorcing the claim language from the specification.

In Vitronics, this court grappled with the same problem and set forth guidelines for reaching the correct claim construction and not imposing improper limitations on claims. 90 F.3d at 1582. The underlying goal of our decision in Vitronics was to increase the likelihood that a court will comprehend how a person of ordinary skill in the art would understand the claim terms. *See* id. at 1584. In that process, we recognized that there is no magic formula or catechism for conducting claim construction. Nor is the court barred from considering any particular sources or required to analyze sources in any specific sequence, as long as those sources are not used to contradict claim meaning that is unambiguous in light of the intrinsic evidence. *See* id. at 1583-84; Intel Corp. v. VIA Techs., Inc., 319 F.3d 1357, 1367 (Fed. Cir. 2003). For example, a judge who encounters a claim term while reading a patent might consult a general purpose or specialized dictionary to begin to understand the meaning of the term, before reviewing the remainder of the patent to determine how the patentee has used the term. The sequence of steps used by the judge in consulting various sources is not important; what matters is for the court to attach the appropriate weight to be assigned to those sources in light of the statutes and policies that inform patent law. Vitronics, 90 F.3d at 1582. In Vitronics, we did not attempt to provide a rigid algorithm for claim construction, but simply attempted to explain why, in general, certain types of evidence are more valuable than others. Today, we adhere to that approach and reaffirm the approach to claim construction outlined in that case, in Markman, and in Innova. We now turn to the application of those principles to the case at bar.

IV

A

The critical language of claim 1 of the '798 patent—"further means disposed inside the shell for increasing its load bearing capacity comprising internal steel baffles extending inwardly from the steel shell walls"—imposes three clear requirements with respect to the baffles. First, the baffles must be made of steel. Second, they must be part of the load-bearing means for the wall section. Third, they must be pointed inward from the walls. Both parties, stipulating to a dictionary definition, also conceded that the term "baffles" refers to objects that check, impede, or obstruct the flow of something.

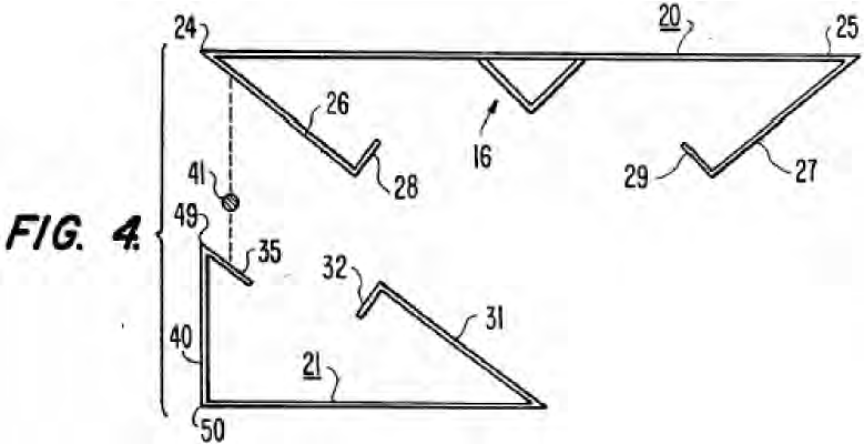
The intrinsic evidence confirms that a person of skill in the art would understand that the term "baffles," as used in the '798 patent, would have that generic meaning.

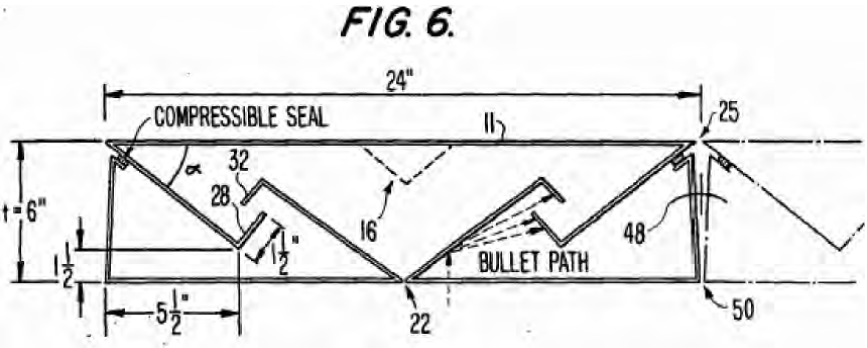
The other claims of the '798 patent specify particular functions to be served by the baffles. For example, dependent claim 2 states that the baffles may be "oriented with the panel sections disposed at angles for deflecting projectiles such as bullets able to penetrate the steel plates." The inclusion of such a specific limitation on the term "baffles" in claim 2 makes it likely that the patentee did not contemplate that the term "baffles" already contained that limitation. *See* Dow Chem. Co. v. United States, 226 F.3d 1334, 1341-42 (Fed. Cir. 2000) (concluding that an independent claim should be given broader scope than a dependent claim to avoid rendering the dependent claim redundant). Independent claim 17 further supports that proposition. It states that baffles are placed "projecting inwardly from the outer shell at angles tending to deflect projectiles that penetrate the outer shell." That limitation would be unnecessary if persons of skill in the art understood that the baffles inherently served such a function. *See* TurboCare, 264 F.3d at 1123 (claim terms should not be read to contain a limitation "where another claim restricts the invention in exactly the [same] manner"). Dependent claim 6 provides an additional requirement for the baffles, stating that "the internal baffles of both outer panel sections overlap and interlock at angles providing deflector panels extending from one end of the module to the other." If the baffles recited in claim 1 were

inherently placed at specific angles, or interlocked to form an intermediate barrier, claim 6 would be redundant.

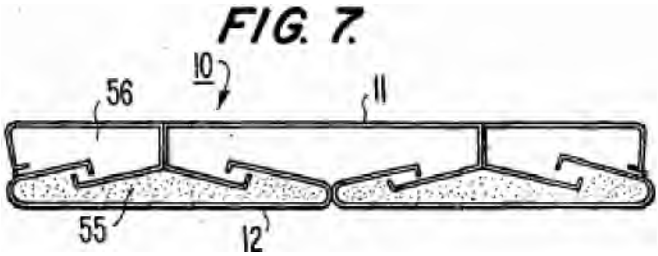
The specification further supports the conclusion that persons of ordinary skill in the art would understand the baffles recited in the '798 patent to be load-bearing objects that serve to check, impede, or obstruct flow. At several points, the specification discusses positioning the baffles so as to deflect projectiles. *See* '798 patent, col. 2, ll. 13-15; id., col. 5, ll. 17-19. The patent states that one advantage of the invention over the prior art is that "[t]here have not been effective ways of dealing with these powerful impact weapons with inexpensive housing." Id., col. 3, ll. 28-30. While that statement makes clear the invention envisions baffles that serve that function, it does not imply that in order to qualify as baffles within the meaning of the claims, the internal support structures must serve the projectile-deflecting function in all the embodiments of all the claims. The specification must teach and enable all the claims, and the section of the written description discussing the use of baffles to deflect projectiles serves that purpose for claims 2, 6, 17, and 23, which specifically claim baffles that deflect projectiles. *See* In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

The specification discusses several other purposes served by the baffles. For example, the baffles are described as providing structural support. The patent states that one way to increase load-bearing capacity is to use "at least in part inwardly directed steel baffles 15, 16." '798 patent, col. 4, ll. 14-15. The baffle 16 is described as a "strengthening triangular baffle." Id., col. 4, line 37. Importantly, Figures 4 and 6 do not show the baffles as part of an "intermediate interlocking, but not solid, internal barrier." In those figures, the baffle 16 simply provides structural support for one of the walls, as depicted below:





Other uses for the baffles are listed in the specification as well. In Figure 7, the overlapping flanges "provide for overlapping and interlocking the baffles to produce substantially an intermediate barrier wall between the opposite [wall] faces":



'798 patent, col. 5, ll. 26-29. Those baffles thus create small compartments that can be filled with either sound and thermal insulation or rock and gravel to stop projectiles. Id., col. 5, ll. 29-34. By separating the interwall area into compartments (*see*, *e.g.*, compartment 55 in Figure 7), the user of the modules can choose different types of material for each compartment, so that the module can be "easily custom tailored for the specific needs of each installation." Id., col. 5, ll. 36-37. When material is placed into the wall during installation, the baffles obstruct the flow of material from one compartment to another so that this "custom tailoring" is possible.

The fact that the written description of the '798 patent sets forth multiple objectives to be served by the baffles recited in the claims confirms that the term "baffles" should not be read restrictively to require that the baffles in each case serve all of the recited functions. We have held that "[t]he fact that a patent asserts that an invention achieves several objectives does not require that each of the claims be construed as limited to structures that are capable of achieving all of the objectives." Liebel-Flarsheim, 358 F.3d at 908; *see also* Resonate Inc. v. Alteon Websystems, Inc., 338 F.3d 1360, 1367 (Fed. Cir. 2003). Although deflecting projectiles is one of the advantages of the baffles of the '798 patent, the patent does not require that the inward extending structures always be capable of performing that function. Accordingly, we conclude that a person of skill in the art would not interpret the disclosure and claims of the '798 patent to mean that a structure extending inward from one of the wall faces is a "baffle" if it is at an acute or obtuse angle, but is not a "baffle" if it is disposed at a right angle.

B

Invoking the principle that "claims should be so construed, if possible, as to sustain their validity," Rhine v. Casio, Inc., 183 F.3d 1342, 1345 (Fed Cir.

1999), AWH argues that the term "baffles" should be given a restrictive meaning because if the term is not construed restrictively, the asserted claims would be invalid.

While we have acknowledged the maxim that claims should be construed to preserve their validity, we have not applied that principle broadly, and we have certainly not endorsed a regime in which validity analysis is a regular component of claim construction. *See* Nazomi Communications, 403 F.3d at 1368-69. Instead, we have limited the maxim to cases in which "the court concludes, after applying all the available tools of claim construction, that the claim is still ambiguous." Liebel-Flarsheim, 358 F.3d at 911; *see also* Generation II Orthonics Inc. v. Med. Tech. Inc., 263 F.3d 1356, 1365 (Fed. Cir. 2001) ("[C]laims can only be construed to preserve their validity where the proposed claim construction is 'practicable,' is based on sound claim construction principles, and does not revise or ignore the explicit language of the claims."); Elekta Instrument S.A. v. O.U.R. Scientific Int'l, Inc., 214 F.3d 1302, 1309 (Fed. Cir. 2000) ("having concluded that the amended claim is susceptible of only one reasonable construction, we cannot construe the claim differently from its plain meaning in order to preserve its validity"); E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co., 849 F.2d 1430, 1434 (Fed. Cir. 1988) (rejecting argument that limitations should be added to claims to preserve the validity of the claims). In such cases, we have looked to whether it is reasonable to infer that the PTO would not have issued an invalid patent, and that the ambiguity in the claim language should therefore be resolved in a manner that would preserve the patent's validity.

That is the rationale that gave rise to the maxim in the first place. In Klein v. Russell, 86 U.S. (19 Wall.) 433, 466 (1873), the owner of a reissued patent argued for a narrow construction of the patent, while the accused infringer argued for a broader construction. The Court noted that the law "required that the reissue should be for the same invention as the original patent." Id. Because the reissue, which was granted under the predecessor to 35 U.S.C. §251, would have been improper under the broader construction, the Court "presumed the Commissioner did his duty" and did not issue an invalid patent. For that reason, among others, the Court construed the disputed claim language in a manner that "sustain[ed] the patent and the construction claimed by the patentee," since that "can be done consistently

with the language which he has employed." Id. The applicability of the doctrine in a particular case therefore depends on the strength of the inference that the PTO would have recognized that one claim interpretation would render the claim invalid, and that the PTO would not have issued the patent assuming that to be the proper construction of the term.

In this case, unlike in Klein and other cases in which the doctrine of construing claims to preserve their validity has been invoked, the claim term at issue is not ambiguous. Thus, it can be construed without the need to consider whether one possible construction would render the claim invalid while the other would not. The doctrine of construing claims to preserve their validity, a doctrine of limited utility in any event, therefore has no applicability here.

In sum, we reject AWH's arguments in favor of a restrictive definition of the term "baffles." Because we disagree with the district court's claim construction, we reverse the summary judgment of non-infringement. In light of our decision on claim construction, it is necessary to remand the infringement claims to the district court for further proceedings.

V

With respect to Mr. Phillips's allegation of misappropriation of trade secrets, we agree with the panel's decision upholding the district court's ruling on that issue, in which the district court dismissed the trade secret claim on statute of limitations grounds. *See* Phillips, 363 F.3d at 1214-1216. Accordingly, based on the panel's disposition of that issue, we affirm the district court's dismissal of the trade secret claim. With respect to AWH's cross-appeal, we also agree with the panel's reasoning and its conclusion that the cross-appeal is improper. *See* id. at 1216. We therefore dismiss the cross-appeal.

VI

In our order granting rehearing en banc, we asked the parties to brief various questions, including the following: "Consistent with the Supreme Court's decision in Markman v. Westview Instruments, 517 U.S. 370 (1996), and our en banc decision in Cybor Corp. v. FAS Technologies, Inc., 138

F.3d 1448 (Fed. Cir. 1998), is it appropriate for this court to accord any deference to any aspect of trial court claim construction rulings? If so, on what aspects, in what circumstances, and to what extent?" After consideration of the matter, we have decided not to address that issue at this time. We therefore leave undisturbed our prior en banc decision in Cybor.

Each party shall bear its own costs for this appeal.

AFFIRMED IN PART, REVERSED IN PART, DISMISSED IN PART, and REMANDED.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

03-1269-1286

EDWARD H. PHILLIPS,
Plaintiff-Appellant
v.
AWH CORPORATION,
HOPEMAN BROTHERS, INC., and LOFTON CORPORATION,
Defendants-Cross Appellants

LOURIE, Circuit Judge, concurring in part and dissenting in part, with whom NEWMAN, Circuit Judge, joins.

I fully join the portion of the court's opinion resolving the relative weights of specification and dictionaries in interpreting patent claims, in favor of the specification. I could elaborate more expansively on that topic, but Judge Bryson's opinion for the majority says it so well, there is little reason for me to repeat its truths. I also agree with the court that claims need not necessarily be limited to specific or preferred embodiments in the specification, although they are limited to what is contained in the overall disclosure of the specification.

However, I do dissent from the court's decision to reverse and remand the district court's decision. The original panel decision of this court, which implicitly decided the case based on the priorities that the en banc court has now reaffirmed, interpreted the claims in light of the specification and found that the defendant did not infringe the claims. We affirmed the district court, which had arrived at a similar conclusion. The dissent from the panel decision relied on the "dictionaries first" procedure, which the court now has decided not to follow. Thus, while the claim construction issue had to be decided by the en banc court, I see no reason for the court, having reaffirmed the principle on which the district judge and the panel originally decided the case, to send it back for further review.

The court premises its reverse-and-remand decision on the concept of claim differentiation and the reasoning that the contested term "baffle"

need not fulfill all of the functions set out for it in the specification. Reasonable people can differ on those points. However, the court did not take this case en banc because the full court differed with the panel majority on those disputable criteria. It did so to resolve the claim construction issue, which it has now done so well. Having done so, I believe that it should simply affirm the district court's decision on the merits, consistently with that court's rationale and that of the panel that affirmed the district court, which it now adopts.

I will not critique in detail particular statements the majority makes in rationalizing its reversal of the district court's decision, such as "that a person of skill in the art would not interpret the disclosure and claims of the '798 patent to mean that a structure extending inward from one of the wall faces is a 'baffle' if it is at an acute or obtuse angle, but is not a 'baffle' if it is disposed at a right angle," or that "the patent does not require that the inward extending structures always be capable of performing that function [deflecting projectiles]" in order to be considered 'baffles.'

I will simply point out that the specification contains no disclosure of baffles at right angles. Moreover, as the majority correctly states, a patent specification is intended to describe one's invention, and it is essential to read a specification in order to interpret the meaning of the claims. This specification makes clear that the "baffles" in this invention are angled. There is no reference to baffles that show them to be other than angled. The abstract refers to "bullet deflecting…baffles." Only angled baffles can deflect. It then mentions "internal baffles at angles for deflecting bullets." That could not be clearer. The specification then refers several times to baffles, often to figures in the drawings, all of which are to angled baffles. A compelling point is that the only numbered references to baffles (15, 16, 26, 27, 30, and 31) all show angled baffles.

The specification further states that steel panels "form the internal baffles at angles for deflecting bullets." It states that the baffles are "disposed at such angles that bullets which might penetrate the outer steel panels are deflected." It explains that if bullets "were to penetrate the outer steel wall, the baffles are disposed at angles which tend to deflect the bullets." There is no specific reference in this patent to a baffle that is not angled at other than 90º.

While, as the majority states, the specification indicates that multiple objectives are achieved by the invention, none of the other objectives is dependent upon whether the baffles are at other than a 90º angle, whereas the constantly stated objective of deflection of bullets is dependent upon such an angle.

Finally, even though claim construction is a question of law, reviewable by this court without formal deference, I do believe that we ought to lean toward affirmance of a claim construction in the absence of a strong conviction of error. I do not have such a conviction in this case, after considering the district court's opinion and the patent specification.

For these reasons, while I wholeheartedly join the majority opinion in its discussion and resolution of the "specification v. dictionaries" issue, I would affirm the decision below.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

03-1269-1286

EDWARD H. PHILLIPS,
Plaintiff-Appellant
v.
AWH CORPORATION,
HOPEMAN BROTHERS, INC., and LOFTON CORPORATION,
Defendants-Cross Appellants

MAYER, Circuit Judge, with whom NEWMAN, Circuit Judge, joins, dissenting.

Now more than ever I am convinced of the futility, indeed the absurdity, of this court's persistence in adhering to the falsehood that claim construction is a matter of law devoid of any factual component. Because any attempt to fashion a coherent standard under this regime is pointless, as illustrated by our many failed attempts to do so, I dissent.

This court was created for the purpose of bringing consistency to the patent field. *See* H.R. Rep. No. 312, 97th Cong., 1st Sess. 20-23 (1981). Instead, we have taken this noble mandate, to reinvigorate the patent and introduce predictability to the field, and focused inappropriate power in this court. In our quest to elevate our importance, we have, however, disregarded our role as an appellate court; the resulting mayhem has seriously undermined the legitimacy of the process, if not the integrity of the institution.

In the name of uniformity, Cybor Corp. v. FAS Technologies, Inc., 138 F.3d 1448 (Fed. Cir. 1998) (en banc), held that claim construction does not involve subsidiary or underlying questions of fact and that we are, therefore, unbridled by either the expertise or efforts of the district court.[1] What we

[1] The Supreme Court did not suggest in affirming Markman v. Westview Instruments, Inc., 52 F.3d 967 (1995) (en banc), that claim construction is a purely legal question. 517 U.S. 370 (1996). It held only that, as a policy matter, the judge, as opposed to the jury, should determine the meaning of a patent claim. *See* Cybor, 138 F.3d at 1464 (Mayer, C.J., dissenting) (explaining that "the [Supreme] Court chose not to accept our formulation of claim construction: as a pure question of law to be decided de novo in all cases on appeal").

have wrought, instead, is the substitution of a black box, as it so pejoratively has been said of the jury, with the black hole of this court. Out of this void we emit "legal" pronouncements by way of "interpretive necromancy"[2]; these rulings resemble reality, if at all, only by chance. Regardless, and with a blind eye to the consequences, we continue to struggle under this irrational and reckless regime, trying every alternative—dictionaries first, dictionaries second, never dictionaries, etc., etc., etc.

Again today we vainly attempt to establish standards by which this court will interpret claims. But after proposing no fewer than seven questions, receiving more than thirty amici curiae briefs, and whipping the bar into a frenzy of expectation, we say nothing new, but merely restate what has become the practice over the last ten years—that we will decide cases according to whatever mode or method results in the outcome we desire, or at least allows us a seemingly plausible way out of the case. I am not surprised by this. Indeed, there can be no workable standards by which this court will interpret claims so long as we are blind to the factual component of the task. *See* Cooter & Gell v. Hartmarx Corp., 496 U.S. 384, 405 (1990) ("Fact-bound resolutions cannot be made uniform through appellate review, de novo or otherwise." (quoting Mars Steel Corp. v. Cont'l Bank N.A., 880 F.2d 928, 936 (7th Cir.1989))).[3]

Federal Rule of Civil Procedure 52(a) states that "[f]indings of fact…shall not be set aside unless clearly erroneous, and due regard shall be given to the opportunity of the trial court to judge of the credibility of witnesses." According to the Supreme Court, this "[r]ule means what it says"—that findings of fact, even "those described as 'ultimate facts' because they may determine the outcome of litigation," are to be reviewed deferentially on

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[2] *See* The Holmes Group, Inc. v. Vornado Air Circulation Sys., Inc., 535 U.S. 826, 833 (2002).

[3] The question asked but not answered by the court which might have allowed it to cure its self-inflicted wound was: "Question 7. Consistent with the Supreme Court's decision in Markman v. Westview Instruments, Inc., 517 U.S. 370 (1996) and our en banc decision in Cybor Corp. v. FAS Technologies, Inc., 138 F.3d 1448 (Fed. Cir. 1998), is it appropriate for this court to accord any deference to any aspect of trial court claim construction rulings? If so, on what aspects, in what circumstances, and to what extent?"

appeal.[4] Bose Corp. v. Consumers Union of United States, 466 U.S. 485, 498 & 501 (1984); *see also* Anderson v. Bessemer City, 470 U.S. 564, 575 (1985) ("[R]eview of factual findings under the clearly-erroneous standard—with its deference to the trier of fact—is the rule, not the exception."); Pullman-Standard v. United Steel Workers of Am., 456 U.S. 273, 287 (1982) ("Rule 52(a) broadly requires that findings of fact not be set aside unless clearly erroneous."); United States v. United States Gypsum Co., 333 U.S. 364, 394 (1948). Even those findings of fact based entirely on documentary evidence are entitled to deference. Anderson, 470 U.S. at 574 ("That [Rule 52(a)] goes on to emphasize the special deference to be paid credibility determinations does not alter its clear command: Rule 52(a) 'does not make exceptions or purport to exclude certain categories of factual findings from the obligation of a court of appeals to accept a district court's findings unless clearly erroneous.'" (quoting Pullman-Standard, 456 U.S. at 287)). In short, we are obligated by Rule 52(a) to review the factual findings of the district court that underlie the determination of claim construction for clear error.

[4] Because some facts are so intertwined with a constitutional standard the Supreme Court has held that de novo review is appropriate. For example, whether a defendant has acted with actual malice in a defamation suit is reviewed de novo because, among other reasons, the scope of the First Amendment is shaped and applied by reference to such factual determinations. Bose, 466 U.S. at 502 ("[T]he content of the rule is not revealed simply by its literal text, but rather is given meaning through the evolutionary process of common-law adjudication."). Similarly, whether there is reasonable suspicion to conduct an investigatory stop or probable cause to perform a search under the Fourth Amendment are reviewed without deference. Ornelas v. United States, 517 U.S. 690, 696 (1996) (holding that the protections afforded by the Fourth Amendment are "fluid concepts that take their substantive content from the particular contexts in which the standards are being assessed"). The reasoning behind these limited exceptions surely does not apply to claim construction. While appearing from the perspective of this court's limited sphere of influence to be dreadfully important, claim construction does not implicate a constitutional value. Cf. Bose, 466 U.S. at 502 ("[T]he constitutional values protected by the rule make it imperative that judges—and in some cases judges of [the Supreme] Court—make sure that it is correctly applied."). This is illustrated by the fact that the outcome of a patent case, unlike a defamation or illegal search case, has little impact on how future cases are decided or on how future parties behave. Cf. id. at 501 n.17 ("Regarding certain largely factual questions in some areas of the law, the stakes—in terms of impact on future cases and future conduct—are too great to entrust them finally to the judgment of the trier of fact."). Even if claim construction did implicate a constitutional value, it, unlike the decisions underlying the First and Fourth Amendments, could readily be reduced, when distinguished from its factual underpinnings, to "a neat set of legal rules." Ornelas, 517 U.S. at 695-96 (quoting Ill. v. Gates, 462 U.S. 213, 232 (1983)).

While this court may persist in the delusion that claim construction is a purely legal determination, unaffected by underlying facts, it is plainly not the case. Claim construction is, or should be, made in context: a claim should be interpreted both from the perspective of one of ordinary skill in the art and in view of the state of the art at the time of invention. *See* Multiform Desiccants, Inc. v. Medzam, Ltd., 133 F.3d 1473, 1477 (Fed. Cir. 1998) ("It is the person of ordinary skill in the field of the invention through whose eyes the claims are construed."). These questions, which are critical to the correct interpretation of a claim, are inherently factual. They are hotly contested by the parties, not by resort to case law as one would expect for legal issues, but based on testimony and documentary evidence.[5] During so called Markman "hearings," which are often longer than jury trials, parties battle over experts offering conflicting evidence regarding who qualifies as one of ordinary skill in the art; the meaning of patent terms to that person; the state of the art at the time of the invention; contradictory dictionary definitions and which would be consulted by the skilled artisan; the scope of specialized terms; the problem a patent was solving; what is related or pertinent art; whether a construction was disallowed during prosecution; how one of skill in the art would understand statements during prosecution; and on and on. In order to reconcile the parties' inconsistent submissions and arrive at a sound interpretation, the district court is required to sift through and weigh volumes of evidence. While this court treats the district court as an intake clerk, whose only role is to collect, shuffle and collate evidence, the reality, as revealed by conventional practice, is far different.

Even if the procedures employed by the district court did not show that it is engaging in fact finding, the nature of the questions underlying claim construction illustrate that they are factual and should be reviewed in accordance with Rule 52(a). For each patent, for example, who qualifies as one of ordinary skill in the art will differ, just as the state of the art at the time of invention will differ. These subsidiary determinations are specific, multifarious and not susceptible to generalization; as such their resolution

[5] That most of the cases now appealed to this court are "summary judgments" is irrelevant. We have artificially renamed findings of fact as legal conclusions; the district courts have dutifully conformed to our fictional characterization, but this does not change the inherent nature of the inquiry. Of course, if the parties do not dispute the material facts, summary judgment is appropriate.

in one case will bear very little, if at all, on the resolution of subsequent cases. *See* Ornelas, 517 U.S. at 703 ("Law clarification requires generalization, and some issues lend themselves to generalization much more than others."); Pierce v. Underwood, 487 U.S. 552, 561-62 (1988) ("Many questions that arise in litigation are not amenable to regulation by rule because they involve multifarious, fleeting, special, narrow facts that utterly resist generalization." (quoting Maurice Rosenberg, Judicial Discretion of the Trial Court, Viewed from Above, 22 Syracuse L. Rev. 635, 662 (1971))); Icicle Seafoods, Inc. v. Worthington, 475 U.S. 709, 714 (1986) (rejecting de novo review of factual questions, even when outcome determinative). That the determination of the meaning of a particular term in one patent will not necessarily bear on the interpretation of the same term in a subsequent patent illustrates this point; while the term is the same, the factual context is different. It further proves that these questions (e.g., who qualifies as one of ordinary skill in the art and what was the state of the art at the time of invention, among others) are implicitly being determined in each case; because we refuse to acknowledge either their existence or importance, however, the manner of their resolution is never elucidated. Finally, that claim construction is dependent on underlying factual determinations has been verified by our experience, which shows that reviewing these questions de novo has not clarified the law, but has instead "distort[ed] the appellate process," causing confusion among the district courts and bar. *See* Cooter, 496 U.S. at 404 (quoting Pierce, 487 U.S. at 561); *see also* Koon v. United States, 518 U.S. 81, 99 (1996).

Our purely de novo review of claim interpretation also cannot be reconciled with the Supreme Court's instructions regarding obviousness. While ultimately a question of law, obviousness depends on several underlying factual inquiries. Graham v. John Deere Co., 383 U.S. 1, 17 (1966); *see also* Dennison Mfg. Co. v. Panduit Corp., 475 U.S. 809, 811 (1986) (holding that Rule 52(a) requires that the district court's subsidiary factual determinations should be reviewed for clear error); cf. Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 336 U.S. 271, 275 (1949) (holding that validity, while ultimately a question of law, is founded on factual determinations that are entitled to deference). "Under [section] 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved." Graham, 383 U.S. at 17.

To a significant degree, each of these factual inquiries is also necessary to claim construction. Before beginning claim construction, "the scope and content of the prior art [should] be determined," id., to establish context. The "differences between the prior art and the claims at issue [should] be ascertained," id., to better define what the inventor holds out as the invention. And, the foundation for both the obviousness and claim construction determinations is "the level of ordinary skill in the pertinent art." Id.; *see* Multiform, 133 F.3d at 1477. These underlying factual considerations receive the level of deference due under Rule 52(a) when considering obviousness, but they are scrutinized de novo in the claim construction context. As directed by the Supreme Court, however, it is especially important in the patent field, "where so much depends upon familiarity with specific scientific problems and principles not usually contained in the general storehouse of knowledge and experience," to give deference to the district court's findings of fact. Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 339 U.S. 605, 609-10 (1950).

While the court flails about in an attempt to solve the claim construction "conundrum," the solution to our plight is straightforward. We simply must follow the example of every other appellate court, which, regarding the vast majority of factual questions, reviews the trial court for clear error.[6] This equilibrium did not come about as the result of chance or permissive appellate personalities, but because two centuries of experience has shown that the trial court's fact finding ability is "unchallenged." Salve Regina Coll. v. Russell, 499 U.S. 225, 233 (1991); Inwood, 456 U.S. at 856 ("Determining the weight and credibility of the evidence is the special province of the trier of fact."). Time has similarly revealed that it is more economical for the district court to find facts. Pierce, 487 U.S. at 560 ("Moreover, even where the district judge's full knowledge of the factual setting can be acquired by the appellate court, that acquisition will often come at unusual expense, requiring the court to undertake the unaccustomed task of reviewing the entire record…").

Therefore, not only is it more efficient for the trial court to construct the record, the trial court is better, that is, more accurate, by way of both

[6] While jurisprudentially sound, the bar also supports this proposition, as evident by the many amici curiae briefs urging adherence to Rule 52(a).

position and practice, at finding facts than appellate judges. Anderson, 470 U.S. at 574 ("The rationale for deference to the original finder of fact is not limited to the superiority of the trial judge's position to make determinations of credibility. The trial judge's major role is the determination of fact, and with experience on fulfilling that role comes expertise."); Zenith Radio Corp. v. Hazeltine Research, Inc., 395 U.S. 100, 123 (1969). Our rejection of this fundamental premise has resulted, not surprisingly, in several serious problems, including increased litigation costs, needless consumption of judicial resources, and uncertainty, as well as diminished respect for the court and less "decisional accuracy." Salve, 499 U.S. at 233. We should abandon this unsound course.[7]

If we persist in deciding the subsidiary factual components of claim construction without deference, there is no reason why litigants should be required to parade their evidence before the district courts or for district courts to waste time and resources evaluating such evidence. It is excessive to require parties, who "have already been forced to concentrate their energies and resources on persuading the trial judge that their account of the facts is the correct one," to "persuade three more judges at the appellate level." Anderson, 470 U.S. at 575. If the proceedings before the district court are merely a "tryout on the road," id. (quoting Wainwright v. Sykes, 433 U.S. 72, 90 (1977)), as they are under our current regimen, it is wasteful to require such proceedings at all. Instead, all patent cases could be filed in this court; we would determine whether claim construction is necessary, and, if so, the meaning of the claims. Those few cases in which claim construction is not dispositive can be remanded to the district court for trial. In this way, we would at least eliminate the time and expense of the charade currently played out before the district court.

Eloquent words can mask much mischief. The court's opinion today is akin to rearranging the deck chairs on the Titanic—the orchestra is playing as if nothing is amiss, but the ship is still heading for Davey Jones' locker.

Courtesy of Patrick H. Higgins, Buchanan Ingersoll & Rooney PC

[7] There are some scenarios where it is difficult to weed facts from law, *see* Pullman-Standard, 456 U.S. at 288, but claim construction is not one of them.

APPENDIX D

UNIVERSITY OF ROCHESTER V. G.D. SEARLE & CO. INC., MONSANTO COMPANY, PHARMACIA CORPORATION, AND PFIZER INC.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

03-1304

UNIVERSITY OF ROCHESTER,
Plaintiff-Appellant
v.
G.D. SEARLE & CO., INC.,
MONSANTO COMPANY, PHARMACIA CORPORATION,
and PFIZER INC.,
Defendants-Appellees

Gerald P. Dodson, Morrison & Foerster, LLP, of Palo Alto, California, argued for plaintiff-appellant. With him on the brief were Emily A. Evans, Erica D. Wilson, and Erik J. Olson. Of counsel on the brief was Jeanine Arden Ornt, Office of Counsel, University of Rochester, of Rochester, New York.

Gerald Sobel, Kaye Scholer LLP, of New York, New York, argued for defendants-appellees. With him on the brief were Richard G. Greco, Sylvia M. Becker, and Daniel L. Reisner. With him on the brief were Robert L. Baechtold, Henry J. Renk, Bruce C. Haas, and Colleen Tracy, Fitzpatrick, Cella, Harper & Scinto, of New York, New York.

Daniel J. Furniss, Townsend and Townsend and Crew LLP, of Palo Alto, California, for amici curiae The Regents of the University of California, et al. With him on the brief were Susan M. Spaeth and Madison C. Jellins.

James J. Kelley, Eli Lilly and Company, of Indianapolis, Indiana, for amicus curiae Eli Lilly and Company. With him on the brief were Steven P.

Caltrider, Michael T. Bates, Robert A. Armitage, Gilbert T. Voy, and Gregory C. Cox.

Appealed from: United States District Court for the Western District of New York

Judge David G. Larimer

G.D. SEARLE & CO., INC., MONSANTO COMPANY,
PHARMACIA CORPORATION, and PFIZER INC.,
Defendants-Appellees.

DECIDED: February 13, 2004

Before LOURIE, BRYSON, and DYK, Circuit Judges.

LOURIE, Circuit Judge.

The University of Rochester ("Rochester") appeals from the decision of the United States District Court for the Western District of New York granting summary judgment that United States Patent 6,048,850 is invalid. Univ. of Rochester v. G.D. Searle & Co., 249 F. Supp. 2d 216 (W.D.N.Y. 2003). Because we conclude that the court did not err in holding the '850 patent invalid for failing to comply with the written description requirement of 35 U.S.C. §112, ¶ 1, and in granting summary judgment on that ground, we affirm.

BACKGROUND

Traditional non-steroidal anti-inflammatory drugs ("NSAIDs") such as aspirin, ibuprofen, ketoprofen, and naproxen are believed to function by inhibiting the activity of enzymes called cyclooxygenases. Cyclooxygenases catalyze the production of a molecule called prostaglandin H2, which is a precursor for other prostaglandins that perform various functions in the human body. Id. at 219.

In the early 1990s, scientists discovered the existence and separate functions of two distinct cyclooxygenases, referred to as "COX-1" and "COX-2."[1] COX-1 is expressed (i.e., produced biologically) in the gastrointestinal tract, where it is involved in the production of prostaglandins that serve a beneficial role by, for example, providing protection for the stomach lining. Id. COX-2 is expressed in response to inflammatory stimuli, and is thought to be responsible for the inflammation associated with diseases such as arthritis. Id. It is now known that the traditional NSAIDs inhibit both COX-1 and COX-2, and as a result they not only reduce inflammation, but also can cause undesirable side effects such as stomach upset, irritation, ulcers, and bleeding. Id.

After the separate functions of COX-1 and COX-2 were discovered, it was hypothesized that it would be possible to reduce inflammation without gastrointestinal side effects if a method could be found for selectively inhibiting the activity of COX-2 (i.e., inhibiting the activity of COX-2 without inhibiting COX-1 activity). Id. To that end, Rochester scientists developed a screening assay for use in determining whether a particular drug displayed such selectivity, and filed a U.S. patent application directed to their developments in 1992. After filing a series of continuation, continuation-in-part, and divisional applications derived from that 1992 application, the scientists eventually received United States Patent 5,837,479 in 1998, covering methods "for identifying a compound that inhibits prostaglandin synthesis catalyzed by mammalian prostaglandin H synthase-2 (PG HS-2)."

From a division of the application that led to the '479 patent, the scientists also obtained, on April 11, 2000, the '850 patent. The '850 patent contains three independent claims and five dependent claims. The three independent claims read as follows:

> 1. A method for selectively inhibiting PGHS-2 activity in a human host, comprising administering a non-steroidal compound that selectively inhibits activity of the

[1] COX-1 and COX-2 are alternatively referred to as "PGHS-1" and "PGHS-2," respectively, where "PGHS" is an abbreviation for "prostaglandin H synthase."

PGHS-2 gene product to a human host in need of such treatment.

5. A method for selectively inhibiting PGHS-2 activity in a human host, comprising administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product in a human host in need of such treatment, wherein the activity of the non-steroidal compound does not result in significant toxic side effects in the human host.

6. A method for selectively inhibiting PGHS-2 activity in a human host, comprising administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product in a human host in need of such treatment, wherein the ability of the non-steroidal compound to selectively inhibit the activity of the PGHS-2 gene product is determined by:

a) contacting a genetically engineered cell that expresses human PGHS-2, and not human PGHS-1, with the compound for 30 minutes, and exposing the cell to a pre-determined-amount of arachidonic acid;

b) contacting a genetically engineered cell that expresses human PGHS-1, and not human PGHS-2, with the compound for 30 minutes, and exposing the cell to a pre-determined amount of arachidonic acid;

c) measuring the conversion of arachidonic acid to its prostaglandin metabolite; and

d) comparing the amount of the converted arachidonic acid converted by each cell exposed to the compound to the amount of the arachidonic acid converted by control cells that were not exposed to the compound, so that the compounds that inhibit PGHS-2 and not PGHS-1 activity are identified.

'850 patent, col. 71, l. 36 - col. 72, l. 51. Thus, all eight claims are directed to methods "for selectively inhibiting PGHS-2 activity in a human host" by "administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product to [or in] a human host in need of such treatment."

On the day the '850 patent issued, Rochester sued G.D. Searle & Co., Inc., Monsanto Co., Pharmacia Corp., and Pfizer Inc. (collectively, "Pfizer"), alleging that Pfizer's sale of its COX-2 inhibitors Celebrex® and Bextra® for treatment of inflammation infringed the '850 patent,[2] and seeking injunctive and monetary relief. Univ. of Rochester, 249 F. Supp. 2d at 220. In May 2002, Pfizer moved for summary judgment of invalidity of the '850 patent for failure to comply with the written description and enablement requirements of 35 U.S.C. §112, ¶ 1. Rochester opposed the motion and filed a cross-motion for summary judgment with respect to the written description issue. Id.

In evaluating the parties' motions, the district court found that, although all of the claims require the use of a "non-steroidal compound that selectively inhibits activity of the PGHS-2 gene," the '850 patent neither discloses any such compound nor provides any suggestion as to how such a compound could be made or otherwise obtained other than by trial-and-error research. Id. at 224-25, 228-29. Indeed, the court found no evidence in the '850 patent that the inventors themselves knew of any such compound at the time their patent application was filed. Id. at 228. Accordingly, the court concluded that the patent's claims are invalid for lack of written description. Id. at 224.

The district court also found that practice of the claimed methods would require "a person of ordinary skill in the art…to engage in undue experimentation, with no assurance of success," and on that basis concluded that the claims are also invalid for lack of enablement. Id. at 232. The court considered, but rejected as conclusory, Rochester's experts'

[2] Celebrex® and Bextra®, generically known as celecoxib and valdecoxib, respectively, were both developed by Searle, which was purchased by Monsanto in 1985. In 2000, Monsanto merged with Pharmacia & Upjohn, Inc. to form Pharmacia Corp. In 2002, Monsanto, sans Searle, was spun off from Pharmacia, and Pharmacia merged with Pfizer in 2003. The combined company has retained the name Pfizer Inc.

opinions that one of skill in the art would have known to start with existing NSAIDs and would have used routine methods to make structural changes to lead compounds to optimize them, citing a general failure to point to any language in the patent supporting those opinions. Id. at 233.

Finding no genuine issue of material fact concerning either written description or enablement, the district court accordingly granted Pfizer's motions for summary judgment of invalidity of the '850 patent for failure to meet the written description and enablement requirements, denied Rochester's cross-motion, and dismissed the complaint. Id. at 235-36.

Rochester now appeals. We have jurisdiction pursuant to 28 U.S.C. §1295(a)(1).

DISCUSSION

Rochester asserts three grounds of error on appeal. First, it argues that the district court erred by granting Pfizer's motion for summary judgment of invalidity for lack of written description. Second, it argues that the court erred by granting Pfizer's motion for summary judgment of invalidity for lack of enablement. Third, Rochester contends that the court erred by denying its cross-motion for summary judgment with regard to written description. Pfizer refutes each of those asserted grounds of error.

Summary judgment is appropriate when there are no genuine issues of material fact and the moving party is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(c); Johns Hopkins Univ. v. Cellpro, Inc., 152 F.3d 1342, 1353 (Fed. Cir. 1998). We review a district court's grant of summary judgment de novo, reapplying the summary judgment standard. Conroy v. Reebok Int'l, 14 F.3d 1570, 1575 (Fed. Cir. 1994). In contrast, "when a district court denies summary judgment, we review that decision with considerable deference to the court," and "will not disturb the trial court's denial…unless we find that the court has indeed abused its discretion in so denying." Suntiger, Inc. v. Scientific Research Funding Group, 189 F.3d 1327, 1333 (Fed. Cir. 1999). Additionally, "[w]hen evaluating a motion for summary judgment, the court views the record evidence through the prism of the evidentiary standard of proof that would pertain at a trial on the merits." Eli Lilly & Co. v. Barr Labs., Inc., 251 F.3d 955, 962 (Fed. Cir.

2001) ("Barr"). In that process, we draw all justifiable inferences in the nonmovant's favor. Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 255 (1986).

An issued patent enjoys a presumption of validity, 35 U.S.C. §282, that can be overcome only through clear and convincing evidence, U.S. Surgical Corp. v. Ethicon, Inc., 103 F.3d 1554, 1563 (Fed. Cir. 1997). Accordingly, a party "seeking to invalidate a patent at summary judgment must submit such clear and convincing evidence of invalidity." Barr, 251 F.3d at 962.

In its first argument, Rochester asserts that the district court effectively—but erroneously—held that a patent claiming a method of obtaining a biological effect in a human by administering a compound cannot, as a matter of law, satisfy the written description requirement without disclosing the identity of any such compound. Indeed, Rochester contends that "no written description requirement exists independent of enablement." In any event, Rochester argues that its patent met the requirements of §112 and is not invalid.[3]

Pfizer responds to Rochester's argument by pointing out that we have "interpreted §112 'as requiring a "written description" of an invention separate from enablement,'" (citing Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 963 (Fed. Cir. 2002)), and that "the many prior precedential decisions" contrary to Rochester's position "cannot be overruled except by an en banc decision." Pfizer also cites Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555 (Fed. Cir. 1991), in which we explained that "[t]he purpose of the written description requirement is broader than to merely explain how to 'make and use' [the invention]," id. at 1563; and Reiffin v. Microsoft Corp., 214 F.3d 1342 (Fed. Cir. 2000), in which we stated that the purpose of the written description requirement is to "ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification," id. at 1345. Pfizer asserts that a patent fails to satisfy the written description requirement if it claims a method of achieving a biological effect, but discloses no compounds that can accomplish that

[3] Rochester is supported by amici curiae the Regents of the University of California, the University of Texas Southwestern Medical Center at Dallas, and the University of Texas M.D. Anderson Cancer Center, which make essentially the same points.

result. It maintains that the district court correctly invalidated Rochester's '850 patent.[4]

We agree with Pfizer that our precedent recognizes a written description requirement and that the '850 patent does not satisfy that requirement. As in any case involving statutory interpretation, we begin with the language of the statute itself. Consumer Prod. Safety Comm'n v. GTE Sylvania, Inc., 447 U.S. 102, 108 (1980). Section 112 provides, in relevant part, that:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. §112, ¶ 1 (2000). Three separate requirements are contained in that provision: (1) "[t]he specification shall contain a written description of the invention"; (2) "[t]he specification shall contain a written description…of the manner and process of making and using it [i.e., the invention] in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same"; and (3) "[t]he specification…shall set forth the best mode contemplated by the inventor of carrying out his invention."

In common parlance, as well as in our and our predecessor court's case law, those three requirements are referred to as the "written description requirement," the "enablement requirement," and the "best mode requirement," respectively. *See* In re Moore, 439 F.2d 1232, 1235 (CCPA 1971) ("Robert Moore") ("This first paragraph analysis in itself contains several inquiries. Considering the language of the statute, it should be evident that these inquiries include determining whether the subject matter defined in the claims is described in the specification, whether the

[4] Pfizer is supported by amicus curiae Eli Lilly & Co., which makes similar arguments.

specification disclosure as a whole is such as to enable one skilled in the art to make and use the claimed invention, and whether the best mode contemplated by the inventor of carrying out that invention is set forth."). The United States Supreme Court also recently acknowledged written description as a statutory requirement distinct not only from the best mode requirement, but also from enablement. *See* Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S. 722, 736 (2002) ("[A] number of statutory requirements must be satisfied before a patent can issue. The claimed subject matter must be useful, novel, and not obvious. 35 U.S.C. §§101-1 03 (1994 ed. and Supp. V). In addition, the patent application must describe, enable, and set forth the best mode of carrying out the invention. §112 (1994 ed.). These latter requirements must be satisfied before issuance of the patent, for exclusive patent rights are given in exchange for disclosing the invention to the public." (emphasis added)).

Although there is often significant overlap between the three requirements, they are nonetheless independent of each other. In re Alton, 76 F.3d 1168, 1172 (Fed. Cir. 1996). Thus, an invention may be described without an enabling disclosure of how to make and use it. A description of a chemical compound without a description of how to make and use it, unless within the skill of one of ordinary skill in the art, is an example. Moreover, an invention may be enabled even though it has not been described. *See*, *e.g.*, In re DiLeone, 436 F.2d 1404, 1405 (CCPA 1971) ("[I]t is possible for a specification to enable the practice of an invention as broadly as it is claimed, and still not describe that invention."). Such can occur when enablement of a closely related invention A that is both described and enabled would similarly enable an invention B if B were described. A specification can likewise describe an invention without enabling the practice of the full breadth of its claims. Finally, still further disclosure might be necessary to satisfy the best mode requirement if otherwise only an inferior mode would be disclosed. Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1535 (Fed. Cir. 1987).

The "written description" requirement serves a teaching function, as a "quid pro quo" in which the public is given "meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time." Enzo, 323 F.3d at 970. Rochester argues, however, that

this teaching, or "public notice," function,[5] although "virtually unchanged since the 1793 Patent Act," in fact "became redundant with the advent of claims in 1870." We disagree. Statutory language does not become redundant unless repealed by Congress, in which case it no longer exists.

In addition, and most significantly, our precedent clearly recognizes a separate written description requirement. In re Ruschig, 379 F.2d 990 (CCPA 1967), our predecessor court affirmed a rejection under 35 U.S.C. §112 of a claim that was added to a patent application during prosecution to provoke an interference. That application had originally included a claim directed to a genus of chemical compounds, all having a central benzenesulphonylurea structure and two variable substituents attached at specified sites on that structure. Id. at 994. As a result of the way in which those substituents were defined in the claim, the genus defined by the claim included thousands of compounds, corresponding to all the possible permutations of the substituents. Id. at 993-94. The added claim, in contrast, was directed to a single member of that genus, N-(p-chlorobenzenesulfonyl)-N-propylurea. Id. at 991. Although that compound was within the literal scope of the originally filed claim, it was never "named or otherwise exemplified" in the appellants' original patent application. Id. at 992. The examiner rejected the added claim on the basis that the specific compound was not adequately supported by the specification as filed. Id.

The Patent Office Board of Appeals, and subsequently the Court of Customs and Patent Appeals, affirmed that rejection. In reaching its decision, the court observed that the claimed compound was not described in the specification and would not "convey clearly to those skilled in the art, to whom it is addressed, in any way, the information that appellants invented that specific compound." Id. at 996. It did not teach the specific compound. Although the appellants had argued that the rejection was improper because one skilled in the art would be enabled by the specification to make the specific compound, the court explained that it was

[5] We and the Supreme Court have frequently used the term "public notice" in connection with claims and discussion of the doctrine of equivalents, the point being that the public is entitled to notice of what the inventor has claimed and the Patent and Trademark Office has agreed should be the subject of a patent's limited right to exclude. However, while the role of the claims is to give public notice of the subject matter that is protected, the role of the specification is to teach, both what the invention is (written description) and how to make and use it (enablement).

"doubt[ful] that the rejection [was] truly based on section 112, at least on the parts relied on by appellants [i.e., the 'language therein about enabling one skilled in the art to make the invention']. If based on section 112, it is on the requirement thereof that 'The specification shall contain a written description of the invention.'" Id. at 995-96.

While it is true that this court and its predecessor have repeatedly held that claimed subject matter "need not be described in haec verba" in the specification to satisfy the written description requirement, *e.g.*, In re Smith, 481 F.2d 910, 914 (CCPA 1973), it is also true that the requirement must still be met in some way so as to "describe the claimed invention so that one skilled in the art can recognize what is claimed." Enzo, 323 F.3d at 968. We have further explained that:

> [T]he appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement…A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its function of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice. [Regents of the Univ. of Cal. v.] Eli Lilly [& Co., Inc.], 119 F.3d [1559,] 1568 [(Fed. Cir. 1997) ("Lilly")]…The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. Id.

Enzo, 323 F.3d at 968. Similarly, for example, in the nineteenth century, use of the word "automobile" would not have sufficed to describe a newly invented automobile; an inventor would need to describe what an automobile is, viz., a chassis, an engine, seats, wheels on axles, etc. Thus, generalized language may not suffice if it does not convey the detailed identity of an invention. In this case, there is no language here, generalized or otherwise, that describes compounds that achieve the claimed effect.

Rochester is also factually incorrect in its assertion that a written description requirement separate from the enablement requirement was not recognized

prior to Ruschig in 1967. For example, in Jepson v. Coleman, 314 F.2d 533 (CCPA 1963), our predecessor court explicitly rejected the notion that an enabling disclosure necessarily satisfies the written description requirement: "It is not a question whether one skilled in the art might be able to construct the patentee's device from the teachings of the disclosure of the application. Rather, it is a question whether the application necessarily discloses that particular device." Id. at 536. Still earlier, that court affirmed a decision of the Board of Appeals of the Patent Office affirming the rejection of an applicant's claims on the basis that those claims were "broader than the disclosure in appellant's application and…were properly rejected for that reason." In re Moore, 155 F.2d 379, 382 (CCPA 1946) ("Wm. Moore"). The court stated that it "is well settled that claims in an application which are broader than the applicant's disclosure are not allowable." Id.

Similarly, in 1962 the court affirmed the Board's rejection of the original claims in a patent application, based on, inter alia, the rejected claims' "fail[ure] to meet the requirements of 35 U.S.C. §112 in that they are broader than the invention described in the written description thereof as set forth in the specification." In re Sus, 306 F.2d 494, 497 (CCPA 1962). In that case, the court specifically identified the "pertinent portions of 35 U.S.C. §112 to be here considered" as the following: ""The specification shall contain a written description of the invention * * *. The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."" Id. at 494 n.1 (ellipsis in original). According to the court, "one skilled in this art would not be taught by the written description of the invention in the specification that any 'aryl or substituted aryl radical' would be suitable for the purposes of the invention but rather that only certain aryl radicals and certain specifically substituted aryl radicals would be suitable for such purposes." Id. at 504.[6] The issues in Jepson, Wm. Moore, and Sus were clearly not confined to a determination whether the enablement requirement was met. They were independent written description issues.

[6] In Sus, the claims at issue were rejected by the patent examiner under 35 U.S.C. §112, ¶ 2. However, the Court of Customs and Patent Appeals pointed out in subsequent cases that that rejection was "more properly considered under the first paragraph of that section." In re Robins, 429 F.2d 452, 457 n. 8 (CCPA 1970).

Rochester's suggestion in its brief that Lilly "compounded Ruschig's error" by "invoking the written description requirement in a case without priority issues" is similarly deficient. Neither Wm. Moore nor Sus, for example, involved any priority issues. Moreover, even if the court had never had occasion to apply the written description requirement to original claims prior to the 1987 Lilly decision, that requirement was nonetheless always present. As explained in Enzo:

> It is said that applying the written description requirement outside of the priority context was novel until several years ago. Maybe so, maybe not; certainly such a holding was not precluded by statute or precedent. New interpretations of old statutes in light of new fact situations occur all the time…
>
> …As for the lack of earlier cases on this issue, it regularly happens in adjudication that issues do not arise until counsel raise them, and, when that occurs, courts are then required to decide them.

323 F.3d at 971-72 (Lourie, J., concurring in Denial of Petition for Rehearing En Banc). In any event, the basic requirement of a written description of an invention exists whether a question of priority has arisen or not. The statute does not limit the requirement to cases in which a priority question arises.

Indeed, as early as 1822 the Supreme Court recognized the existence of separate written description and enablement requirements:

> [T]he patent act requires…that the party [i.e., the inventor] "shall deliver a written description of his invention, in such full, clear, and exact terms, as to distinguish the same from all other things before know[n], and to enable any person skilled in the art or science, &c. &c. to make, compound, and use the same." The specification, then has two objects: one is to make known the manner of constructing the machine (if the invention is of a machine) so as to enable artizans [sic] to make and use it, and thus to give the public

> the full benefit of the discovery after the expiration of the patent…The other object of the specification is, to put the public in possession of what the party claims as his own invention, so as to ascertain if he claim anything that is in common use, or is already known, and to guard against prejudice or injury from the use of an invention which the party may otherwise innocently suppose not to be patented.

Evans v. Eaton, 20 U.S. (7 Wheat.) 356, 433-34 (1822). The Patent Act of 1793, 1 Stat. 318, which was in force at the time Evans was decided, required, in relevant part, that every inventor "deliver a written description of his invention, and of the manner of using, or process of compounding the same, in such full, clear, and exact terms, as to distinguish the same from all other things before known, and to enable any person skilled in the art or science…to make, compound, and use the same…" In re Barker, 559 F.2d 588, 592 (CCPA 1977) (ellipses in original). Although the patent statutes have been extensively revised since 1822, most notably in the addition of the requirement of claims, the language of the present statute is not very different in its articulation of the written description requirement. Id. at 592-94.

Rochester also argues that Fiers v. Revel, 984 F.2d 1164 (Fed. Cir. 1993), Lilly, and Enzo are all distinguishable because they were limited to DNA-based inventions. Rochester asserts that undisputed evidence shows that, based on the '850 patent's teachings, skilled artisans would be able to recognize COX-2-selective inhibitors.

We agree with Rochester that Fiers, Lilly, and Enzo differ from this case in that they all related to genetic material whereas this case does not, but we find that distinction to be unhelpful to Rochester's position. It is irrelevant; the statute applies to all types of inventions. We see no reason for the rule to be any different when non-genetic materials are at issue; in fact, where there might be some basis for finding a written description requirement to be satisfied in a genetics case based on the complementariness of a nucleic acid and, for example, a protein, that correspondence might be less clear in a non-genetic situation. In Enzo, we explained that functional descriptions of genetic material can, in some cases, meet the written description

requirement if those functional characteristics are "coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." 323 F.3d at 964 (quoting from the PTO's Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106). DNA and RNA are each made up of just four building blocks that interact with each other in a highly predictable manner. Each of those building blocks, or "nucleotides," is characterized by a unique "base": In the case of DNA, the four nucleotides include the bases adenine, thymine, cytosine, and guanine; RNA also includes adenine, cytosine, and guanine, but contains the base uracil in place of thymine. Adenine on one strand of DNA binds, or "hybridizes," to thymine on the other; in RNA, adenine binds to uracil; and in either DNA or RNA, cytosine binds to guanine. Given the sequence of a single strand of DNA or RNA, it may therefore have become a routine matter to envision the precise sequence of a "complementary" strand that will bind to it. Therefore, disclosure of a DNA sequence might support a claim to the complementary molecules that can hybridize to it.

The same is not necessarily true in the chemical arts more generally. Even with the three-dimensional structures of enzymes such as COX-1 and COX-2 in hand, it may even now not be within the ordinary skill in the art to predict what compounds might bind to and inhibit them, let alone have been within the purview of one of ordinary skill in the art in the 1993-1 995 period in which the applications that led to the '850 patent were filed. Rochester and its experts do not offer any persuasive evidence to the contrary. As the district court pointed out:

> Tellingly,…what plaintiff's experts' [sic] do not say is that one of skill in the art would, from reading the patent, understand what compound or compounds—which, as the patent makes clear, are necessary to practice the claimed method—would be suitable, nor would one know how to find such a compound except through trial and error…Plaintiff's experts opine that a person of ordinary skill in the art would understand from reading the '850 patent what method is claimed, but it is clear from reading the patent that one critical aspect of the method—a

> compound that selectively inhibits PGHS-2 activity—was hypothetical, for it is clear that the inventors had neither possession nor knowledge of such a compound.

Univ. of Rochester, 249 F. Supp. 2d at 229.

Rochester also attempts to distinguish Fiers, Lilly, and Enzo by suggesting that the holdings in those cases were limited to composition of matter claims, whereas the '850 patent is directed to a method. We agree with the district court that that is "a semantic distinction without a difference." Univ. of Rochester, 249 F. Supp. 2d at 228. Regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods. As the district court observed, "[t]he claimed method depends upon finding a compound that selectively inhibits PGHS-2 activity. Without such a compound, it is impossible to practice the claimed method of treatment." Id.

We of course do not mean to suggest that the written description requirement can be satisfied only by providing a description of an actual reduction to practice. Constructive reduction to practice is an established method of disclosure, but the application must nonetheless "describe the claimed subject matter in terms that establish that [the applicant] was in possession of the…claimed invention, including all of the elements and limitations." Hyatt v. Boone, 146 F.3d 1348, 1353 (Fed. Cir. 1998). But *see* Enzo, 323 F.3d at 969 ("Application of the written description requirement, however, is not subsumed by the 'possession' inquiry. A showing of 'possession' is ancillary to the statutory mandate that '[t]he specification shall contain a written description of the invention,' and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the invention."). The specification must teach the invention by describing it.

Rochester also contends that "[t]he patent-in-suit cannot be per se invalid," because written description is a question of fact. Rochester further argues that:

> [C]onsistent with written description's fact-intensive nature, this Court has recognized diverse forms of description, including description primarily (if not entirely) based on functional characteristics. In Union Oil [Co. v. Atlantic Richfield Co., 208 F.3d 989 (Fed. Cir. 2000) ("Unocal")], for example, the Court rejected the argument that the patent-in-suit was invalid because it described claimed gasoline mixtures by their "desired characteristics," rather than by their "exact chemical component[s]."

In response, Pfizer argues that the district court did not apply a per se rule, and that written description of a method of selectively inhibiting the activity of an enzyme by administering a chemical compound is insufficient unless a skilled artisan can recognize the identity of the compound, and the description must convey what the compound is, not just what it does. Pfizer points out that the district court found that the '850 patent does not disclose the structure or physical properties of any of the compounds required to practice the claimed methods, and that the structure of such compounds cannot be deduced from any known structure-function correlation. Pfizer agrees with the district court that the '850 patent discloses nothing more than a hoped-for function for an as-yet-to-be-discovered compound, and a research plan for trying to find it.

We agree with Pfizer that the '850 patent is deficient in failing to adequately describe the claimed invention. First, although compliance with the written description requirement is a question of fact, Vas-Cath, 935 F.2d at 1116, Rochester's argument that a patent may not be held invalid on its face is contrary to our case law. In PIN/NIP, Inc. v. Platte Chemical Co., 304 F.3d 1235 (Fed. Cir. 2002), for example, we held that a patent can be held invalid for failure to meet the written description requirement, based solely on the language of the patent specification. After all, it is in the patent specification where the written description requirement must be met. Similarly, in TurboCare Division of Demag Delaval Turbomachinery Corp. v. General Electric Co., 264 F.3d 1111 (Fed. Cir. 2001), we held that "[n]o reasonable juror could find that [an appellant's] original disclosure was sufficiently detailed to enable one of skill in the art to recognize that [the appellant]

invented what is claimed," and accordingly upheld a grant of summary judgment. Id. at 1119.

Second, it is undisputed that the '850 patent does not disclose any compounds that can be used in its claimed methods. The claimed methods thus cannot be practiced based on the patent's specification, even considering the knowledge of one skilled in the art. No compounds that will perform the claimed method are disclosed, nor has any evidence been shown that such a compound was known. The '850 patent does contain substantial description of the cyclooxygenases, including the nucleotide sequences of coding and promoter regions of the genes that encode human COX-1 and COX-2 and a comparison of those sequences. *See*, *e.g.*, '850 patent, figs. 6A-6B, 10A-1 0D, and 11A-11C. The patent also describes in detail how to make cells that express either COX-1 or COX-2, but not both, id. §5.2, at cols. 8-20, as well as "assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product; and methods of treating diseases characterized by aberrant PGHS-2 activity using such compounds," id. at col. 8, ll. 2-7; *see also* id. §5.6, at cols. 24-25. Such assay methods are in fact claimed in the '479 patent, i.e., Rochester's other patent based on the same disclosure. The '850 patent specification also describes what can be done with any compounds that may potentially be identified through those assays, including formulation into pharmaceuticals, routes of administration, estimation of effective dosage, and suitable dosage forms. Id. §5.8, at cols. 27-34. As pointed out by the district court, however, the '850 patent does not disclose just "which 'peptides, polynucleotides, and small organic molecules' have the desired characteristic of selectively inhibiting PGHS-2." Univ. of Rochester, 249 F. Supp. 2d at 224. Without such disclosure, the claimed methods cannot be said to have been described. As we held in Lilly, "[a]n adequate written description of a DNA…'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." 119 F.3d at 1566 (quoting Fiers, 984 F.2d at 1171). For reasons stated above, that requirement applies just as well to non-DNA (or -RNA) chemical inventions.

Third, Rochester's reliance on Unocal is unavailing. Although we held in that case that a "descri[ption] of the exact chemical component of each

combination that falls within the range claims of the…patent" is not necessary to comply with §112, we explained that the patentee is nonetheless required to provide sufficient description to show one of skill in the art that the inventor possessed the claimed invention at the time of filing. Unocal, 208 F.3d at 997. Evidence was adduced in that case that artisans skilled in petroleum refining were aware of the properties of raw petroleum sources and knew how to mix streams of such sources to achieve a final product with desired characteristics. Accordingly, we held that the written description requirement was satisfied in that case by specifying the ranges of properties of the claimed gasolines, reflecting the way that oil refiners actually formulate gasoline, such that one skilled in the art could recognize what was being claimed. Id. at 992. The present case is not analogous. Rochester did not present any evidence that the ordinarily skilled artisan would be able to identify any compound based on its vague functional description as "a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product."[7]

Rochester also cites In re Edwards, 568 F.2d 1349 (CCPA 1978), and In re Herschler, 591 F.2d 693 (CCPA 1979), in support of its arguments. Those cases are also inapposite. In Edwards, the court held that the written description requirement was satisfied by a specification that described a claimed compound by the process by which it was made, rather than by its structure, because the court found that Edwards' application, "taken as a whole, reasonably leads persons skilled in the art to the [recited reactions] and, concomitantly, to the claimed compound." 568 F.2d at 1354. In marked contrast to the Edwards application, the specification of the '850 patent contains no disclosure of any method for making even a single "non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product." In Herschler, the court found adequate written description support for broad claims to processes for topically administering a physiologically active steroidal agent to a human or animal by concurrently administering the steroidal agent and dimethyl sulfoxide ("DMSO"), even

[7] Indeed, if compounds that selectively inhibit activity of the PGHS-2 gene product had been known in the art, it is difficult to see how the claims of the '850 patent would have satisfied the novelty requirement of 35 U.S.C. §102. After all, the novelty of those claims, if any, would appear to reside in the fact that COX-2-selective inhibitors were previously unknown. The issue of patentability under §102, however, was not decided by the district court, and we do not address it further.

though the specification disclosed only one example of a "physiologically active steroidal agent." Critically, however, there was no question in that case that, unlike "non-steroidal compound[s] that selectively inhibit[ ] activity of the PGHS-2 gene product," numerous physiologically active steroidal agents were known to those of ordinary skill in the art. As the court there noted, [w]ere this application drawn to novel 'steroidal agents,' a different question would be posed." 591 F.2d at 701. The novelty in that invention was the DMSO solvent, not the steroids.

Although cases such as Unocal, Enzo, Edwards, and Herschler demonstrate that patent applicants have some flexibility in the "mode selected for compliance" with the written description requirement, neither those cases nor any other cases cited by Rochester eliminate the requirement that the patent specification set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed. The only claims that appear to be supported by the specification are claims to assay methods, but those claims were already issued in the '479 patent.

Rochester argues that "[t]he appealed decision vitiates universities' ability to bring pioneering innovations to the public," and that:

> Congress has determined that licensing of academia's inventions to industry is the best way to bring groundbreaking inventions to the public. *See* 35 U.S.C. §200. By vesting in universities the patent rights to their federally funded research, the Bayh-Dole Act of 1980 encouraged "private industry to utilize government funded inventions through the commitment of the risk capital necessary to develop such inventions to the point of commercial application." H.R. Rep. No. 96-1 307, pt. 1, at 3 (1980).

Further, amici the University of California and the University of Texas assert that "[t]his Court's decision will have a significant impact on the continuing viability of technology transfer programs at universities and on the equitable allocation of intellectual property rights between universities and the private sector."

That argument is unsound. The Bayh-Dole Act was intended to enable universities to profit from their federally-funded research. It was not intended to relax the statutory requirements for patentability. As pointed out by amicus Eli Lilly, "no connection exists between the Bayh-Dole Act and the legal standards that courts employ to assess patentability. Furthermore, none of the eight policy objectives of the Bayh-Dole Act encourages or condones less stringent application of the patent laws to universities than to other entities. *See* 35 U.S.C. §200."[8]

In sum, because the '850 patent does not provide any guidance that would steer the skilled practitioner toward compounds that can be used to carry out the claimed methods—an essential element of every claim of that patent—and has not provided evidence that any such compounds were otherwise within the knowledge of a person of ordinary skill in the art[9] at the relevant time, Rochester has failed to raise any question of material fact whether the named inventors disclosed the claimed invention. Accordingly, we affirm the district court's grant of Pfizer's motion for summary judgment.

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[8] Section 200, entitled "Policy and objective," provides that:

It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise without unduly encumbering future research and discovery; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.

35 U.S.C. §200 (2000).

[9] In O'Reilly v. Morse, 56 U.S. 62 (1853), the Supreme Court stated "[Morse] claims an exclusive right to use a manner and process which he has not described and indeed had not invented, and therefore could not describe when he obtained his patent. The court is of the opinion that the claim is too broad, and not warranted by law." Id. at 113. Likewise, Rochester has claimed a method that could not be adequately described at the time its application was filed. As we explained in Fiers, "one cannot describe what one has not conceived." 984 F.2d at 22 1171.

In view of our affirmance of the district court's decision on the written description ground, we consider the enablement issue to be moot and will not discuss it further.

With respect to the third asserted error, relating to the denial of Rochester's cross-motion for summary judgment, Rochester argues that because Pfizer adduced no evidence, other than the patent in suit, to support its written description defense, Rochester was entitled to summary judgment on that issue. Rochester contends that, because all issued patents are presumed to be valid, the district court was wrong to conclude that the '850 patent constitutes clear and convincing proof of its own invalidity.

Pfizer responds by arguing that there is no issue of material fact in dispute and that the '850 patent is invalid as a matter of law. Pfizer argues further that the district court properly found that Rochester's experts' declarations did not raise any issue of material fact, because they focused only on the use and function of the screening assay, rather than on the disclosure in the specification of a suitable compound. According to Pfizer, common sense dictates that one has not described a method of treating a disease with a drug if he has not disclosed any such drug or even if one exists, and there is accordingly no need for any evidence of invalidity beyond the '850 patent itself.

Although section 282 of the Patent Act places the burden of proof on the party seeking to invalidate a patent, it does not foreclose the possibility of that party demonstrating that the patent in suit proves its own invalidity, *see*, *e.g.*, PIN/NIP, 304 F.3d at 1235; TurboCare, 264 F.3d at 1111, and as detailed in section I above, we conclude that the '850 patent clearly and convincingly does just that. The patent's claims all require a COX-2-selective compound, but no COX-2-selective compound is disclosed in the patent, and it is undisputed that there was no pre-existing awareness in the art of any compound having COX-2-selective activity. Accordingly,

we hold that the district court did not abuse its discretion by denying Rochester's cross-motion for summary judgment.[10]

CONCLUSION

Because the court did not err in holding the '850 patent to be invalid for failing to comply with the written description requirement of 35 U.S.C. §112, ¶ 1, and in granting summary judgment in favor of Pfizer on that ground, the decision of the district court is

AFFIRMED.

Courtesy of Patrick H. Higgins, Buchanan Ingersoll & Rooney PC

[10] Although we have treated the issue in this case as one of written description, as it was argued and decided below, underlying that question is the fundamental issue whether Rochester actually invented the subject matter it claimed in the '850 patent as required by 35 U.S.C. §102(f). As the Supreme Court has cautioned, "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Brenner v. Manson, 383 U.S. 519, 536 (1966). Here the patentee has done no more than invent a search method, i.e., a method of identifying a selective COX-2 inhibitor, much less did it invent, as claimed in the '850 patent, a method of using any such compound to selectively inhibit COX-2 in humans. Under these circumstances, it might appear that the patentee also failed to satisfy the requirements of section 102(f).

APPENDIX E

MERCK KGAA, PETITIONER V. INTEGRA LIFE SCIENCES I LTD., ET AL.

OPINION OF THE COURT

NOTICE: This opinion is subject to formal revision before publication in the preliminary print of the United States Reports. Readers are requested to notify the Reporter of Decisions, Supreme Court of the United States, Washington, D.C. 20543, of any typographical or other formal errors, in order that corrections be made before the preliminary print goes to press.

SUPREME COURT OF THE UNITED STATES

No. 03-1237

MERCK KGAA, PETITIONER v.
INTEGRA LIFE SCIENCES I, LTD., ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

[June 13, 2005]

JUSTICE SCALIA delivered the opinion of the Court.

This case presents the question whether uses of patented inventions in preclinical research, the results of which are not ultimately included in a submission to the Food and Drug Administration (FDA), are exempted from infringement by 35 U. S. C. ß271(e)(1).

I

It is generally an act of patent infringement to mak[e], us[e], offe[r] to sell, or sel[l] any patented invention…during the term of the patent therefore ß271(a). In 1984, Congress enacted an exemption to this general rule, *see*

Drug Price Competition and Patent Term Restoration Act of 1984, ß202, 98 Stat. 1585, as amended, 35 U. S. C. ß271(e)(1), which provides:

> It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) . . .) 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…

The Federal Food, Drug, and Cosmetic Act (FDCA), ch. 675, 52 Stat. 1040, as amended, 21 U. S. C. ß301 et seq., is "a Federal law which regulates the manufacture, use, or sale of drugs. *See* 21 U. S. C. ß355(a); Eli Lilly & Co. v. Medtronic, Inc., 496 U. S. 661, 665-666, 674 (1990). Under the FDCA, a drug-maker must submit research data to the FDA at two general stages of new-drug development.[11] First, a drug-maker must gain authorization to conduct clinical trials (tests on humans) by submitting an investigational new drug application (IND). *See* 21 U. S. C. ß355(i); 21 CFRß 312.1 et seq. (2005).[12] The IND must describe "preclinical tests (including tests on animals) of [the] drug adequate to justify the proposed clinical testing." 21 U. S. C. ß355(i)(1)(A); *see* 21 CFR ßß312.23(a)(5) and (a)(8) (specifying necessary information from preclinical tests). Second, to obtain authorization to market a new drug, a drug-maker must submit a new drug application (NDA), containing "full reports of investigations which have been made to show whether or not [the] drug is safe for use and whether [the] drug is effective in use. 21 U. S. C. ß355(b)(1). Pursuant to FDA

[11] Drugmakers that desire to market a generic drug (a drug containing the same active ingredients as a drug already approved for the market) may file an abbreviated new drug application (ANDA) with the FDA. *See* 21 U. S. C. ß355(j). The sponsor of a generic drug does not have to make an independent showing that the drug is safe and effective, either in preclinical or clinical studies. *See* ß355(j)(2)(A). It need only show that the drug includes the same active ingredients as, and is bioequivalent to, the drug that it is mimicking. *See* ßß355(j)(2)(A)(ii) and (iv); ß355(j)(8)(B).

[12] We cite the current versions of federal statutes and regulations. The provisions cited are materially unchanged since the period of petitioner's alleged infringement.

regulations, the NDA must include all clinical studies, as well as preclinical studies related to a drug's efficacy, toxicity, and pharmacological properties. *See* 21 CFR ßß314.50(d)(2) (pre-clinical studies) and (d)(5) (clinical studies).

II A

Respondents Integra Lifesciences I, Ltd., and the Burn-ham Institute, own five patents related to the tripeptide sequence Arg-Gly-Asp, known in single-letter notation as the "RGD peptide." U. S. Patent Nos. 4,988,621, 4,792,525, 5,695,997, 4,879,237, and 4,789,734, Supp. App. SA11-SA19. The RGD peptide promotes cell adhesion by attaching to αvβ3 integrins, receptors commonly located on the outer surface of certain endothelial cells. 331 F. 3d 860, 862-863 (CA Fed. 2003).

Beginning in 1988, petitioner Merck KGAA provided funding for angiogenesis research conducted by Dr. David Cheresh at the Scripps Research Institute (Scripps). Telios Pharmaceuticals, et al. v. Merck KGaA, et al., Case No. 96-CV-1307 (SD Cal., Sept. 9, 1997), App. 30a. Angiogenesis is the process by which new blood vessels sprout from existing vessels; it plays a critical role in many diseases, including solid tumor cancers, diabetic retinopathy, and rheumatoid arthritis. 331 F. 3d, at 863. In the course of his research, Dr. Cheresh discovered that it was possible to inhibit angiogenesis by blocking the αvβ3 integrins on proliferating endothelial cells. Ibid. In 1994, Dr. Cheresh succeeded in reversing tumor growth in chicken embryos, first using a monoclonal antibody (LM609) he developed himself and later using a cyclic RGD peptide (EMD 66203) provided by petitioner.[13] App. 190a. Dr. Cheresh's discoveries were announced in leading medical journals and received attention in the general media. *See* Altman, Scientists Report Finding a Way to Shrink Tumors, N. Y. Times, Dec. 30, 1994, p. A1; Brooks, et al., Integrin αvβ3 Antagonists Promote Tumor Regression by Inducing Apoptosis of Angiogenic Blood Vessels, 79 Cell 1157 (Dec. 30, 1994); Brooks, Clark, and Cheresh, Requirement of Vascular Integrin αvβ3 for Angiogenesis, 264 Science 569 (Apr. 22, 1994).

[13] In the proceedings below, the Court of Appeals held that respondents' patents covered the cyclic RGD peptides developed by petitioner. 331 F. 3d 860, 869 (CA Fed. 2003). Petitioner does not contest that ruling here.

With petitioner's agreement to fund research at Scripps due to expire in July 1995, Dr. Cheresh submitted a de-tailed proposal for expanded collaboration between Scripps and petitioner on February 1, 1995. App. 95-107a. The proposal set forth a 3-year timetable in which to develop "integrin antagonists as angiogenesis inhibitors," id., at 105a, beginning with in vitro and in vivo testing of RGD peptides at Scripps in year one and culminating with the submission of an IND to the FDA in year three, id., at 106-107a. Petitioner agreed to the material terms of the proposal on February 20, 1995, id., at 124-125a, and on April 13, 1995, pledged $6 million over three years to fund research at Scripps, id., at 126a. Petitioner's April 13 letter specified that Scripps would be responsible for testing RGD peptides produced by petitioner as potential drug candidates but that, once a primary candidate for clinical testing was in "the pipeline," petitioner would perform the toxicology tests necessary for FDA approval to proceed to clinical trials. Id., at 127a; *see* 21 CFR ß312.2 3(a)(8)(iii) (2005) (requirement that "non-clinical laboratory study" include a certification that it was per-formed under good laboratory practices); *see also* ß58.3(d) (2004) (defining "[n]on-clinical laboratory study"). Scripps and petitioner concluded an agreement of continued collaboration in September 1995. Case No. 96-CV-1307, App. 31a.

Pursuant to the agreement, Dr. Cheresh directed in vitro and in vivo experiments on RGD peptides provided by petitioner from 1995 to 1998. These experiments focused on EMD 66203 and two closely related derivatives, EMD 85189 and EMD 121974, and were designed to evaluate the suitability of each of the peptides as potential drug candidates. 331 F. 3d, at 863. Accordingly, the tests measured the efficacy, specificity, and toxicity of the particular peptides as angiogenesis inhibitors, and evaluated their mechanism of action and pharmacokinetics in animals. Ibid. Based on the test results, Scripps decided in 1997 that EMD 121974 was the most promising candidate for testing in humans. Ibid. Over the same period, Scripps performed similar tests on LM609, a monoclonal antibody developed by Dr. Cheresh.[14] App. 277a, 285-298a. Scripps also conducted more basic research

[14] Scripps licensed the patent for the monoclonal antibody to Ixsys, a California biotechnology company. App. 271a. Based on research conducted at Scripps and at Ixsys in consultation with Dr. Cheresh, an IND application for a humanized version of the antibody called Vitaxin was filed with the FDA on December 30, 1996. Id., at 271-274a, 404a. In addition to toxicology tests, the application included information from Dr. Cheresh's in vitro and in vivo experiments related to the antibody's mechanism of action and efficacy as an inhibitor of angiogenesis. Id., at 399-404a. Ixsys began clinical testing of the antibody as an angiogenesis inhibitor in February 1997. Id., at 304a.

on organic mimetics designed to block αvβ3 integrins in a manner similar to the RGD peptides, id., at 223-224a; it appears that Scripps used the RGD peptides in these tests as "positive controls" against which to measure the efficacy of the mimetics, id., at 188a.

In November 1996, petitioner initiated a formal project to guide one of its RGD peptides through the regulatory approval process in the United States and Europe. Id., at 129a. Petitioner originally directed its efforts at EMD 85189, but switched focus in April 1997 to EMD 121974. Case No. 96-CV-1307, App. 31a. Petitioner subsequently discussed EMD 121974 with officials at the FDA. Id., at 397a. In October 1998, petitioner shared its research on RGD peptides with the National Cancer Institute (NCI), which agreed to sponsor clinical trials. Id., at 214-217a. Although the fact was excluded from evidence at trial, the lower court's opinion reflects that NCI filed an IND for EMD 121974 in 1998. 331 F. 3d, at 874 (Newman, J., dissenting).

B

On July 18, 1996, respondents filed a patent-infringement suit against petitioner, Scripps, and Dr. Cheresh in the District Court for the Southern District of California. Respondents' complaint alleged that petitioner willfully infringed and induced others to infringe respondents' patents by supplying the RGD peptide to Scripps, and that Dr. Cheresh and Scripps infringed the same patents by using the RGD peptide in experiments related to angiogenesis. Respondents sought damages from petitioner and a declaratory judgment against Dr. Cheresh and Scripps. Id., at 863. Petitioner answered that its actions involving the RGD peptides did not infringe respondents' patents, and that in any event they were protected by the common-law research exemption and 35 U. S. C. ß271(e)(1). 331 F. 3d, at 863.

At the conclusion of trial, the District Court held that, with one exception, petitioner's pre-1995 actions related to the RGD peptides were protected by the common-law research exemption, but that a question of fact remained as to whether petitioner's use of the RGD peptides after 1995 fell within the ß271(e)(1) safe harbor. With the consent of the parties, the

District Court gave the following instruction regarding the ß271(e)(1) exemption:

> To prevail on this defense, [petitioner] must prove by a preponderance of the evidence that it would be objectively reasonable for a party in [petitioner's] and Scripps' situation to believe that there was a decent prospect that the accused activities would contribute, relatively directly, to the generation of the kinds of in-formation that are likely to be relevant in the processes by which the FDA would decide whether to approve the product in question.
>
> Each of the accused activities must be evaluated separately to determine whether the exemption applies.
>
> Petitioner] does not need to show that the information gathered from a particular activity was actually submitted to the FDA. App. 57a.

The jury found that petitioner, Dr. Cheresh, and Scripps infringed respondents' patents and that petitioner had failed to show that its activities were protected by ß271(e)(1). It awarded damages of $15 million.

In response to post-trial motions, the District Court dismissed respondents' suit against Dr. Cheresh and Scripps, but affirmed the jury's damage award as sup-ported by substantial evidence, Civ. Action No. 961307 JMF (SD Cal. Mar. 26, 2001), App. to Pet. for Cert. 52a, and denied petitioner's motion for judgment as a matter of law, Civ. Action No. 96CV-1307 JMF (SD Cal., Mar. 6, 2001), App. to Pet. for Cert. 50a. With respect to the last, the District Court explained that the evidence was sufficient to show that "any connection between the infringing Scripps experiments and FDA review was insufficiently direct to qualify for the [ß271(e)(1) exemption]." Id., at 49a.

A divided panel of the Court of Appeals for the Federal Circuit affirmed in part, and reversed in part. The panel majority affirmed the denial of judgment as a matter of law to petitioner, on the ground that ß271(e)(1)'s safe harbor did not apply because "the Scripps work sponsored by

[petitioner] was not clinical testing to supply information to the FDA, but only general biomedical research to identify new pharmaceutical compounds." 331 F. 3d, at 866. It reversed the District Court's refusal to modify the damages award, and remanded for further proceedings.[15] Id., at 872. Judge Newman dissented on both points. *See* id., at 874, 877. The panel unanimously affirmed the District Court's ruling that respondents' patents covered the cyclic RGD peptides developed by petitioner. Id., at 868-869; id., at 873, n. 7 (Newman, J., dissenting). We granted certiorari to review the Court of Appeals' construction of ß271(e)(1). 543 U. S. _ (2004).

III

As described earlier, 35 U. S. C. ß271(e)(1) provides that "[i]t shall not be an act of infringement to…use…or import into the United States a patented invention…solely for uses reasonably related to the development and submission of information under a Federal law which regulates the…use…of drugs." Though the contours of this provision are not exact in every respect, the statutory text makes clear that it provides a wide berth for the use of patented drugs in activities related to the federal regulatory process.

As an initial matter, we think it apparent from the statutory text that ß271(e)(1)'s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of any information under the FDCA. Cf. Eli Lilly, 496 U. S., at 665-669 (declining to limit ß271(e)(1)'s exemption from infringement to submissions under particular statutory provisions that regulate drugs). This necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process. There is simply no room in the statute for excluding certain information from the exemption on the basis of the phase of research in which it is developed or the particular submission in which it could be included.[16]

[15] On remand, the District Court reduced the damages award to $6.375 million. Civ. Action No. CV.96 CV 1307-B(AJB), 2004 WL 2284001, *1 (SD Cal., Sept. 7, 2004).

[16] Although the Court of Appeals' opinion suggests in places that ß271(e)(1)'s exemption from infringement is limited to research con-ducted in clinical trials, *see* 331 F. 3d, at 866, we do not understand it to have adopted that position. The Court of Appeals recognized that information included in an IND would come within ß271(e)(1)'s safe harbor. Ibid. Because an IND must be filed before clinical trials may begin, such information would necessarily be developed in preclinical studies.

Respondents concede the breadth of ß271(e)(1) in this regard, but argue that the only preclinical data of interest to the FDA is that which pertains to the safety of the drug in humans. In respondents' view, preclinical studies related to a drug's efficacy, mechanism of action, pharmacokinetics, and pharmacology are not reasonably included in an IND or an NDA, and are therefore outside the scope of the exemption. We do not understand the FDA's interest in information gathered in preclinical studies to be so constrained. To be sure, its regulations provide that the agency's "primary objectives in reviewing an IND are…to assure the safety and rights of subjects," 21 CFR 312.22(a) (2005), but it does not follow that the FDA is not interested in reviewing information related to other characteristics of a drug. To the contrary, the FDA requires that applicants include in an IND summaries of the pharmacological, toxicological, pharmacokinetic, and biological qualities of the drug in animals. *See* ß312.23(a)(5); Department of Health and Human Services, Guidance for Industry, Good Clinical Practice: Consolidated Guidance 45 (Apr. 1996) ("The results of all relevant non-clinical pharmacology, toxicology, pharmacokinetic, and investigational product metabolism studies should be provided in summary form. This summary should address the methodology used, the results, and a discussion of the relevance of the findings to the investigated therapeutic and the possible unfavorable and unintended effects in humans"). The primary (and, in some cases, only) way in which a drug-maker may obtain such information is through preclinical in vitro and in vivo studies.

Moreover, the FDA does not evaluate the safety of pro-posed clinical experiments in a vacuum; rather, as the statute and regulations reflect, it asks whether the pro-posed clinical trial poses an "unreasonable risk." 21 U. S. C. ß355(i)(3)(B)(i); *see also* 21 CFR ß312.23(a)(8) (2005) (requiring applicants to include pharmacological and toxicological studies that serve as the basis of their conclusion that clinical testing would be "reasonably safe"); ß56.111(a)(2) (2004) (providing that the Institutional Review Boards that oversee clinical trials must consider whether the "[r]isks to subjects are reasonable in relation to anticipated benefits"). This assessment involves a comparison of the risks and the benefits associated with the proposed clinical trials. As the Government's brief, filed on behalf of the FDA, explains, the "FDA might allow clinical testing of a drug that posed significant safety concerns if the drug had a sufficiently positive potential to address a serious disease, although the agency would not accept similar risks

for a drug that was less likely to succeed or that would treat a less serious medical condition." Brief for United States as Amicus Curiae 10. Accordingly, the FDA directs that an IND must provide sufficient information for the investigator to "make his/her own unbiased risk-benefit assessment of the appropriateness of the proposed trial." Guidance for Industry, supra, at 43. Such information necessarily includes preclinical studies of a drug's efficacy in achieving particular results.

Respondents contend that, even accepting that the FDA is interested in preclinical research concerning drug characteristics other than safety, the experiments in question here are necessarily disqualified because they were not conducted in conformity with the FDA's good laboratory practices regulations. This argument fails for at least two reasons. First, the FDA's requirement that preclinical studies be conducted under "good laboratory practices" applies only to experiments on drugs "to determine their safety," 21 CFR ß58.3(d). *See* 21 CFR ß58.1(a); ß312.23(a)(8)(iii) (2005) (only "non-clinical laboratory study subject to the good laboratory practice regulations under part 58" must certify compliance with good laboratory practice regulations). The good laboratory practice regulations do not apply to preclinical studies of a drug's efficacy, mechanism of action, pharmacology, or pharmacokinetics. Second, FDA regulations do not provide that even safety-related experiments not conducted in compliance with good laboratory practices regulations are not suitable for submission in an IND. Rather, such studies must include "a brief statement of the reason for the noncompliance." Ibid.

The Court of Appeals' conclusion that ß271(e)(1) did not protect petitioner's provision of the patented RGD pep-tides for research at Scripps appeared to rest on two somewhat related propositions. First, the court credited the fact that the "Scripps-Merck experiments did not supply information for submission to the [FDA], but in-stead identified the best drug candidate to subject to future clinical testing under the FDA processes." 331 F. 3d, at 865; *see also* id., at 866 (similar). The court explained:

> "The FDA has no interest in the hunt for drugs that may or may not later undergo clinical testing for FDA approval. For instance, the FDA does not require in-formation

> about drugs other than the compound featured in an [IND] application. Thus, the Scripps work sponsored by [petitioner] was not solely for uses reasonably related to' clinical testing for FDA." Ibid.

Second, the court concluded that the exemption "does not globally embrace all experimental activity that at some point, however attenuated, may lead to an FDA approval process." Id., at 867.[17]

We do not quibble with the latter statement. Basic scientific research on a particular compound, performed without the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce, is surely not "reasonably related to the development and submission of information" to the FDA. It does not follow from this, however, that ß271(e)(1)'s exemption from infringement categorically excludes either (1) experimentation on drugs that are not ultimately the subject of an FDA submission or (2) use of patented compounds in experiments that are not ultimately submitted to the FDA. Under certain conditions, we think the exemption is sufficiently broad to protect the use of patented compounds in both situations.

As to the first proposition, it disregards the reality that, even at late stages in the development of a new drug, scientific testing is a process of trial and error. In the vast majority of cases, neither the drug-maker nor its scientists have any way of knowing whether an initially promising candidate will prove successful over a battery of experiments. That is the reason they conduct the experiments. Thus, to construe ß271(e)(1), as the Court of Appeals did, not to protect research conducted on patented compounds for which an IND is not ultimately filed is effectively to limit assurance of exemption to the activities necessary to seek approval of a generic drug:

[17] The Court of Appeals also suggested that a limited construction of ß271(e)(1) is necessary to avoid depriving so-called "research tools" of the complete value of their patents. Respondents have never argued the RGD peptides were used at Scripps as research tools, and it is apparent from the record that they were not. *See* 331 F. 3d, at 878 (Newman, J., dissenting) ("Use of an existing tool in one's research is quite different from study of the tool itself"). We therefore need not and do not express a view about whether, or to what extent, ß271(e)(1) exempts from infringement the use of "research tools" in the development of information for the regulatory process.

One can know at the outset that a particular compound will be the subject of an eventual application to the FDA only if the active ingredient in the drug being tested is identical to that in a drug that has already been approved.

The statutory text does not require such a result. Congress did not limit ß271(e)(1)'s safe harbor to the development of information for inclusion in a submission to the FDA; nor did it create an exemption applicable only to the research relevant to filing an ANDA for approval of a generic drug. Rather, it exempted from infringement all uses of patented compounds "reasonably related" to the process of developing information for submission under any federal law regulating the manufacture, use, or distribution of drugs. *See* Eli Lilly, 496 U. S., at 674. We de-cline to read the "reasonable relation" requirement so narrowly as to render ß271(e)(1)'s stated protection of activities leading to FDA approval for all drugs illusory. Properly construed, ß271(e)(1) leaves adequate space for experimentation and failure on the road to regulatory approval: At least where a drug-maker has a reasonable basis for believing that a patented compound may work, through a particular biological process, to produce a particular physiological effect, and uses the compound in research that, if successful, would be appropriate to include in a submission to the FDA, that use is "reasonably related" to the "development and submission of information under…Federal law." ß271(e)(1).

For similar reasons, the use of a patented compound in experiments that are not themselves included in a "submission of information" to the FDA does not, standing alone, render the use infringing. The relationship of the use of a patented compound in a particular experiment to the "development and submission of information" to the FDA does not become more attenuated (or less reasonable) simply because the data from that experiment are left out of the submission that is ultimately passed along to the FDA. Moreover, many of the uncertainties that exist with respect to the selection of a specific drug exist as well with respect to the decision of what research to include in an IND or NDA. As a District Court has observed, "[I]t will not always be clear to parties setting out to seek FDA approval for their new product exactly which kinds of information, and in what quantities, it will take to win that agency's approval." Intermedics, Inc. v. Ventritex, Inc., 775 F. Supp. 1269, 1280 (ND

Cal. 1991), aff'd, 991 F. 2d 808 (CA Fed. 1993). This is especially true at the preclinical stage of drug approval. FDA regulations pro-vide only that "[t]he amount of information on a particular drug that must be submitted in an IND…depends upon such factors as the novelty of the drug, the extent to which it has been studied previously, the known or suspected risks, and the developmental phase of the drug." 21 CFR ß312.22(b). We thus agree with the Government that the use of patented compounds in preclinical studies is protected under ß271(e)(1) as long as there is a reasonable basis for believing that the experiments will produce "the types of information that are relevant to an IND or NDA." Brief of United States as Amicus Curiae 23.

* * *

Before the Court of Appeals, petitioner challenged the sufficiency of the evidence supporting the jury's finding that it failed to show that "all of the accused activities are covered by [ß271(e)(1)]." App. 62a. That court rejected the challenge on the basis of a construction of ß271(e)(1) that was not consistent with the text of that provision or the relevant jury instruction.[18] Thus, the evidence presented at trial has yet to be reviewed under the standards set forth in the jury instruction, which we believe to be consistent with, if less detailed than, the construction of ß271(e)(1) that we adopt today. We decline to undertake a review of the sufficiency of the evidence under a proper construction of ß27 1(e)(1) for the first time here. Accordingly, we vacate the judgment of the Court of Appeals and remand the case for proceedings consistent with this opinion.

It is so ordered.

Courtesy of Patrick H. Higgins, Buchanan Ingersoll & Rooney PC

[18] The relevant jury instruction provided only that there must be a "decent prospect that the accused activities would contribute, relatively directly, to the generation of the kinds of information that are likely to be relevant in the processes by which the FDA would decide whether to approve the product in question." App. 57a. It did not say that, to fall within ß271(e)(1)'s exemption from infringement, the patented compound used in experimentation must be the subject of an eventual application to the FDA. And it expressly rejected the notion that the exemption only included experiments that produced information included in an IND or NDA. Ibid.

APPENDIX F

SCHERING CORPORATION V. GENEVA PHARMACEUTICALS INC. AND NOVARTIS CORPORATION, ET. AL.

02-1540,-1541,-1542,-1543,-1544,-1545,-1546,-1547,-1548,-1549,
03-1021,-1022,-1023,-1025,-1027

SCHERING CORPORATION, Plaintiff-Appellant,

v.

GENEVA PHARMACEUTICALS, INC. and
NOVARTIS CORPORATION,
and
TEVA PHARMACEUTICALS USA, INC.,
and
ANDRX CORPORATION, ANDRX PHARMACEUTICALS LLC,
and ANDRX PHARMACEUTICALS, INC.,
and
MYLAN PHARMACEUTICALS, INC.,
and
WYETH, ESI-LEDERLE, WYETH PHARMACEUTICALS,
and WYETH
CONSUM ER HEALTHCARE
(formerly American Home Products Corporation,
Wyeth-Ayerst Laboratories, and Whitehall Robbins Healthcare),
and
IMPAX LABORATORIES, INC.,
APOTEX, INC. and NOVEX PHARMA,
COPLEY PHARMACEUTICAL, INC.,
and
GENPHARM, INC.,
Defendants-Appellees.

Robert G. Krupka, Kirkland & Ellis LLP, of Los Angeles California, filed a combined petition for panel rehearing and rehearing en banc for plaintiff-appellant. Of counsel on the petition were David P. Swenson, Kirkland & Ellis, of Washington, DC; John M. Desmarais, Peter J. Armenio, Maxine Y. Graham, Monica V. Bhattacharyya, Young J. Park, and Eric W. Dittmann, Kirkland & Ellis, of New York, New York. Also of counsel on the petition were John F. Hoffman and Arthur Mann, Schering Corporation, of Ken ilworth, New Jersey.

Robert D. Bajefsky, Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., of Washington, DC, filed a response to the petition for defendants-appellees Wyeth, ESI¬Lederle, Wyeth Pharmaceuticals and Wyeth Consumer Healthcare (formerly American Home Products Corporation, Wyeth-Ayerst Laboratories, and Whitehall Robbins Healthcare). With him on the response was Barbara R. Rudolph. Of counsel on the response were David A. Manspeizer and Lawrence Alaburda, WYETH, of Madison, New Jersey. On the response was Julie A. Petruzzelli, Venable, LLP, of Washington, DC, for defendant-appellee Impax Laboratories, Inc. Also on the response were Edgar H. Haug, Daniel G. Brown, and Porter F. Fleming, Frommer Lawrence & Haug LLP, of New York, New York; and Robert J. Stickles, Klett Roonery Lieber & Schorling, of Newark, New Jersey, for defendant-appellee Genpharm Inc.; Colin A. Underwood, Proskauer Rose LLP, of New York, New York, for defendants-appellees Andrx Corporation, Andrx Pharmaceuticals LLC, and Andrx Pharmaceuticals, Inc.; E. Anthony Figg, and Joseph A. Hynds, Rothwell, Figg, Ernst & Manbeck, of Washington, DC, for defendant-appellee Mylan Pharmaceuticals, Inc.; and Thomas L. Creel, Frederick H. Rein, and Keith A. Zullow, Goodwin Procter LLP, of New York, New York, for defendants-appellees Teva Pharmaceuticals USA, Inc., and Copley Pharmaceuticals, Inc.

Robert S. Silver and William J. Castillo, Caesar, Rivise, Bernstein, Cohen & Pokotilow, Ltd., of Philadelphia, Pennsylvania for defendants-appellees Apotex, Inc. and Novex Pharma.

Douglass C. Hochstetler, Schiff, Hardin & Waite, of Chicago, Illinois, filed a response to the petition for defendants-appellees Geneva Pharmaceuticals, Inc. and Novartis Corporation. With him on the response

were Patricia J. Thompson and Jo-Anne M. Kokoski. Of counsel on the response was Kevin M. Flowers, Ph.D., Marshall Gerstein & Borun, of Chicago, Illinois.

Appealed from: United States District Court for the District of New Jersey

Chief Judge John W. Bissell

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

02-1540,-1541,-1542,-1543,-1544,-1545,-1546,-1547,-1548,-1549,
03-1021,-1022,-1023,-1025,-1027

SCHERING CORPORATION, Plaintiff-Appellant,

v.

GENEVA PHARMACEUTICALS, INC. and
NOVARTIS CORPORATION,
and
TEVA PHARMACEUTICALS USA, INC.,
and
ANDRX CORPORATION, ANDRX PHARMACEUTICALS LLC,
and ANDRX PHARMACEUTICALS, INC.,
and
MYLAN PHARMACEUTICALS, INC.,
and
WYETH, ESI-LEDERLE, WYETH PHARMACEUTICALS,
and WYETH
CONSUM ER HEALTHCARE
(formerly American Home Products Corporation,
Wyeth-Ayerst Laboratories, and Whitehall Robbins Healthcare),
and
IMPAX LABORATORIES, INC.,
APOTEX, INC. and NOVEX PHARMA,
COPLEY PHARMACEUTICAL, INC.,
and
GENPHARM, INC.,
Defendants-Appellees.

O R D E R

A combined petition for panel rehearing and rehearing en banc was filed by the Appellant, and responses thereto were invited by the court and filed by the Appellees. This petition for panel rehearing was referred to the panel that heard the appeal, and thereafter the petition for rehearing en banc and responses were referred to the circuit judges who are authorized to request a poll whether to rehear the appeal en banc. A poll was requested, taken, and failed.

Upon consideration thereof,

IT IS ORDERED THAT:

(1) The petition for panel rehearing is denied.
(2) The petition for rehearing en banc is denied.

NEWMAN, Circuit Judge, dissents from the denial of rehearing en banc in a separate opinion.

LOURIE, Circuit Judge, dissents from denial of the petition for rehearing en banc in a separate opinion.

GAJARSA, Circuit Judge, would rehear the appeals en banc.

SCHALL, Circuit Judge, did not participate in the vote.

The mandate of the court will issue on November 4, 2003.

ON COMBINED PETITION FOR PANEL REHEARING
AND REHEARING EN BANC

Date: October 28, 2003

FOR THE COURT
Jan Horbaly Clerk

cc: Robert G. Krupka, Esq.
Robert D. Bajefsky, Esq.
Douglass C. Hochstetler, Esq.
Thomas L. Creel, Esq.

E. Anthony Figg, Esq.
Robert S. Silver, Esq.
Edgar H. Haug, Esq.
Julie Ann Petruzzelli, Esq.
Colin A. Underwood, Esq.

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and
GENPHARM, INC.,
Defendants-Appellees.

NEWMAN, Circuit Judge, dissenting from denial of rehearing en banc.

I write to state my concern for the panel's departure from the established law of anticipation. The court holds "anticipated" a novel chemical compound (descarbethoxyloratidine or DCL), a compound not known to

the prior art and that did not previously exist. The Schering inventor discovered it in vivo as a degradation product of loratidine, isolated it, determined its structure, and found its biologic properties. The panel nonetheless holds that this new compound is unpatentable on the ground of "inherent anticipation."

The law is that a product is "anticipated" if it is not new. Conversely, it is not anticipated if it is new. A new product may of course be unpatentable based on obviousness, but it is not subject to unpatentability for lack of novelty. No precedent supports the position that a product whose existence was not previously known and is not in the prior art is always unpatentable on the ground that it existed undiscovered. If the law is to be changed in this direction it must be done en banc.

DISCUSSION

The panel appears to have reached the correct result of no liability for infringement, but for the wrong reason. According to the briefs, the defendants are doing only what was claimed in the expired loratidine patent, not in suit. However, instead of simply ruling that Schering cannot prevent the practice of the expired patent in accordance with its teachings, the panel strains to hold that this newly discovered, previously unknown product cannot be validly patented. That is not the law. I also point out that the issue here is validity, not infringement.

Note the word "discovery" in the patent statute. "The term 'invention' means invention or discovery." 35 U.S.C. §100(a). It was and is well understood that an inventor may discover something that already existed. That the thing was there, undiscovered, does not render it "inherently anticipated." The panel's proposed rule may have particular impact on the discovery of biological products. Does the panel intend that no newly discovered product found in an organism can be patented? Such a ruling does not comport with either the patent statute or the incentive purposes of the patent system.

Precedent concerning "anticipation" has dealt with diverse factual situations, applying the common thread that novel subject matter may or may not be patentable, depending on whether it is also unobvious, while

subject matter that is not novel cannot be patented. A newly discovered attribute or property of something that was already known is patentable only as a method-of-use, but does not impart patentability to the known product. However, a previously unknown product does not become unpatentable simply because it existed before it was discovered. Precedent deals primarily with application of the law to situations where (1) a single prior art reference teaches all the elements of a product as claimed; in such case, the discovery of a new use or function does not render the product itself patentable; and (2) a single prior art reference does not teach all of the claimed elements; in such case the factual question arises of whether the omitted element is shown elsewhere (in which event the issue is obviousness) or whether the omitted element would have been known to be present in the reference subject matter, in which case the issue is anticipation. For example, in In re Schreiber, 128 F.3d 1473 (Fed. Cir. 1997) the applicant sought to patent a conical spout to dispense popped popcorn; the same conical spout was shown in the prior art as an oil dispenser. The product itself was thus held unpatentable as anticipated. In MEHL/Biophile International Corp. v. Milgraum, 192 F.3d 1362 (Fed. Cir. 1999) the prior art showed all of the claimed steps of laser irradiation of hair follicles, but did not mention hair removal; the court held that this effect was inherent in the prior art process, and that the same process steps could not be claimed, the court stating that "nothing in the claim limits the method's reach to human skin." Id. at 1366. In Titanium Metals Corp. v. Banner, 778 F.2d 775 (Fed. Cir. 1985) the court held that the discovery of the property of corrosion resistance of a known alloy did not impart patentability to the known alloy, for the property was inherent in the alloy.

In all applications of the law of anticipation, the initial consideration is whether the thing that is claimed was disclosed in a single prior art reference. When all of the elements of the claim are not shown in the prior art, precedent requires that the missing element was nonetheless known to be present in the subject matter of the reference, and that the claim is directed to the known subject matter. Although the panel now purports to disavow this precedent, such a change of law requires en banc action of the court. *See*, *e.g.*, the precedent represented by and cited in such cases as Continental Can Co. USA v. Monsanto Co., 948 F.2d 1264 (Fed. Cir. 1991), where the law of "inherency" is applied to subject matter wherein all of the elements of the claim are not shown in the prior art:

> To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill…
>
> This modest flexibility in the rule that "anticipation" requires that every element of the claims appear in a single reference accommodates situations where the common knowledge of technologists is not recorded in the reference; that is, where technological facts are known to those in the field of the invention, albeit not known to judges.

Id. at 1269-70. The analytic tool of "inherency" allows determination of whether subject matter that is not taught in the single reference was nonetheless known in the field of the invention. This was acknowledged in EMI Group North America, Inc. v. Cypress Semiconductor Corp., 268 F.3d 1342 (Fed. Cir. 2001):

> This requirement, that a person of ordinary skill in the art must recognize that the missing descriptive matter is necessarily present in the reference, may be sensible for claims that recite limitations of structure, compositions of matter, and method steps which could be inherently found in the prior art. Such recognition by one of ordinary skill may be important for establishing that the descriptive matter would inherently exist for every combination of a claim's limitation.

Id. at 1350-51. The panel now contradicts this body of precedent, stating that it "rejects the contention that inherent anticipation requires recognition in the prior art." A rejection of precedent requires en banc action, not panel disruption.

No reference shows the claimed descarbethoxyloratidine, or that a person of ordinary skill would have known that DCL is formed in vivo upon ingestion of loratidine. Precedent is directly contrary to the panel's holding that although no one knew of the existence of DCL, it is unpatentable because it in fact existed.

Whether it is desirable new policy to bar the patentability of products that have not yet been discovered is a result I seriously doubt. The court should speak with one voice on this important question. Thus I must, respectfully, dissent from the court's refusal to review this case en banc.

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LOURIE, Circuit Judge, dissenting from denial of petition for rehearing en banc.

I respectfully dissent from the court's decision not to hear this case en banc. I do so because it is an extraordinary decision, effectively precluding

virtually all patents on human metabolites of drugs. It thus qualifies as an issue of exceptional importance, justifying en banc consideration.

The holding of the panel, which the full court left standing, is that an issued patent on a pharmaceutical product provides an enabling disclosure of all of that product's metabolites (i.e., compounds that are formed in a patient's body upon ingestion of the pharmaceutical product), simply by disclosing that the product can be used by administration to a human. Because product patents covering pharmaceutical products generally issue before clinical trials on the product have revealed the identity or nature of any metabolites, this decision will preclude protection of those metabolites, as the issued patent will be effective prior art against such application.

I do not question that when a pharmaceutical product has been in actual public use prior to the filing of a patent application on its metabolite, the metabolite will also have been in public use and hence will be unpatentable. The holding of this case, however, goes much further, mandating that the mere issuance of the patent on the product—or any other publication of that product—inherently anticipates claims to the metabolite merely by disclosing that the product can be administered to a patient, on the theory that such administration would inevitably cause the human body to "make" the metabolite. The decision holds that an enabling disclosure of "how to make" metabolites is provided by the mere recitation that one can administer a prior art compound to humans.

If U.S. Patent 4,282,233 really taught how to make metabolites, it might be another story. However, that patent simply included a minimal, boilerplate statement of how to use the claimed products, sufficient to satisfy the requirements of 35 U.S.C. §112, but far from the careful and thorough prescribing information required by the FDA. The disclosure of the patent, like similar disclosures in other such patents, merely stated:

> The compounds of the present invention are useful as non-sedating antihistamines. These compounds act as anti-allergic agents in the treatment of such conditions as perennial and seasonal allergic rhinitis and chronic urticaria.

> The compounds of the present invention are administered in pharmaceutical formulations comprising the compound in admixture with a pharmaceutical carrier suitable for enteral or parenteral administration. The formulations may be in solid form…or in liquid form…
>
> Although the required dosage will be determined by such factors as the patient's age, sex, weight and the severity of the allergic reaction to be treated, the preferred human dosage range is likely to be 4 to 50 mg of the effective compound 1 to 3 times per day. The preferred dosage ranges for other animals can readily be determined by using standard testing methods.

'233 patent, col. 4, ll. 42-66. That is hardly an enabling disclosure of how to make any metabolites, whatever they might turn out to be, sufficient to anticipate them by inherency. The '233 patent does not identify or even mention any of the claimed products' metabolites. Yet the court here sweepingly holds that the patent anticipates those metabolites.

It may be asked why, if a developer of a new product has a patent on that product, does it also need a patent on its metabolite. However, that is not the patent law question before us. Moreover, another company might hold a patent on the metabolite, having independently invented it before the product patent issued and before the product went into public use. In any event, we deal here with issues of patent law, not policy or equity, and to hold that a patent on a product, with a minimal disclosure of administering it to a human or other subject, anticipates a later application on a metabolite, of which no mention appears whatsoever in the patent, cannot be correct.

Courtesy of Patrick H. Higgins, Buchanan Ingersoll & Rooney PC

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