Appeal No. 06-1261

IN THE
UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

PFIZER INC.,

Plaintiff-Appellee-Petitioner,

v.

APOTEX, INC.,

Defendant-Appellant-Respondent

Appeal from the United States District Court for the Northern District Of Illinois, in Case No. 03-CV-5289, Judge James M. Rosenbaum

CORRECTED BRIEF *AMICI CURIAE* OF SMITHKLINE BEECHAM CORPORATION (d/b/a GLAXOSMITHKLINE) AND ELI LILLY AND COMPANY IN SUPPORT OF PETITIONER PFIZER INC.

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2. The name of the real party in interest (if the parties named in the caption are not the real parties in interest) represented by me is: None.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or *amicus curiae* represented by me are: GlaxoSmithKline plc.

4. The names of all law firms and the partners or associates that appeared for the party or *amicus curiae* now represented by me in the trial court or agency or are expected to appear in this Court are: Carter G. Phillips, David T Pritikin, John W. Treece, Constantine L. Trela, Jr., Jeffrey P. Kushan, and Peter S. Choi – all of Sidley Austin LLP. And Sherry M. Knowles of GlaxoSmithKline.

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2. The name of the real party in interest (if the parties named in the caption are not the real parties in interest) represented by me is: None.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or *amicus curiae* represented by me are. None.

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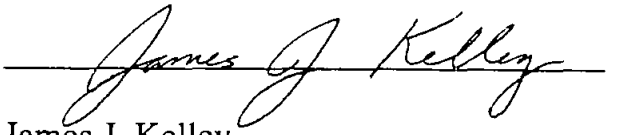

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

FEDERAL STATUTES

MISCELLANEOUS

STATEMENT OF INTEREST OF *AMICI CURIAE*

Amici curiae SmithKline Beecham Corporation (d/b/a GlaxoSmithKline) and Eli Lilly and Company are leading, global research-based companies whose medicines and healthcare products are used to treat a variety of serious and potentially life-threatening illnesses. *Amici* invest billions of dollars each year to discover and develop novel, pharmacologically active chemical compounds and to address practical, but equally significant concerns, such as drug product processing, manufacturing, and storage. Like Petitioner Pfizer Inc., *Amici* own many patents that cover discoveries in both areas. Accordingly, *Amici* have a vital interest in the proper application of the patent laws in this case.[1]

INTRODUCTION

The panel held that Pfizer's patent on amlodipine besylate, a previously unknown pharmaceutical composition, is invalid as obvious in view of the prior art. The panel found that the "problem to be solved" provided a motivation to combine the prior art teachings (slip op. 24) and that there was a reasonable expectation that the combination would work (*id.* at 27). The panel went on to find that the process the inventors employed to arrive at their discovery involved nothing more than routine testing, which, for the panel, confirmed the non-inventive nature of what they had done. (*Id.* at 31.)

[1] Petitioner has consented to the filing of this *amicus* brief, but Respondent has not. *Amici* accordingly have submitted a motion for leave to file this brief.

The panel's decision is contrary to long-settled principles of law. The panel based its obviousness determination upon the *inventors' own confidential, experimental work and insights gleaned from that work.* The problem the inventors recognized and then solved was not publicly known at the time of the invention. The expectation of success found by the panel was not the objective expectation of one of ordinary skill, but rather the inventors' own subjective thoughts concerning their experiments. Further, the panel's dismissal of the inventors' work as "routine" ignores both the statutory directive that the "manner in which the invention was made" shall not defeat patentability, 35 U.S.C. § 103(a), and the fact that much scientific work inside and outside the pharmaceutical industry involves use of "routine" testing procedures in the course of developing patentable inventions.

In short, the panel's decision holds an inventor's efforts obvious and unworthy of a patent not because of the content of the prior art and what it suggested, but because of the content of the inventor's own mind and work. Moreover, the panel effectively adopted an "obvious to try" standard and reinterpreted the requirement of reasonable expectation of success. This decision thus stands obviousness jurisprudence on its head and calls into question countless patents in every area of technology. The decision does not apply only to "the

particularized facts of this case" (slip op. 31), but rather has broad ramifications that should be addressed by the Court *en banc*.

ARGUMENT

The factual circumstances giving rise to this case go the core of pharmaceutical research. While a drug compound selected for development, by definition, has favorable pharmacological properties, it also *must* have additional characteristics that enable it (i) to be effective at non-toxic doses; (ii) to be chemically stable upon processing and storage; and (iii) to exist in a form that is easily handled and measured and can endure the rigors of industrial manufacturing processes. Because a novel salt has the potential to change the "solid state" properties relevant to these characteristics, salt formation with the "active" compound to be administered is one approach that may be investigated if problems arise. However, the formation and properties of salts of drug compounds are notoriously unpredictable, as emphasized in the key reference cited by the panel. *See* Berge, *J Pharm Sci* 66:1 (1977). In addition, while any potential solution may target any one property, the real difficulty lies in the multi-faceted nature of the problem -- obtaining a compound that exhibits a *balance* of these characteristics against this backdrop of uncertainty. Thus, identifying a suitable salt can be a crucial step in the process of commercializing a viable *drug product.*

This does not mean, as the panel suggests, that all salt forms are patentable. Only that improper means cannot be used to make an obviousness determination.

I. AN INVENTOR'S OWN PATH TO DISCOVERY CANNOT BE USED TO DEFEAT PATENTABILITY.

A. The Problem Solved By The Inventors Was Unexpected And Not Generally Known By Those Having Ordinary Skill.

The law has long been clear that the question of obviousness is an objective one to be determined from the perspective of the person of ordinary skill in the art. *See Hotchkiss v. Greenwood*, 52 U.S. (11 How.) 248, 267 (1851); *Standard Oil Co v. Am Cyanamid Co* , 774 F.2d 448, 454 (Fed. Cir. 1985). Improperly finding that there was a motivation to combine the prior art references and a reasonable expectation that the combination would succeed, the panel ignored this established principle.

The panel relied on the "problem to be solved" -- *i.e* , the susceptibility of amlodipine maleate to chemical degradation via a "Michael addition reaction" -- to find a motivation to combine the prior art. (Slip op. 21.) According to the panel, this problem, which was actually only one of several, would have led the skilled artisan away from certain types of structures and toward compounds such as besylate. The error in this analysis is that the problem was not known in the art. Instead, it was discovered as a result of confidential work by one of the inventors, Dr. Wells, to develop a suitable formulation for amlodipine. (*Id.* at 5.) The

Michael addition reaction, in this case, is a disfavored reaction that a skilled artisan would not have expected.[2] Thus, one of ordinary skill would not have predicted the degradation observed by Dr. Wells, and thus would not have appreciated the problem to be solved. *Cf In re Huang*, 100 F.3d 135, 139 n.5 (Fed. Cir. 1996) (problem was "well known"). Dr. Wells' identification of the problem was part of the invention. *In re Sponnoble,* 405 F.2d 578, 832 (C.C.P.A. 1969).

B. The Inventors' Own Subjective Expectations Cannot Support A Finding That The Success Of Their Efforts Was Predictable.

The panel also erred by looking to the inventors' own subjective beliefs to find a reasonable expectation of success. In particular, the panel relied on Dr. Wells' testimony that, after compiling a list of potential compounds, he had an "expectation" that he could form a salt with one of them and "believed" one of these could solve the problems of amlodipine maleate. (Slip op. 25-26.)

Every inventor has an "expectation" as to what his or her experiments *may* accomplish -- otherwise, why perform the experiments at all? The relevant inquiry for obviousness, however, must focus on the expectations of persons other than the inventor. "Because patentability is assessed from the perspective of the hypothetical person of ordinary skill in the art, information regarding the

[2] Michael addition reactions to unsaturated negatively charged carboxylates such as maleates are extremely sluggish and not favored, given that the Michael addition itself generates an anion, which in the case of a maleate leads to a compound bearing two negative charges.

subjective motivations of inventors is not material." *Life Techs , Inc v Clontech Labs., Inc.*, 224 F.3d 1320, 1325 (Fed. Cir. 2000). Here, it is undisputed that the prior art provides "no reliable way of predicting the influence of a particular salt species on the behavior of a parent compound," a teaching accepted by experts from *both* sides. (Slip op. 10-11.) This is consistent with the fact that Dr. Wells did not know which salt, *if any*, would solve the problem he had discovered (and so he was forced to test numerous alternatives).

C. The Nature Of The Effort Undertaken By The Inventors Is Legally Irrelevant To The Obviousness Inquiry.

Although the panel acknowledged the statutory mandate that "[p]atentability shall not be negatived by the manner in which the invention was made," it devoted nearly seven pages to the question: "[W]hen the skilled artisan must test, how far does that need for testing go toward supporting a conclusion of non-obviousness?" (Slip op. 28, 30.) Because the panel had erroneously concluded that the prior art "predicted the results" of salt formation, it found that the inventors "merely had to verify [the results] through routine testing" using "standard techniques" (*id.* at 31); and that the inventors engaged in nothing more than "optimization of the acid addition salt" (*id.* at 32). These appellate findings are both procedurally improper and legally irrelevant under § 103. *See Standard Oil*, 774 F.2d at 454.

Even if the nature of the inventors' experimentation were relevant, the panel's minimization of their work as mere "optimization" or "verification" of an

expected result is factually incorrect. As discussed, the inventors' own expectations cannot rebut the undisputed prior art teaching that the properties of a salt cannot be predicted in advance. Moreover, every court that has considered the issue, *including this Court*, has found the unpredictability of salt selection to be a factor supporting the patentability of specific salt forms.[3] Thus, testing of salts is necessary to identify those, *if any*, possessing the proper characteristics

Nor does the selection of a pharmaceutical salt necessarily involve the "optimization of a range or other variable within the claims." (*See* slip op. 32.) In parameter cases involving optimization, the quantity or degree of a recited *numerical* parameter in a *known* process or composition was varied to arrive at an "optimized" *numerical* value. There was never any question that the modified process or composition would work for its intended purpose. *See, e g , In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003) (*prima facie* obviousness exists when "one skilled in the art would have expected them to have the same properties"). Here, however, a new chemical compound was formed possessing properties that were distinct from its parents. Prior to making and testing any new salt compound, the person of ordinary skill does not know whether that salt will work for its intended purpose, *i.e* , will have the proper balance of solid-state

[3] *See, e g., Sanofi-Synthelabo v. Apotex, Inc* , 470 F.3d 1368, 1379 (Fed. Cir. 2006); *Pfizer Inc v Mylan Labs., Inc* , No. 02-1628, 2007 WL 654274, at *30 (W.D. Pa. Feb. 27, 2007).

properties. This uncertainty did not exist in the optimization cases cited by the panel.

The panel's misunderstanding concerning the significance of salts is reflected in its references to *Pfizer Inc v. Dr. Reddy's Labs, Ltd*, 359 F.3d 1361 (Fed. Cir. 2004). There, this Court found that "drug product," as used in 35 U.S.C. § 156(f), refers to the "active moiety" and that this encompassed two products that contained this active ingredient (*i.e*, amlodipine besylate and amlodipine maleate). *Id.* at 1366. Relying on that finding, the panel here concluded that the besylate salt component of amlodipine besylate is inconsequential because it has no therapeutic effect. (*See* slip op. 26, 29, 32.) This is a misreading of *Dr Reddy's* The policy behind § 156(f), restoration of time lost as a result of the regulatory process needed to obtain marketing approval for the component "*responsible for the physiological or pharmacological action*," 359 F.3d at 1366 (emphasis added) -- here, amlodipine, has no bearing on whether any particular salt form of amlodipine exhibits nonobvious manufacturing properties when that compound is considered "as a whole." *In re Dillon*, 919 F.2d 688, 694 (Fed. Cir. 1990). As discussed, properties other than pharmacological effect are crucial to commercializing a drug product, and these properties must be evaluated. *Id.*

The panel reasoned that there is a material difference between the trial and error used to "discover" new drug compounds and the trial and error procedures at

issue here. (Slip op. 31.) In reality, the process necessary to identify a salt form of a drug compound bears similarities to that used for "discovery" of the drug compound itself. In the latter, the discovery of compounds exhibiting biological properties relevant to pharmacological efficacy and toxicity is important; in the former, the discovery of compounds exhibiting solid-state properties relevant to safety, stability, handling, and manufacturing is important. In each case, numerous possible compounds exist that must be made and tested to find the species possessing the proper combination of properties, but the properties -- when considered individually and *as a whole* -- cannot be predicted in advance. Nor can it be known if any compound will be suitable at all. To find the new result unpatentable in these circumstances equates "obvious to try" with obviousness.

II. THE DECISION'S RATIONALE CALLS INTO QUESTION THE VALIDITY OF NUMEROUS ISSUED PATENTS.

The panel opinion has broad ramifications that cast a cloud over countless patents. By confusing the subjective research objectives of inventors trying to solve a unique and unexpected problem with the objective standard for obviousness, the panel has upended settled case law on obviousness. An invention cannot be unpatentable because the inventor recognized a problem as part of a confidential work project, proposed a solution, and confirmed it by testing. If this were the case, only discoveries made "by accident," and not through purposeful experimentation, would be patentable. This cannot be reconciled with § 103(a).

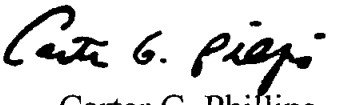
In addition, the panel's emphasis upon the nature of the testing used to confirm an inventor's suspicions and its characterization of it as "routine" have the potential to create further mischief Many inventions flow from well-known means of experimentation and testing, which can be performed by laboratory technicians. Until now, this has never been thought to raise the specter of obviousness. To find obviousness under these circumstances calls into question the patentability of every invention discovered through methodical trial and error and will unsettle the reliance interests of countless patentholders.

In sum, although the panel disavows the "obvious to try" standard, it actually applies that very standard in this case As Judge Rich stated in *In re Tomlinson*, 363 F.2d 928, 931 (C.C.P.A. 1966), "there is usually an element of 'obviousness to try' in any research endeavor, that . . . is not undertaken with complete blindness but rather with some semblance of a chance of success . . . . [To make] patentability determinations based on that as the test would not only be contrary to the statute but result in a marked deterioration of the entire patent system as an incentive to invest in those efforts and attempts which go by the name 'research.'"

CONCLUSION

For the foregoing reasons, *amici curiae* respectfully submit that the Court should grant Pfizer's petition for rehearing *en banc*.

Respectfully submitted,



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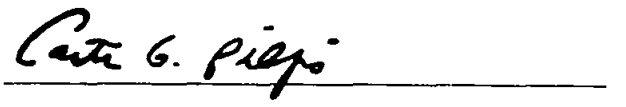
CERTIFICATE OF COMPLIANCE WITH FRAP 29(d) AND 32(a)(7)(B)

Counsel for *Amici* certifies that the body of this corrected brief, beginning with the "Statement of Interest of *Amici Curiae*" on page 1 and ending with the last line of the "Conclusion" on page 10, contains 3,249 words, as measured by the word-processing system used to prepare this brief, in compliance with Federal Rules of Appellate Procedure 29(d) and 30(a)(7)B).



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