UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

PFIZER INC., PHARMACIA CORP., PHARMACIA & UPJOHN INC., PHARMACIA& UPJOHN COMPANY, G.D. SEARLE & CO, G.D. SEARLE LLC, SEARLE LLC (DELAWARE) and SEARLE LLC (NEVADA) Plaintiffs, v. TEVA PHARMACEUTICALS USA, INC. Defendant.	:	CIV. ACTION NO. 04-754 (JCL) **FINDINGS OF FACT AND CONCLUSIONS OF LAW**

LIFLAND, District Judge

Plaintiffs, Pfizer, Inc., Pharmacia Corp., Pharmacia & Upjohn Inc., Pharmacia & Upjohn Company, G.D. Searle & Co., G.D. Searle LLC, Searle LLC (Delaware), and Searle LLC (Nevada) (collectively "Pfizer" or "Plaintiffs") allege infringement of U.S. Patent Nos. 5,466,823 (the "'823 Patent"); 5,563,165 (the "'165 Patent"); and 5,760,068 (the "'068 Patent) (collectively the "patents-in-suit") by Teva Pharmaceuticals U.S.A., Inc. ("Teva" or "Defendant"). The patents-in-suit are directed toward celecoxib, the active ingredient in Celebrex, and a broad genus of compounds that includes celecoxib, pharmaceutical

compositions including such compounds, and methods of using such compounds.

For the reasons set forth below,[1] the Court finds that Teva has failed to prove obviousness, inequitable conduct, a violation of the best mode requirement, or obvious-type double patenting by clear and convincing evidence. Thus, the patents are neither invalid nor unenforceable, and Teva has infringed the patents under 35 U.S.C. § 271(e)(2).

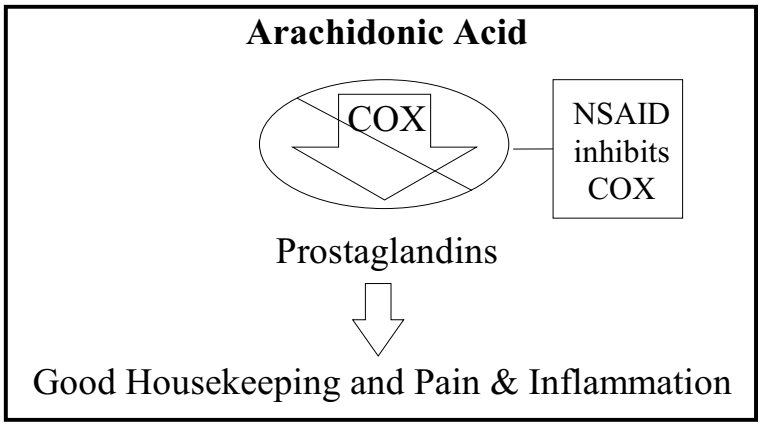
BACKGROUND

I. A Brief History of Anti-Inflammatory Drugs

The precise biological reason people suffer from pain and inflammation is not yet fully understood. However, great progress has been made in recent decades toward understanding and treating the pain and other symptoms associated with inflammatory conditions. Around the turn of the century, researchers at Friedrich Bayer & Co. invented aspirin, which quickly gained popularity as a painkiller. Over the next several decades similar drugs—classified as traditional non-steroidal anti-inflammatory drugs ("NSAIDs")—were introduced into the market, including ibuprofen and naproxen. Yet it was not until

[1] This opinion shall constitute the Court's findings of fact and conclusions of law pursuant to Federal Rule of Civil Procedure 52(a).

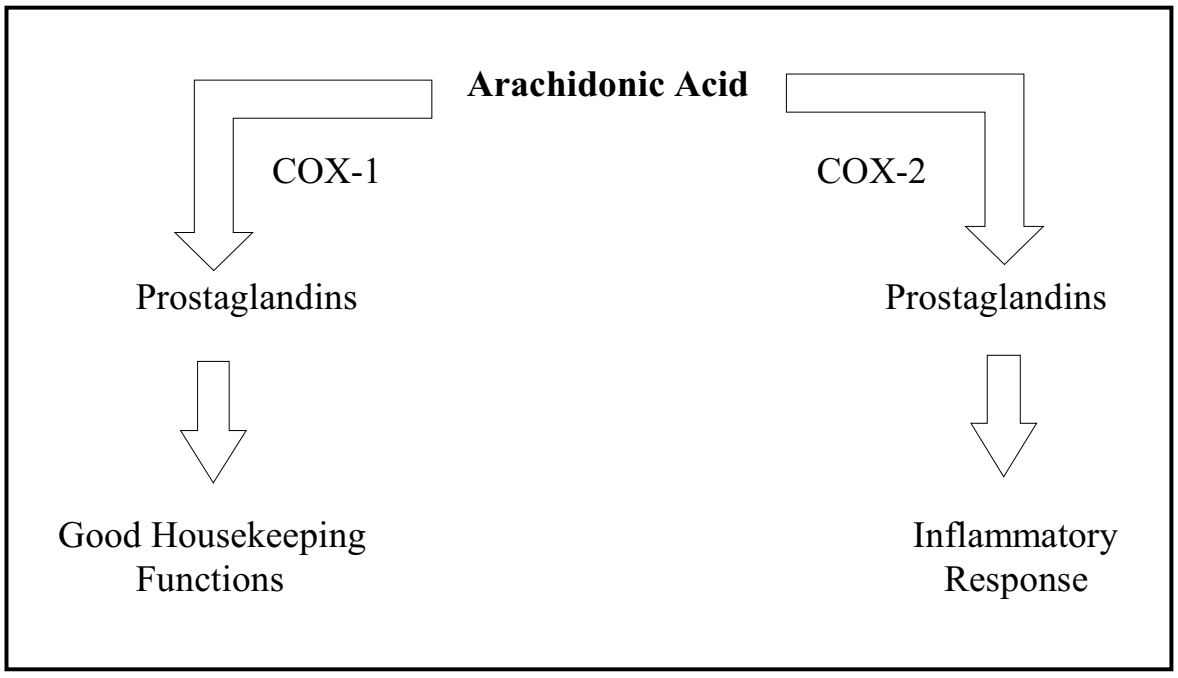
the early 1970s that the mechanism of action of these drugs was understood. In simplified terms, scientists eventually discerned that traditional NSAIDs worked by blocking the production of prostaglandins in cells. Prostaglandins are small molecules that are associated with both pain and inflammation, and with "good housekeeping" functions, such as contributing to good gastrointestinal physiology and blood clotting. These prostaglandin molecules are produced in the body when arachidonic acid (a fat found in cell membranes) is catalyzed by cyclooxygenase (COX) enzymes. Traditional NSAIDs inhibited the COX enzyme, thus preventing the creation of prostaglandins and the associated pain and inflammation.



This discovery also shed light on the cause of some of the reported side effects of traditional NSAIDs. It had been known for some time that NSAIDs were associated with gastrointestinal ("GI") side effects, ranging from discomfort to serious life threatening ulcers, yet the cause of these GI risks was unclear. With

the discovery of the prostaglandin pathway, it became clear that in addition to reducing the negative effects of prostaglandins, traditional NSAIDs like aspirin also reduced the positive "housekeeping" functions, thus causing potentially severe GI risks. This new knowledge was an important step in the ongoing effort to invent a new kind of NSAID that would treat pain and inflammation without causing GI side effects.

The next breakthrough in anti-inflammatory drug development came in the 1970s and 1980s when scientists established that there were in fact two different kinds of COX enzymes: one responsible for producing good housekeeping prostaglandins (COX-1), and one responsible for producing prostaglandins associated with pain and inflammation (COX-2). (See figure below.)



COX-1 was fully identified and sequenced in 1988. COX-2 was sequenced in 1991. Once both enzymes were sequenced, scientists hypothesized that it might be possible to selectively inhibit COX-2, thus creating a GI sparing NSAID. However, due to the similarity of the two enzymes, there was significant skepticism as to whether it would be possible to develop a drug that selectively inhibited either enzyme.

Scientists became more hopeful in 1992 after Dr. William Galbraith of DuPont-Merck gave a presentation at a prostaglandin conference in Keystone, Colorado ("the Keystone Conference"). Dr. Galbraith's presentation focused on a compound called DuP 697, which he reported might be a COX-2 selective inhibitor. Following the Keystone Conference, pharmaceutical companies stepped up their efforts to create a COX-2 selective compound, and thus began what Teva has characterized as a "race" to develop the first COX-2 selective inhibitor, with Pfizer and Merck as the two frontrunners.

II. Celebrex and the Patents-in-Suit

For Pfizer, the finish line of the COX-2 selective inhibitor race was Celebrex. Sometime between August and November 1993,[2] Pfizer scientists

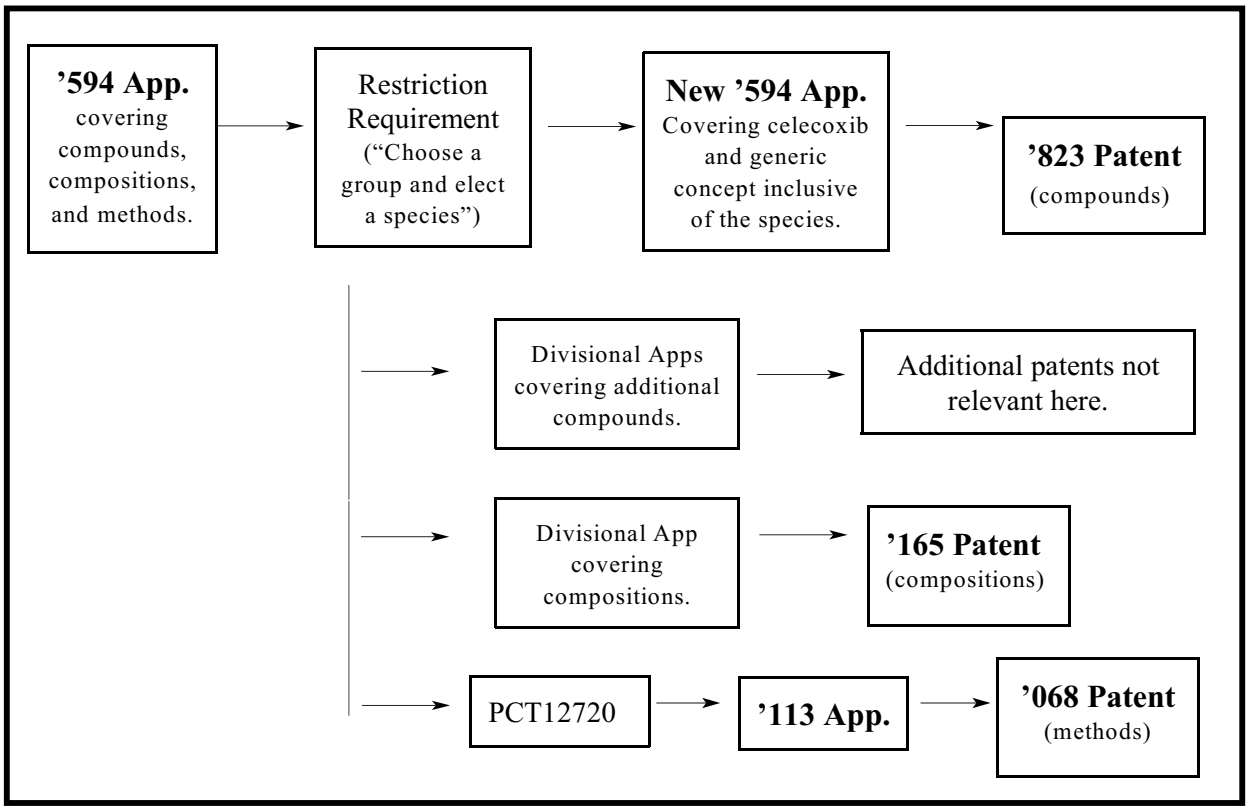
[2] The precise invention date of celecoxib is disputed. This issue is addressed in detail below. See *infra* Section I.A.

invented several new compounds they believed would selectively inhibit the COX-2 enzyme. One of the compounds was celecoxib.

On November 30, 1993, Pfizer filed U.S. Application No. 08/160,594 (the "'594 Application"), covering a broad range of chemical compounds, as well as pharmaceutical compositions utilizing the compounds, and methods of treatment. On July 12, 1994, the Patent Examiner issued a restriction requirement requiring Pfizer to select either the compound claims, the composition claims, or the method claims to prosecute, and further required Pfizer to elect a single species within the chosen group for examination.

Pfizer elected to prosecute the compound claims and chose the species described in example #1c (celecoxib) as the elected species. The Examiner then defined a "generic concept inclusive of the elected species . . . for examination along with the elected species." The '594 Application, as narrowed, was approved and ultimately issued as the '823 Patent. Pfizer filed several divisional applications covering the compounds that were not embraced by the '823 Patent. These patents were issued, but are not relevant here. Pfizer also filed a divisional application covering compositions. This divisional application issued as the '165 Patent. Finally, Pfizer also filed international application PCT12720 covering methods. This application entered the national stage as the '113 Application, and

ultimately issued as the ’068 Patent. (See figure below.)



After the patents-in-suit were issued, Pfizer scientists conducted further testing of the compounds covered by the patents to identify a compound to develop into a commercial drug. Several compounds that initially seemed to be promising candidates were discarded after further testing revealed unacceptable properties such as excessive half-life or liver toxicity. Eventually, scientists selected celecoxib as the preferred compound and, following clinical trials, submitted a New Drug Application to the Food and Drug Administration (“FDA”) for Celebrex. The FDA approved Celebrex as a COX-2 selective NSAID for the

treatment of osteoarthritis and rheumatoid arthritis on December 31, 1998. Celebrex was launched the following year, and almost immediately achieved enormous and sustained success in the marketplace.

III. Teva's Abbreviated New Drug Application

The Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act permit an applicant to file an Abbreviated New Drug Application ("ANDA") with the Food and Drug Administration ("FDA") requesting approval of a bioequivalent ("generic") version of a drug that is already listed by the FDA as approved for safety and effectiveness without having to submit additional safety and efficacy data. See 21 U.S.C. § 355(j)(2)(A). An ANDA may be filed for drugs currently protected by patents. In its filing, the applicant must certify either (1) that it will not market its drug prior to the expiration of the relevant patents, or (2) that the relevant patents "are invalid or will not be infringed by the manufacture, use or sale of the new drug for which the ANDA is submitted." 21 U.S.C. § 355(j) (2)(A)(vii)(IV). An ANDA applicant filing its application with the FDA and making a Section IV certification must notify the holder of the patent, who may then bring an action against the applicant for infringement under 35U.S.C. § 271(e)(2). See 21 U.S.C. §§ 355(j)(2)(B)(i) and (j)(5)(B)(iii); see also, e.g., SmithKline Beecham Corp. v. Apotex Corp., 439 F.3d 1312, 1314 (Fed. Cir.

2006). Submission of an ANDA is an act of patent infringement if the ANDA seeks approval to manufacture, use, or sell a drug that is claimed in a patent or the use of which is claimed in a patent. 35 U.S.C. § 271(e).

Teva filed Abbreviated New Drug Application No. 76-898 with the FDA. The application was addressed to a proposed drug March 19, 2007 product identified as "Celecoxib Capsules, 100 mg, 200 mg, and 400 mg." The ANDA contained a Section IV certification challenging the validity of the patents covering celecoxib.

IV. The Current Litigation

In February 2004, Pfizer filed an action against Teva for infringement. In May 2004, Teva filed an answer and asserted an affirmative defense claiming that the patents-in-suit are invalid or unenforceable due to obviousness under 35 U.S.C. § 103(a), inequitable conduct, and violation of the best mode requirement, and that the '068 Patent (covering methods of use) is invalid for obvious-type double patenting over the '165 Patent (covering pharmaceutical compositions).

The parties tried the case before the Court from November 13 through December 8, 2006 and on December 13, 2006. Written closing statements were submitted to the Court on February 1, 2007.

JURISDICTION, VENUE AND APPLICABLE LAW

This Court has subject matter jurisdiction over Pfizer's patent infringement claims pursuant to 28 U.S.C. §§ 1331 and 1338(a). Venue is proper under 28 U.S.C. §§ 1391 and 1400(b).

Because this action arises under the patent laws of the United States, this Court must apply the precedents of the United States Court of Appeals for the Federal Circuit, which has jurisdiction over any appeal of this judgment. See 28 U.S.C. § 1295(a).

STANDARD OF REVIEW

Patents enjoy a presumption of validity. 35 U.S.C. § 282 ("A patent shall be presumed valid."). The party challenging the patent bears the burden of proving by clear and convincing evidence the invalidity or unenforceability of the claims of a patent. See id; see also Alza Corp. v. Mylan Labs., Inc., 464 F.3d 1286, 1289 (Fed. Cir. 2006). "The 'clear and convincing' standard of proof of facts is an intermediate standard which lies somewhere between 'beyond a reasonable doubt' and a 'preponderance of the evidence,'" and "has been described as evidence which produces in the mind of the trier of fact an abiding conviction that the truth

of [the] factual contentions [is] 'highly probable.'" Buildex, Inc. v. Kason Indus., Inc., 849 F.2d 1461, 1463 (Fed. Cir. 1988) (internal quotation omitted). Thus, Teva bears the burden of proving each of its defenses of patent invalidity/unenforceability, and each element of those defenses, by clear and convincing evidence.

ANALYSIS

I. OBVIOUSNESS

Pursuant to § 103 of the United States Code, a patent is invalid if the claimed invention was "obvious" at the time it was created. The test for obviousness is "whether the claim at issue would have been obvious to one of ordinary skill in the art at the time of the patent." Avia Group Int'l, Inc. v. L.A. Gear California, Inc., 853 F.2d 1557, 1563 (Fed. Cir. 1988); see also Alza Corp. v. Mylan Labs., Inc., 464 F.3d 1286, 1289 (Fed. Cir. 2006) ("[A] claimed invention is unpatentable if the differences between it 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.'") (quoting 35 U.S.C. § 103(a)). In adjudicating obviousness, four factors—called the Graham factors—must be considered: "(1) the scope and content of the prior art; (2) the level of ordinary

skill in the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness." In re Dembiczak, 175 F.3d 994, 998 (Fed. Cir. 1999) (citing Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966)).

"For a chemical compound, a *prima facie* case of obviousness requires 'structural similarity between claimed and prior art subject matter . . . *where the prior art gives reason or motivation to make the claimed compositions*.'" Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc,, 231 F.3d 1339, 1343 (Fed. Cir. 2000) (emphasis added) (quoting In re Dillon, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc)). Accordingly, this Court must apply the "motivation-suggestion-teaching" test, which asks "whether a person of ordinary skill in the art, possessed with the understandings and knowledge reflected in the prior art, and motivated by the general problem facing the inventor, would have been led to make the combination recited in the claims." In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006). In other words, a *prima facie* case of obviousness requires the party to "explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious." Id. at 986 (internal quotations omitted). Evidence of motivation to combine need not be found explicitly in the prior art—it "may be

implicit from the prior art as a whole," In re Kotzab, 217 F.3d 1365, 1370 (Fed. Cir. 2000), or evident from the general knowledge of a person of ordinary skill, Alza Corp. v. Mylan Labs., Inc., 464 F.3d 1286, 1291 (Fed. Cir. 2006); In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006).[3]

Importantly, "[b]ecause 35 U.S.C. § 103(a) orders a Court to determine whether the subject matter was obvious 'at the time the invention was made,' the obviousness inquiry cannot be performed using hindsight." Janssen Pharmaceutica N.V. v. Mylan Pharms., Inc., 456 F. Supp.2d 644, 654-55 (D.N.J. 2006); see also Orthopedic Equipment Co., Inc. v. United States, 702 F.2d 1005, 1012 (Fed. Cir. 1983) ("It is wrong to use the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit. Monday morning quarterbacking is

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[3] This Court is aware that the Supreme Court has recently granted *certiorari* and heard oral argument in KSR International Co. v. Teleflex, Inc., No. 04-1350, to address the following question: "Whether the Federal Circuit has erred in holding that a claimed invention cannot be held 'obvious,' and thus unpatentable under 35 U.S.C. § 103(a), in the absence of some proven 'teaching, suggestion, or motivation' that would have led a person of ordinary skill in the art to combine the relevant prior art teachings in the manner claimed." Whether and to what extent the Supreme Court's decision in that case will affect the proper analysis of this case is impossible to anticipate. But the "teaching, suggestion, motivation" test does not come into play with respect to many of the reasons articulated in this opinion for rejecting Teva's obviousness defense. Those reasons would remain unchanged regardless of the outcome of KSR.

quite improper when resolving the question of nonobviousness in a court of law."). The motivation-suggestion-teaching test "stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness." In re Rouffet, 149 F.3d 1350, 1358 (Fed. Cir. 1998).

Teva contends that celecoxib and other compounds within the genus of the '823 Patent would have been obvious to a person of ordinary skill in the art in November of 1993. In brief, Teva's theory of obviousness is that the person of ordinary skill would have derived a pharmacophore from the disclosure of the Merck '196 Application/'995 Patent,[4] and then used the pharmacophore, his/her general knowledge of pharmaceutical chemistry, and the teachings of two other references—the '142 Patent and the Fujisawa '829 Application—to create twelve obvious compounds, including celecoxib.

As an initial matter, the Court finds that the '196 Application/'995 Patent is not prior art to the patents-in-suit because the Merck '995 Patent is not entitled to claim priority to the filing date of the '196 Application. This finding alone warrants a ruling for Pfizer since Teva's entire theory of obviousness hinges on this reference. However, even assuming *arguendo* that the '196 Application/'995

[4] As explained in more detail herein, a pharmacophore is a structural framework used to define the essential features of one or more molecules with the same biological activity.

Patent is prior art, the Court finds that Teva has failed to meet its burden of proving a *prima facie* case of obviousness. As explained in detail below, Teva has not shown that the person of ordinary skill would derive the proposed pharmacophore or that the pharmacophore would inexorably lead to the creation of celecoxib as one of the twelve allegedly obvious compounds.

Accordingly, the Court finds that the patents-in-suit are not invalid for obviousness.

A. The Date of Invention

At the outset, the Court must determine the precise invention date for celecoxib. Because the Court must evaluate obviousness "at the time the invention was made," the invention date is a threshold question that will guide the entire obviousness analysis. "A general rule in patent law is that the date of invention . . . is presumed to be the date [the applicant] files a complete patent application in the Patent and Trademark Office disclosing the invention." 1 Chisum on Patents § 3.08. This presumption can be overcome by proof of either: (1) an earlier reduction to practice of the invention, or (2) an earlier conception of the invention coupled with due diligence from the date of conception to a subsequent reduction to practice or to the filing of the application. Id.; Dow

Chemical Co. v. Halliburton Co., 631 F.Supp. 666, 704 (N.D. Miss. 1985), aff'd 740 F.2d 93 (Fed. Cir. 1986). "[This earlier] date, if established, is the 'time the invention was made' used in determining obviousness under 35 U.S.C. § 103." Dow Chemical, 631 F.Supp. at 704 (N.D. Miss. 1985) (citing Lockheed Aircraft Corp. v. United States, 553 F.2d 69, 74 (Ct. Cl. 1977)).

Here, the invention date has been an issue of considerable dispute. The filing date for the application was November 30, 1993. However, shortly before the trial began, Pfizer asserted an earlier invention date of August 2, 1993 on the ground of earlier conception of the invention coupled with due diligence from the date of conception to a subsequent reduction to practice or to the filing of the application (*i.e.*, ground (2) above). Specifically, Pfizer asserted that "it conceived the invention claimed in the patents-in-suit at least as early as August 2, 1993 and worked with reasonable diligence continuously through the time it filed for patent protection." (Decl. of Michael Patunas in Support of Teva's in Limine Motion No. 1, Ex. G at ¶ 9; see also Opinion on Teva's Motion in Limine No. 1.)[5]

[5] Pfizer did not disclose this argument until after the close of discovery despite the existence of an interrogatory requesting "the conception and first reduction to practice of each of the alleged inventions recited in the asserted claims." (Decl. of Michael E. Patunas in Support of Teva's in Limine Motion No. 1, Ex. A, Interrogatory No. 27.) Accordingly, Teva moved in limine to preclude Pfizer from submitting evidence to support the August 2 invention date. The Court denied Teva's request to preclude the evidence, but granted Teva's alternative request to submit additional expert reports on the issue of the proper

To support its assertion of an August 2, 1993 conception date, Pfizer relied upon pages from the laboratory notebook of Dr. Bertenshaw, one of the inventors of celecoxib. The notebook pages, dated August 2, 1993, disclosed a broad genus of chemical compounds with several substituents in several positions. Celecoxib was within the genus (*i.e.*, one could derive celecoxib by picking certain groups out of the possibilities listed in notebook pages), but the notebook pages provided no direction to celecoxib—no instruction or even suggestion to select these groups out of the plethora of possibilities provided.

Pfizer initially sought this earlier invention date in order to antedate the Fujisawa '829 Application (with a publication date of August 11, 1993), which Teva originally indicated was an important piece of its obviousness theory. At trial, however, the parties' respective positions began to shift. Teva did not rely heavily on the '829 Application. Pfizer meanwhile questioned the appropriateness of starting with the '196 Application/'995 Patent by introducing other patents—with effective dates later than August 2, 1993—that the person of ordinary skill could have started with instead. These patents would not have been available to the person of ordinary skill if the date of invention was set at August 2, 1993, as Pfizer initially argued it should be. On the second day of trial, Teva's

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invention date for the patents-in-suit. See Opinion on Teva's Motion in Limine No. 1.

counsel "concede[d] the invention date is at least in October," but did not elaborate further. (Trial Trans. II 30:6.) The trial concluded without further elaboration from either party as to the invention date they respectively believed should be accepted by the Court.

Teva elaborated for the first time in its response to a Rule 52 motion filed by Pfizer at the close of Teva's case-in-chief. In its response papers Teva argued that the proper invention date was October 4, 1993, since Pfizer scientists first synthesized celecoxib (*i.e.*, reduced it to practice) no later than that date. An October 4, 1993 invention date would benefit Teva's obviousness argument in two ways. First, it would make the '829 Application viable prior art to the patents-in-suit. See *infra* Section I.B.2. Second, as discussed in Section I.D.1(c), Pfizer proffers several possible starting points for the development of new NSAIDs that it contends would have been more appealing to the person of ordinary skill than the one Teva relies on. Two of these proposed starting points are patents that resulted from applications which were filed in November 1993. These patents would not have been available to the person of ordinary skill on October 4, 1993.

Since the invention date had been a "moving target" throughout the trial and pre-trial proceedings, the Court sent a letter to counsel requesting that Pfizer "include a clear explication of [its] position regarding the proper invention date in

its reply papers." Letter to Counsel re: Pfizer v. Teva, Civ. Action No. 04-754 (Dec. 26, 2006). Pfizer did address the invention date in its reply papers—and moved the target once again. Pfizer abandoned its August 2 invention date argument, and urged the Court to adopt November 30, 1993 (the filing date of the patents-in-suit) as the default invention date.

Accordingly, there are three potential invention dates on the table. As noted, Pfizer no longer asserts an invention date of August 2, 1993. Nor does the Court find there to be adequate support for conception of the invention on that date.[6] This leaves October 4, 1993, and November 30, 1993, as the possible

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[6] Conception of a broad genus that includes hundreds of thousands of compounds, including the specific compound at issue, is not sufficient to establish conception of the compound. The Federal Circuit has explained that

> [c]onception is the touchstone of inventorship, the completion of the mental part of invention. It is the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention . . . . Conception is complete only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation. . . .
>
> Thus, the test for conception is whether the inventor had an idea that was definite and permanent . . . . The conception analysis necessarily turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot prove possession of the complete mental picture of the invention. These rules ensure that patent rights attach only when an idea is so far developed that the inventor can point to a definite, particular invention.

Burroughs Wellcome Co. v. Barr Lab., 40 F.3d 1223, 1228-29 (Fed. Cir. 1994)

invention dates. As per the general rule, see *supra*, the Court will use November 30, 1993, as the default invention date unless there is clear and convincing evidence of the earlier October 4th date. The Court finds that there is.

This case presents a unique situation. Generally, it is the patent holder who seeks to assert an earlier invention date in order to antedate a prior art reference or to establish priority in the context of an interference. Here, however, it is Teva that asserts the earlier invention date of October 4, 1993, based on Pfizer's reduction to practice on or before that date. In support of its assertion, Teva cites several pieces of evidence, including Pfizer's own statement in an interrogatory response that Pfizer scientists synthesized celecoxib at least as early as October 4, 1993:

> Interrogatory No. 28
> Identify when, where and how the compound [celecoxib], and any pharmaceutically acceptable salts thereof, were first synthesized, the individual(s) that conducted such synthesis, the individual(s) that directed such synthesis, and any analysis of the results of such synthesis.

(internal quotation marks and citations omitted). The broad genus conceived by Dr. Bertenshaw on August 2, 1993 does not meet this high standard. It does not "describe [celecoxib] with particularity." It does not demonstrate "possession of the complete mental picture of [celecoxib.]" It does not illustrate a "definite and permanent idea of the complete and operative invention." Id. Accordingly, the Court is not persuaded that the notebook pages constitute clear and convincing evidence of the conception of celecoxib on August 2, 1993.

> Response to Interrogatory No. 28
> Plaintiffs object to the term "any analysis of the results of such synthesis" as vague and ambiguous. Subject to the general and specific objections, *plaintiffs respond that celecoxib was first synthesized at least as early as October 4, 1993* by Julie M. Miyashiro at G.D. Searle & Co.'s facilities in Skokie, Illinois.

(Declaration of Michael E. Patunas in Support of Teva's Post-Trial Brief, Exh. 3, at 3 (emphasis added).) In the typical scenario, there are concerns over the credibility of the patent holder's own self-serving testimony regarding an earlier date of conception or reduction to practice. Chen v. Bouchard, 347 F.3d 1299, 1309 (Fed. Cir. 2003); Mahurkar v. C.R. Bard, Inc., 79 F.3d 1572, 1577 (Fed. Cir. 1996). However, those concerns are inapplicable in the current situation where the earlier invention date hurts, rather than helps, the patent holder. Accordingly, the Court will give due weight to Pfizer's own *self-defeating* statements regarding an earlier reduction to practice.

Furthermore, Pfizer's statement is not the only evidence in the record that supports the October 4th date. There is documentary and testimonial evidence that corroborates the reduction to practice of celecoxib on this date. A page from the laboratory notebook of inventor Julie Miyashiro describes the synthesis (reduction to practice) of celecoxib. The page is dated October 4, 1993, and was signed and witnessed in accordance with Pfizer's "Guidelines for Research Records." See

DTX 53; see also Deposition of Julie Marion Miyashiro Vol. 1 (Nov. 3, 2005), at 109:21-112:12. Accordingly, there is ample evidence to support the October 4th reduction to practice date, and the Court finds October 4, 1993 to be the correct invention date *for the individual compound celecoxib*.

The next issue, therefore, is whether the synthesis of one species, celecoxib, supports an invention date of October 4, 1993, for all of the asserted claims of the '823 Patent. The Court finds that it does. One of the asserted claims of the '823 Patent (claim 9) covers only celecoxib.[7] Synthesis of celecoxib on October 4 certainly supports an October 4, 1993 invention date for this claim. The remaining asserted claims cover genuses of compounds that include celecoxib. The Court finds that the synthesis of celecoxib—an individual species within those genuses—on October 4, 1993 is sufficient to establish that date as the proper invention date for the genus claims as well.

The Board of Patent Appeals has held that the first party to conceive a species is the first to conceive of the generic invention. Miller v. Walker, 214 U.S.P.Q. 845, 847 (Bd. Pat. App. 1982). Although the Federal Circuit has not

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[7] Claim 9 reads: "Compound of claim 8 where the compound is 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide, or a pharmaceutically-acceptable salt thereof." This is the chemical structure of celecoxib.

made such a definitive statement, it has held that "conception of a species within a genus may constitute conception of the genus."[8] Oka v. Youssefyeh, 849 F.2d 581, 584 (Fed. Cir. 1988) (emphasis added); see also In re Jolley, 308 F.3d 1317, 1232 n.2 (Fed. Cir. 2002). Moreover, the predecessor to the Federal Circuit has held that a prior reduction to practice of a species establishes priority to the genus in the context of an interference and "precludes another party from claiming that he is the first inventor of the genus containing the species." Mikus v. Wachtel, 504 F.2d 1150, 1151 (C.C.P.A. 1974). Based on this caselaw, the Court finds that the date on which an individual species within a genus is reduced to practice constitutes the invention date for genus claims that include the species.

In re Zletz, cited by Pfizer, is not to the contrary. In Zletz, the Federal Circuit stated: "Priority to a genus may indeed be shown by prior invention of a single species, but the genus will not be patentable to an applicant unless he has generic support therefor." In re Zletz, 893 F.2d 319, 323 (Fed. Cir. 1989) (internal citation omitted). The first caluse of this quotation simply restates the rule explained above and adopted by this Court that invention of a species can establish invention of a genus containing that species. The second clause of the

[8] The Federal Circuit has not elaborated on when conception of a species will constitute conception of a genus and when it will not.

sentence— contrary to Pfizer's interpretation—does not negate this sentiment. The import of the second clause is that even though a party can establish priority to a genus by showing earlier invention of an individual species, he will not ultimately be able to obtain a patent for the genus unless he can provide adequate § 112 support therefor. See id. (citing In re Grimme, 274 F.2d 949, 952 (C.C.P.A. 1960) (discussing the disclosure required to support a generic claim in the field of chemistry)).

Accordingly, the Court finds the invention date for celecoxib and the asserted claims of the '823 Patent to be October 4, 1993.[9]

B. The Scope and Content of the Prior Art

"The scope and content of the prior art is limited to art that is analogous to the claimed invention. Analogous art is that which is from the same field of endeavor or, if not within the field of endeavor, is still reasonably pertinent to the particular problem with which the inventor is involved." Janssen Pharmaceutica

[9] Because neither party has presented any evidence of an earlier invention date for the methods-of-use or compositions covered by the '165 and '068 Patents, the Court finds the appropriate invention date for those patents to be November 30, 1993. Nevertheless, October 4 remains the relevant date for the purposes of determining the obviousness of celecoxib and other compounds within the claims of the '823 patent.

N.V. v. Mylan Pharms., Inc., 456 F. Supp.2d 644, 652 (D.N.J. 2006). As explained above, Teva argues that the patents-in-suit are obvious in light of three prior art references: the Merck '196 Application/'995 Patent, the Fujisawa '142 Patent, and the Fujisawa '829 Application. Pfizer disputes that the '196 Application and the '829 Application are prior art to the patents-in-suit. The prior art status of these two references is discussed below.

1. ___The Merck '196 Application/'995 Patent Is Not Prior Art

On June 24, 1993, Merck and Co., Inc. ("Merck") filed U.S. Patent Application 08/082,196 (the "'196 Application") entitled "Phenyl Heterocycles as COX-2 Inhibitors." In early November 1993, Merck withdrew several claims of the '196 Application from consideration. On November 23, 1993, the Patent Examiner rejected the remaining claims under 35 U.S.C. § 112 for failing to adequately teach how to use the claimed invention (*i.e.*, for failure to satisfy the enablement requirement). The Examiner explained:

> the claims are directed to compounds which selectively inhibit COX-2, compositions containing them, and methods of treating cyclooxegenase mediated diseases using said compounds. The discovery of COX-2 is a recent development in the art, as indicated in the instant specification, and relatively little is known about it and its properties. . . . Relatively little is known regarding the activity of COX-2, and there is no predictability as to which

> compounds will inhibit COX-2. In such a field, the data found in the specification regarding the activity of the claimed compounds is not sufficient to enable the full scope of the invention as claimed. Even within the limited set of compounds tested for activity, the variation of activity is so great that the data cannot be said to create the expectation that the multitude of compounds claimed will have the claimed activity.

(PTX 34 at PFC 02019556.)

On January 10, 1994, Merck filed a continuation-in-part ("CIP") application Serial No. 08/179,467 (the "'467 Application"). The '467 Application included substantial additional data, including *in vivo* data. Shortly thereafter, on February 22, 1994, Merck expressly abandoned the '196 Application. In the remarks section of the express abandonment, Merck stated as follows:

> In an informal interview [the patent examiner] clarified that with regard to the compounds and their use as anti-inflammatory agents, she is concerned that there is insufficient proof that inhibition of COX-2 would translate into anti-inflammatory activity.
>
> In response, applicants point out that this is a question [of] utility (35 USC 101) rather than a failure to teach how to use under 35 USC 112. Indeed, applicants have extensively taught "how to use." See for Example pages 10-16 of the specification. In that there is no 101 rejection, Applicants must assume that the Examiner is not concerned about utility. Accordingly, the present rejection is traversed.
>
> In any event, the above mentioned CIP renders the Examiner's concern moot, in that rat paw edema assay data are provided demonstrating that applicants['] compounds are useful anti-inflammatory agents.

(Id. at PFC 02019560-61.) On December 12, 1995, CIP Application '467 issued as U.S. Patent No. 5,474,995 (the "'995 Patent").

A patent is available as prior art as of the actual filing date of the application that resulted in the patent. See In re Wertheim, 646 F.2d 527, 534 (C.C.P.A. 1981). The reasoning underlying this rule is that the patent could have issued on that day but for delays in the patent office, and "[a]s Justice Holmes said in Milburn, 'The delays in the patent office ought not to cut down the effect of what has been done.'" Id. A question arises where, as here, the patent issues from a CIP application: Is the patent considered prior art as of the date the original parent application was filed (here, June 24, 1993), or only as of the filing date of the CIP (here, January 10, 1994)? This distinction is critical here because the CIP was filed after the invention date for the claims at issue in this case.[10] As such, the '995 Patent can only be prior art if it is entitled to claim priority to the June 24, 1993 filing date of its original '196 Application.

The Federal Circuit has addressed this question, and has held that a patent

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[10] As explained above, see *supra* Section I.A, the Court finds the proper invention date for the claims of the '823 Patent to be October 4, 1993. Notably, however, all three of the proposed invention dates—August 2, October 4, and November 30, 1993—fall in between the filing dates of the original '196 Application and the CIP application. Accordingly, this distinction would be critical with any of these invention dates.

issuing from a CIP is entitled to the earlier filing date of its parent application if—and only if—the disclosures of the parent provide adequate § 112 support for the claims that actually appear in the patent as issued.[11] See, e.g., Go Med. Indus. PTY, Ltd. v. Inmed Corp., 471 F.3d 1264, 1270 (Fed. Cir. 2006) ("A patent application for an invention disclosed in a previously-filed application in a manner that satisfies all the requirements of 35 U.S.C. § 112 is entitled to the benefit of the earlier filing date."); see also In re Wertheim, 646 F.2d at 538 (holding that entitlement to an "earlier U.S. filing date for the patent necessarily depends on further compliance with §§ 120 and 112").[12] Accordingly, determining whether a patent is entitled to claim priority to its parent's filing date generally requires the Court to examine both the parent application and the resulting patent and independently evaluate whether the patent claims were fully supported by the disclosures of the parent application; as applied to this case, the question is

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[11] Section 112 contains three separate requirements: (1) a written description requirement; (2) an enablement requirement; and (3) a best mode requirement. See 35 U.S.C. § 112; see also Univ. of Rochester v. Searle, 358 F.3d 916, 921 (Fed. Cir. 2004). "Although there is often significant overlap between the three requirements, they are nonetheless independent of each other." Univ. of Rochester, 358 F.3d at 921. These requirements are discussed in detail *infra*.

[12] If this condition is met, then any disclosures in the parent application that are "carried forward" into the final patent may be considered prior art. See In re Lund, 376 F.2d 982 (C.C.P.A. 1966).

whether the disclosures of the '196 Application provide adequate § 112 support for the claims of the '995 Patent.

Entitlement to claim priority to the filing date of a parent application may not be available under certain circumstances. See Pennwalt Corp. v. Akzona Inc., 740 F.2d 1573, 1579 (Fed. Cir. 1984). In Pennwalt, the plaintiff's subsidiary filed a patent application that was rejected by the Patent and Trademark Office ("PTO") under 35 U.S.C. § 112 for failure to satisfy the enablement requirement. Id. at 1579. Following this rejection, the subsidiary abandoned the original application and filed a CIP application describing the claims in more detail. Id. The Federal Circuit held that (1) the filing of a CIP in response to a § 112 rejection creates a rebuttable presumption of acquiescence in the PTO's determination that the original application did not comply with the requirements of § 112, and (2) that a finding of acquiescence precludes an inventor from claiming entitlement to the filing date of the original application. Id. at 1579-80. The reason for this preclusion is simple: An inventor who acquiesced in the PTO's conclusion that the claims did not meet the statutory requirements for patentability is estopped from later claiming that these requirements were in fact met. See, e.g., 4 Chisum on Patents § 11.03.

The Pennwalt Court thus made clear that a finding of acquiescence is a

threshold finding, which eliminates the need to independently evaluate whether the claims of an issued patent are supported by the disclosure of a rejected application. Id. at 1280 n.13; see also Moll v. Northern Telecom. Inc., No. 94-5451, 1995 U.S. Dist. LEXIS 17053, at * 10 (E.D. Pa. Nov. 5, 1995) (explaining that a finding that the inventor acquiesced in the PTO's final rejection of the earlier parent application "eliminates the need to [independently evaluate] whether the claims of the patent that issued were supported by the disclosure of the rejected application.").

Notably, Pennwalt and other cases that apply the acquiescence rule generally involve a different factual situation from the instant case. Typically, a patent holder seeks the benefit of the parent application's earlier filing date in order to antedate a potentially invalidating reference. See, e.g., Max Daetwyler Corp. v. Input Graphics, Inc., 608 F. Supp. 1549 (E.D. Pa. 1985). Here, by contrast, an alleged infringer is seeking the benefit of a parent application's earlier filing date in order to make a third party's patent available as a prior art reference to the patents-in-suit.

Pfizer urges the Court to apply the Pennwalt framework here, and argues that the Court need not independently evaluate whether the claims of the '995 Patent are fully supported by the disclosures of the '196 Application because

"[t]he 'filing of a CIP application to overcome a PTO rejection' gives rise to a rebuttable 'presumption of acquiescence in the rejection,' resulting in a presumption that the applicant is not entitled to the earlier filing date." (Pfizer's Post-Trial Brief at 8 (citing Pennwalt, 740 F.2d at 1578).) Teva disagrees, arguing that the Pennwalt framework is not applicable in this factual situation.

The Court finds that the first step of the Pennwalt framework is applicable here, but not the second. The Court agrees with Teva that the estoppel reasoning underlying step two does not apply where, as here, the party arguing for the earlier filing date is not the party that allegedly acquiesced in the PTO rejection. In other words, Teva should not be estopped from arguing that the § 112 requirements were satisfied with respect to the relevant claims of the Merck '196 Application just because Merck (an entirely unrelated party) acquiesced in the PTO's conclusion that the claims did not meet those requirements. C.f. Arkla, Inc. v. U.S., 37 F.3d 621, 624 (Fed. Cir. 1994) (explaining that the parties must have had a full and fair opportunity to litigate the subject at issue for estoppel to apply); Bd. of Trs. of Trucking Employees of New Jersey Welfare Fund, Inc. v. Centra, 983 F.2d 495, 505 (3d Cir. 1992) (same).

There is no similar reason to ignore the first step of the Pennwalt framework. The idea that the filing of a CIP in response to a § 112 rejection

creates a rebuttable presumption of acquiescence in the PTO's determination that the original application did not comply with the requirements of § 112 is equally applicable in the factual context presented here. And although an ultimate finding of acquiescence would not have a step-two preclusive effect in this context, the Court finds that it would still be relevant as evidence that the rejected application did not fully support the claims of the issued patent.

In sum, the Court will apply the following framework to answer the question of whether the '995 Patent is entitled to claim priority to the filing date of the '196 Application: The Court will evaluate the prosecution history of the '196 Application to determine whether there is a *prima facie* case of acquiescence, and if so, whether it is rebutted. Regardless of the Court's finding on this issue, Teva will not be precluded from arguing that the disclosure of the '196 Application provides adequate § 112 support for the claims of the '995 Patent. The Court will undertake an independent evaluation of this question, but will consider a finding of acquiescence as part of its analysis.

(a) Merck Acquiesced in the PTO's Rejection of the '196 Application

There is *prima facie* evidence that Merck acquiesced in the PTO's rejection of the '196 Application based on the fact that Merck filed a CIP (with additional

data) in response to the PTO's § 112 rejection of the Application on enablement grounds. See *supra*. Teva argues that the elements of a *prima facie* case of acquiescence cannot be established because Merck never faced a "final rejection" during prosecution of the Merck '196 Application.[13] The Court is not persuaded by this argument.

Mr. Ronald Smith, Teva's expert on patent office practice and procedure, defined a "final rejection" as a rejection made in a "second office action, after the examiner had already rejected the claims, at least once, and an applicant has had a chance to respond to the rejection. If the examiner still feels the rejection is appropriate he would make the second action final." (Trial Trans. XII 19:13-18.) Mr. Smith also stated that the November 23, 1993 rejection by the patent examiner was not a "final rejection." (Trial Trans. XII 19:19-21.) Teva points to Federal Circuit caselaw stating that "[e]stoppel does not occur . . . in the absence of an explicit *final rejection* under 35 U.S.C. § 112, first paragraph." Waldemar Link, GmbH & Co. v. Osteonics Corp., 32 F.3d 556, 560 (Fed. Cir. 1994).

The Court agrees that the November 23, 1993 rejection of the '196 Application was not a "final rejection," but finds that fact to be irrelevant to

[13] Although Teva does not provide substantial discussion of this point in its Post-Trial Brief, Teva did address this argument in detail in an earlier filing and in its arguments before the Court during trial.

determining the existence of a *prima facie* case of acquiescence. Teva mis-uses the relevant caselaw. Certainly there are cases stating that only a final rejection will give rise to a presumption of acquiescence. See, e.g., Paperless Accounting, Inc. v. Bay Area Rapid Transit System, 804 F.2d 659, 662-64 (Fed. Cir. 1986); Waldemar, 32 F.3d at 560. But in both Paperless Accounting and Waldemar a preliminary § 112 rejection was later withdrawn by the patent examiner in subsequent rejections. "In both cases, the patentee filed the CIP application after the PTO had withdrawn the § 112 objections. Thus, in both cases, there was no acquiescence in a § 112 rejection because there was no pending § 112 rejection when the continuation-in-part application was filed." B&S Plastics, Inc. v. Hydro Air Indus., Inc., No. SA CV 95-492), 1995 U.S. Dist. LEXIS 20791, at *8-*9 (C.D. Cal. Oct. 10, 1995).[14] Without a pending § 112 rejection at the time the CIP

[14] See also 4 Chisum on Patents § 11.03:

> In Paperless Accounting . . . the Federal Circuit . . . held that the filing of a continuation-in-part application ("c-i-p") that added text to the specification of a parent application ("parent") did not constitute a binding admission that the parent did not support the claims in the patent issuing on the c-i-p when the examiner withdrew a previous Section 112 rejection of the claims of the parent that were carried forward in the c-i-p. The applicant did not acquiesce in the examiner's initial Section 112 rejection during the prosecution of the parent because that rejection, not forming the basis of the final rejection, could not have been appealed.

was filed, the applicants were not faced with the choice to fight or submit—and it is the decision to submit rather than fight that gives rise to the *prima facie* case of acquiescence.

In the present case, by contrast, there was an unambiguous rejection of the '196 Application under § 112. Merck could have chosen to fight the rejection or submit to it. As Mr. Smith conceded, Merck could have responded to the rejection and asked the patent examiner to reconsider. It did not do so. It filed a CIP that addressed the examiner's concerns. It chose to submit, impliedly conceding that the disclosure of the application was insufficient. Thus, the elements of a *prima facie* case can be established despite the fact that the rejection was not technically "final."

Moreover, Teva has offered no alternative explanation for Merck's decision to file a CIP. In fact, Mr. Smith, Teva's own witness, conceded that Merck abandoned the '196 Application in favor of the CIP *in response to* the examiner's rejection:

> Q: Then what did the applicants do *in response to the rejection*? . . .
> A: Applicants abandoned the application in favor of the co-pending continuation in part application filed January 10,

1994.[15]

(Trial Trans. XI 66:25-67:8 (emphasis added).)

Accordingly, the Court finds that there is *prima facie* evidence of acquiescence, and will turn to the question of whether there is "countervailing evidence" of non-acquiescence. Pennwalt, 740 F.2d at 1579. Teva vigorously argues that there is ample countervailing evidence in the prosecution history of the '196 Application to rebut a finding of acquiescence. Teva points specifically to Merck's response to the Examiner's rejection, in which Merck stated that it disagreed with the decision and traversed the rejection.

"Traverse" is a term of art in the patent office. It means that the applicant disagrees with the position of the examiner and requests reconsideration. (Trial Trans. X 157:6-13; see also XI 67:22-68:3 ("[Travserse] means that they disagree with the rejection and request that it be withdrawn.").) Mr. Smith testified that "if an applicant was acquiescing in a rejection, he wouldn't file a traversal." (Trial Trans. XII 20:22-23.)

The Court does not find travsersal—in the circumstances presented here—to

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[15] It is important to note that the although the CIP application was "co-pending" at the time Merck abandoned the '196 Application, it was filed on January 10, 1994—nearly two months after the examiner rejected the '196 Application.

be compelling evidence of non-acquiescence. There are two reasons for this finding: one substantive and one procedural. As to the substance of the traversal, Merck never actually disputed the idea that the data was insufficient to establish the utility of the claimed compounds. It merely argued (erroneously) that this was not a § 112 problem. (PTX 34 at PFC 02019560-61 ("[A]pplicants point out that this is a question [of] utility (35 USC 101) rather than a failure to teach how to use under 35 USC 112. Indeed, applicants have extensively taught 'how to use.' In that there is no 101 rejection, Applicants must assume that the Examiner is not concerned about utility. Accordingly, the present rejection is traversed.").) Thus, the traversal does not illustrate disagreement—*i.e.*, non-acquiescence—with the fundamental finding that the disclosed data was insufficient. Moreover, Merck's argument was legally inaccurate. As discussed further *infra*, it is well established that the "use" element of the enablement requirement incorporates the utility requirement of 35 U.S.C. § 101. See *infra*; see also, e.g., In re Fisher, 421 F.3d 1365, 1378 (Fed. Cir. 2005).

The procedural consideration involves the context of the traversal. Merck traversed *in an express abandonment*. As Mr. Smith explained, because Merck set forth its traversal and accompanying argument in an express abandonment, the PTO was never going to consider or act on the traversal in any way:

Q: [The traversal] is in a document where they [Merck] are expressly abandoning the application, right?
A: Yes.
Q: So they are not going to get the examiner to remove or change the rejection at the time that they are abandoning, right?
A: At the time – no, not at the time.
Q: . . . After you file an express abandonment, the Patent Office doesn't have to do anything in that application other than [mark] it as abandoned, right?
A: I think they send out a letter acknowledging the express abandonment, then send the case the abandoned files.

(Trial Trans. XII 29:22-30:9.) This was not Merck's only option. The company could have chosen to simply traverse the rejection *without* abandoning the application. Since the rejection was not final, the examiner could have withdrawn or amended the rejection. By traversing in an express abandonment, Merck effectively eliminated this possibility.

For both of these reasons, the Court is not persuaded that Merck's traversal rebuts the *prima facie* evidence of acquiescence. Accordingly, the Court finds that Merck acquiesced in the PTO's § 112 rejection of the '196 Application.

As explained above, the inquiry does not end here. The Court must still conduct an independent evaluation of whether the claims of the '995 Patent are fully supported by the disclosure of the '196 Application. If so, then all disclosures of the '196 Application that were carried forward into the '995 Patent

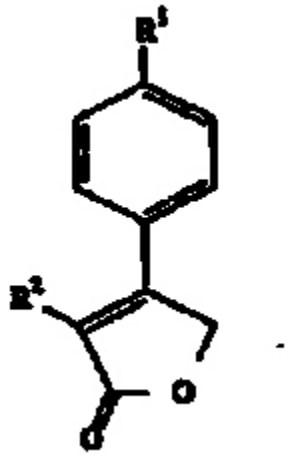
will properly be considered prior art. See In re Lund, 376 F.2d 982 (C.C.P.A. 1966). If not, then the '196 Application/'995 Patent is not prior art, and Teva's entire theory of obviousness will be effectively eviscerated. Merck's acquiescence is but one factor that the Court will consider when conducting this analysis.

(b) Claim 6 of the '995 Patent is Not Supported By the Disclosure of the '196 Application

Teva contends that claim 6 of the '995 Patent is fully supported by the disclosure of the '196 Application. The Court disagrees. The parties do not dispute the relevant facts, only the legal conclusions to be derived therefrom.

i. *Undisputed Facts*

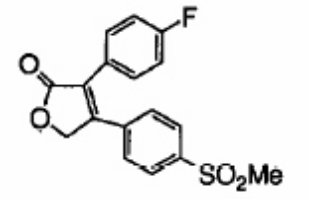
Claim 6 of the '995 Patent is a genus claim covering dozens of chemical compounds:

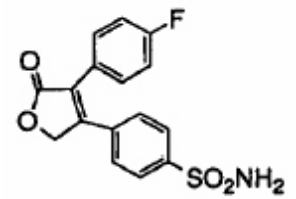


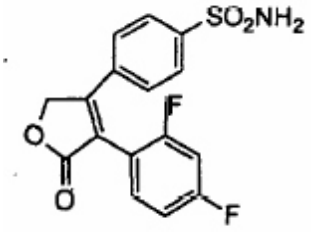
6. A compound according to claim 5 wherein R^1 is selected from the group consisting of
(a) $S(O)_2CH_3$, and
(b) $S(O)_2NH_2$,
R^2 is mono or di-substituted phenyl wherein the substituents are selected from the group consisting of
(1) hydrogen,
(2) halo, selected from the group consisting of fluoro, chloro and bromo.

The claim requires a furanone core,[16] one phenyl ring with a sulfonamide or methylsulfone substituent, and another phenyl ring with one or two substituents chosen from hydrogen (H), flouro (F), chloro (Cl), or bromo (Br) in any of the available positions. Finally, claim 6 requires that the two phenyl rings be attached at a double bond.

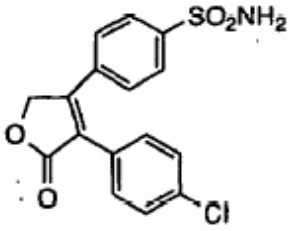
The '196 Application covers several thousand compounds. Tables 1 and 2 of the '196 Application include several examples of covered compounds. (DTX 302 at 31-43.) Examples # 9 and # 10 in table 1 of the '196 Application are within the genus disclosed in claim 6 of '995 Patent. (Id. at 33.) Three (unnumbered) examples in table 2 of the '196 Application are also within the genus disclosed in claim 6 of '995 Patent. (Id. at 39.) Thus, five—and only five—compounds within the genus of claim 6 of the '995 Patent are disclosed in the '196 Application. These five compounds are reproduced below:

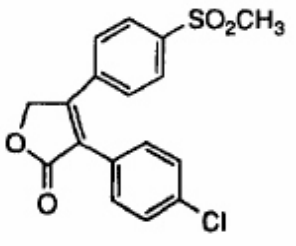






[16] A furanone is a five sided ring with one oxygen atom on the ring and another oxygen atom attached to the ring by a double bond.





These five compounds show diphenyl furanones with one phenyl substituted with a sulfonamide or methylsulfone and with a flourine or chlorine on the second phenyl. Importantly, however, the compounds do not cover the full scope of claim 6. (Trial Trans. VII 126:13-20.) For example, none of the five compounds use a bromine substituent. None of them include two different substituents. Nor do they cover the full range of possible positions for the mono- or di-substituted substituents.

As for data, the '196 Application includes in vitro data for two of the examples (examples 9 and 10). (Id. at 45-46.) There is no in vivo data disclosed in the '196 Application, but it does include a description, written in the past tense, of a rat paw edema assay.[17] (Id. at 44.)

[17] The rat paw edema assay is a common in vivo test to evaluate the anti-inflammatory activity of a compound. The import of Merck's use of the past tense to describe the protocol for this assay is hotly disputed by the parties, and is

Finally, the '196 Application provides a detailed description for synthesizing example 9, and a general method for synthesizing example 10. Notably, the synthesis procedure for example 9 set forth in the '196 application is not included in the CIP application or the '995 Patent. It was replaced by a different procedure.

ii. *The Disclosure of the '196 Application Does Not Satisfy the Written Description Requirement for Claim 6 of the '995 Patent*

A patent must contain a written description of the claimed invention. See 35 U.S.C. § 112 (stating that the "specification shall contain a written description of the invention"). The written description must reasonably convey to a person of ordinary skill that the inventor possessed the entire invention—here, the entire genus covered by claim 6 of the '995 Patent—as of the application filing date. Eiselstein v. Frank, 52 F.3d 1035, 1039 (Fed. Cir. 1995); see also In re Reiffin, No. 06-1063, 2006 U.S. App. LEXIS 25246, at *5 (Fed. Cir. Oct. 6, 2006) (not precedential) (The "disclosure as originally filed must convey with reasonable clarity to those skilled in the art that [another] was in possession of the invention.") (internal quotations omitted). Thus, the question in this case is

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discussed in detail in Section I.D.1(b), *infra*.

whether the five examples disclosed in the '196 Application would convey to a person of ordinary skill that Merck possessed the entire genus of claim 6 of the '995 Patent as of the filing date of the '196 Application.

It is well established that the written description requirement does not require a description of every possible embodiment falling within the scope of a genus claim, and that disclosure of a few species can reasonably convey possession of a genus and thus satisfy the written description requirement. See, e.g., In re Curtis, 354 F.3d 1347 (Fed. Cir. 2004); Bilstad v. Wakalopulos, 386 F.3d 1116, 1124 (Fed. Cir. 2004). Indeed, "disclosure of [even a single] species *may be* sufficient written description support for a later claimed genus including that species." Bilstad, 386 F.3d at 1124. But it is not always sufficient. "There are . . . exceptions to the general rule that disclosure of a species provides sufficient written description support for a later filed claim directed to the genus." Id. at 1125. In Bilstad, the Federal Circuit surveyed several cases that considered the issue of written description support for an added genus claim when only a species was disclosed. The Court determined that the critical distinction between cases where disclosure of a species sufficed and those where it did not was the level of predictability in the relevant art:

> The distinction in these cases is based upon what would be

> reasonably conveyed to a person skilled in the art at the time of the original disclosure. If the difference between members of the group is such that the person skilled in the art would not readily discern that other members of the genus would perform similarly to the disclosed members, i.e., if the art is unpredictable, then the disclosure of more species is necessary to adequately show possession of the entire genus.

Id. In other words, the primary exception to the general rule that disclosure of a species is a sufficient written description of a later claimed genus involves inventions in unpredictable fields. Id. ("[U]npredictability in the particular field may warrant closer scrutiny of whether disclosure of a species is sufficient to describe a genus."). In an unpredictable field, a broader disclosure is required.

Pharmaceutical chemistry is a highly unpredictable field. See, e.g., 2 Chisum on Patents § 5.04 ("Because of the unpredictable nature of chemical reactions, a newly-synthesized compound may be very similar in structure to known and existing compounds and yet exhibit very different properties."). Indeed, the Federal Circuit has expressly stated that the particular chemistry involved in the development of celecoxib was and is highly unpredictable. In an opinion in separate case involving the development of celecoxib, the Federal Circuit wrote:

> 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 1993-1995 period . . . .

Univ. of Rochester v. Searle, 358 F.3d 916, 925 (Fed. Cir. 2004). Moreover, the evidence presented in this case confirms the unpredictability of the field. For example, Dr. Talley—one of the inventors of celecoxib—testified about two compounds that were produced by his team. The two compounds were identical except that the positions of two substituent groups were reversed. With the groups in one position, the compound was a good inhibitor. With the groups in the reverse position, the compound was devoid of activity. (Trial Trans. XV 57:15-58:8; see also id. at XII 71:18-80:23 (Dr. Seibert); *infra* Section I.D.4.)

In its Post-Trial Brief, Teva contends Dr. Trummlitz testified that based on the disclosure of the '196 Application, the person of ordinary skill would have understood that the inventors of the '196 Application possessed all of the compounds of Claim 6 of the '995 Patent. (Teva's Post-Trial Brief at 130.) Teva cites volume four of the trial transcript at 92:17-94:2 and 103:19-114:2. The Court has reviewed the transcript and does not find any such assertion in Dr. Trummlitz's testimony. Moreover, even if such a statement could be extrapolated from Dr. Trummlitz's testimony, Teva has offered no persuasive reasoning or supporting evidence as to why or how disclosure of five examples would

reasonably convey to a person of ordinary skill that Merck actually possessed the entire genus of claim 6 on June 24, 1993.

Teva also argues that three additional compounds that were disclosed on page 41 of the '196 Application provide written description support for claim 6 of the '995 Patent. The Court disagrees. The three compounds at issue are 4,5 diphenyl furanones. In other words, they are diphenyl furanones with a double bond between the carbon atoms in the 4 and 5 positions. Teva admits that these compounds are not within the scope of claim 6, but nevertheless argues that they should be considered because they are "in equilibrium" with three 3,4 furanones that are within the scope of the claim.

When compounds are in equilibrium, it means that if one compound is present, both will be present. Thus, according to Teva, when looking at the 4,5 furanones in the '196 Application, the person of ordinary skill would "immediately envision the 3,4 furanones" as well. (Teva's Post-Trial Brief at 132.) By way of evidence in support of this assertion, Teva cites to the testimony of Pfizer's medicinal chemistry expert, Dr. William Jorgensen. Teva asserts that Dr. Jorgensen admitted the different compounds could be in equilibrium, but the Court does not read Dr. Jorgensen's testimony to support this assertion. The relevant testimony was as follows:

> Q: That furanone, the 4, 5 configured furanone, would be in equilibrium with a 3, 4 furanone, wouldn't it?
>
> A: I am not sure you want to go there. For compounds like this you can imagine multiple equilibrium. . . . They are [in] [e]quilibrium in the sense that any two isomers, if you have enough heat, it will convert it. That is a better way to do it. If you think about 3, 4, and the 4,5[] furanone, they are different molecules. . . . And there is some barrier in between them. If there is enough heat you might be able to get them over that barrier or they might decompose on you. So in principal . . . now, quote, they are in equilibrium in the sense that they are isomers. And maybe you could equilibriate thermally. Maybe not. Maybe they would decompose.

(Trial Trans. XVI 111:24-112:15.) Dr. Jorgensen clearly stated that the 4,5 furanones and the 3,4 furanones are different molecules," and that although "they are isomers," they might "decompose" if one tries to equilibrate them. (Id.)

Teva offers no evidence other than Dr. Jorgensen's testimony that the compounds are in equilibrium. Teva's expert's did not address the idea. There are no documents that support it. Moreover, Teva offered no evidence, other than its bald assertion, to support the idea that the person of ordinary skill would immediately envision the 3,4 furanones even if the compounds were in equilibrium. Accordingly, the Court will not consider the 4,5 furanones as providing support for claim 6 of the '995 Patent.

In sum, given the unpredictability of the art, the Court finds that the written

description requirement for claim 6 of the '995 Patent is not satisfied by the disclosure of five individual compounds in the '196 Application. This finding alone would be sufficient to hold that claim 6 is not fully supported by the disclosure of the '196 Application; however, the Court also finds that other § 112 requirements are not met.

iii. *The Disclosure of the '196 Application Does Not Satisfy the Enablement Requirement for Claim 6 of the '995 Patent*

Section 112 also includes an enablement requirement. See 35 U.S.C. § 112 ("[T]he specification shall contain a written description . . . of the manner and process of making and using [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."). Although related, the written description and enablement requirements are distinct and must be analyzed separately. See, e.g., 3 Chisum on Patents § 7.04; Invitrogen Corp. v. Clontech Labs. Inc., 429 F.3d 1052, 1071 n.17 (stating that the "written description requirement is distinct from the enablement requirement"). Even assuming *arguendo* that the disclosure of the '196 Application satisfies the written description requirement with respect to claim 6 of the '995 Patent, the claim would

not be fully supported because the enablement requirement is not met.

To satisfy the enablement requirement, the disclosure "must teach those skilled in the art how to *make* and *use* the full scope of the claimed invention without 'undue experimentation.'" Univ. of Rochester v. Searle, 249 F. Supp.2d 216, 231 (W.D.N.Y. 2003). The Federal Circuit has explained the "undue experimentation" standard as follows:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564 (Fed. Cir. 1996) (quotation and citation omitted). The Federal Circuit has also set forth factors to consider in determining whether a disclosure would require undue experimentation: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

Importantly, the "use" element of the enablement requirement also

incorporates the utility requirement of 35 U.S.C. § 101:

> The how to use prong of *section 112* incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention. If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112.

In re Ziegler, 992 F.2d 1197, 1200-01 (Fed. Cir. 1993) (citations omitted); see also In re Fisher, 421 F.3d 1365, 1378 (Fed. Cir. 2005) ("It is well established that the enablement requirement of § 112 incorporates the utility requirement of § 101."). In other words, a showing of practical utility of the claimed invention is necessary to satisfy the enablement requirement.

As best as the Court can tell, Teva's argument is essentially as follows: (1) the synthesis information and in vitro data included in the '196 Application are sufficient to enable a person of ordinary skill to make and use the five examples disclosed in the '196 Application, and (2) this is sufficient to enable a person of ordinary skill to make and use all of the compounds covered by claim 6 of the '995 Patent without undue experimentation.

Turning to the first step of Teva's argument, Teva asserts that the synthesis information included in the '196 Application would enable a person of ordinary skill to make the disclosed examples, and that the in vitro data disclosed in table 3

of the '196 Application would be sufficient to prove the utility of the examples, and enable the person of ordinary skill to use them. Pfizer contends that the "use" element of the requirement is not satisfied because, due to the large number of compounds disclosed in the '196 Application and the lack of any in vivo data, there was no basis to conclude that any particular compound of the Application was in fact anti-inflammatory as asserted in the specification.

In vitro data can be sufficient to establish the utility of a chemical compound. In vivo data is not always required. See, e.g., In re Fisher, 421 F.3d at 1376-78; Cross v. Iizuka, 753 F.2d 1040 (Fed. Cir. 1985). In Cross, Iizuka filed an application claiming thromboxane synthetase inhibitors, which were alleged to be useful in treating inflammation, asthma, hypertension, and other health problems. Cross filed an application claiming the same compounds two months later, and the PTO declared an interference. The dispositive issue in the case was whether Iizuka's application, which included in vitro, but not in vivo, data, was sufficient to comply with the practical utility requirement of § 101. Id. at 1050. The Board of Patent Appeals held that it was, and the Federal Circuit agreed. Id. ("Based upon the facts of this case, we are not persuaded that the Board erred in finding that the *in vitro* utility disclosed in the [Iizuka application] is sufficient to establish a practical utility."). The Court explained its reasoning as follows:

> Opinions of our predecessor court have recognized the fact that pharmacological testing of animals is a screening procedure for testing new drugs for practical utility. This in vivo testing is but an intermediate link in a screening chain which may eventually lead to the use of the drug as a therapeutic agent in humans. We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question. Successful in vitro testing will marshal resources and direct the expenditure of effort to further in vivo testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an in vivo utility.
>
> Today, under the circumstances of the instant case, where the Japanese priority application discloses an in vitro utility, *i.e.*, the inhibition of thromboxane synthetase in human or bovine platelet microsomes, and where the disclosed in vitro utility is supplemented by the similar in vitro and in vivo pharmacological activity of structurally similar compounds, *i.e.*, the parent imidazole and 1-methylimidazole compounds, we agree with the Board that this in vitro utility is sufficient to comply with the practical utility requirement of § 101.

Id. at 1051 (internal citations omitted).

The Court understands the opinion in Cross to stand for the proposition that in vitro data can suffice to establish practical utility when "the disclosed in vitro utility is supplemented by the similar in vitro and in vivo pharmacological activity of structurally similar compounds." In these circumstances, the person of ordinary skill can be reasonably confident that the disclosed compounds will work as claimed despite the lack of in vivo data for the specific compounds covered by the

claim. Teva argues that these circumstances are present here because there was published in vitro and in vivo data for the type of compounds claimed in the '196 Application, substituted diphenyl heterocycles, which would lead the person of ordinary skill to assume a correlation between in vitro and in vivo efficacy in the claimed compounds. The Court disagrees.

The only evidence supporting Teva's argument is the testimony of Dr. Trummlitz. Dr. Trummlitz testified that the person of ordinary skill could have concluded that the compounds of the '196 Application were anti-inflammatory despite the lack of in vivo data. He explained that the Fujisawa '142 Patent and WO 708 Patent both included in vitro and in vivo data for similar compounds, and that DuP 697 was known by 1993 to be anti-inflammatory and believed to be COX-2 selective. Based on this published data, Dr. Trummlitz asserted that "one could conclude that this type of compound will work." (Trial Trans. IV 107:8-9.) He also stated:

> I think the general method if we are working in a new area, if you have new compounds, you need very early the link between in [vitro] and in vivo. If you have already data showing good correlation, then it is not so important, you will do it later, the in vivo studies.

(Trial Trans. IV 107:9-13; see also Trial Trans. IV 109:24-114:21.)

The Court is not persuaded by this testimony. As an initial matter, COX-2

selective anti-inflammatory development was a "new area" in 1993. As the Patent Examiner who reviewed the '196 Application stated: "The discovery of COX-2 is a recent development in the art, as indicated in the instant specification, and relatively little is known about it and its properties." (PTX 34 at PFC 02019556.) Thus, even according to Dr. Trummlitz's own testimony, the person of ordinary skill would have needed to see the link between in vitro and in vivo activity at the time the '196 Application was filed.

Moreover, several of Pfizer's witnesses testified that without in vivo data, the person of ordinary skill would not have known whether the compounds were anti-inflammatory. Dr. Jorgensen testified that the lack of in vivo data in the Application "means that the compounds that are disclosed are not necessarily antiinflammatory," and that "antiinflammatory [activity] would have to be determined in an in vivo experiment." (Trial Trans. XVI 51:6-12.) Dr. Seibert, who spoke about her experiences on the team that developed celecoxib, testified that not all compounds that "worked" in vitro were anti-inflammatory in vivo. She stated that they could not predict on the basis of in vitro data whether a compound would be active in vivo: "[Y]ou had to do the study. You could not predict." (Id. XII 74:5-16.) Dr. Talley, another inventor of celecoxib, testified that even when a compound performed well in in vitro assays, he could not tell whether it would be

anti-inflammatory until the compound was tested in a laboratory animal. (Id. XV 67:7-13.) Dr. Galbraith, who gave the presentation on DuP 697 at the Keystone conference, testified that anti-inflammatory activity must be determined based on in vivo studies and data. (Id. XVII 10:22-11:4 (explaining the need for "in vivo data where you actually had animal, experimental results showing that the compounds were antiinflammatory in nature").) Indeed, even Dr. Wolfe—one of Teva's own medical experts—testified that in vitro and in vivo test results do not always match up. (Trial Trans. V 147:9-23.)

Finally, the Patent examiner who reviewed the '196 Application also agreed with this assessment. She rejected the Application on the ground that "there [was] insufficient proof that the inhibition of COX-2 would translate into anti-inflammatory activity." PTX 34 at PFC 02019560; see also Trial Trans. XVI 51:16-52:24. Merck's acquiescence in this rejection is the proverbial last nail in the coffin; the final piece of evidence that the disclosure of the '196 Application does not enable even its own claimed compounds.

Turning to step two of Teva's argument as set forth above, the Court finds that even assuming the disclosure of the '196 Application would have enabled the person of ordinary skill to make and use the five examples, this would not have enabled a person of ordinary skill to make and use the entire scope of claim 6 of

the ‘995 Patent.

As discussed *supra*, the examples and supporting information in the ‘196 application do not cover the entire genus of claim 6. This is not always fatal to enablement of a claim, but as with the written description requirement, the amount of disclosure required to enable the full scope of a genus claim depends, in large part, on the degree of predictability in the relevant field. The Federal Circuit has highlighted the importance of unpredictability in evaluating the enablement of generic claims:

> In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. Enablement is lacking in those cases, the court has explained, because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation.

PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564 (Fed. Cir. 1996) (internal citations omitted)

Given the unpredictability of pharmaceutical chemistry in general, and of COX-2 selectivity in particular, information and data on more than a handful of species was necessary to enable a person of ordinary skill to make and use the full scope of the genus claimed in claim 6 of the ‘995 Patent without undue

experimentation, and to be confident in its utility. Teva offers virtually no evidence in support of its conclusory statement that a person of ordinary skill would be able to generalize the information provided to cover the full scope of the claim. Teva once again cites to Dr. Trummlitz's testimony reproduced in volume 4 of the transcript at 92:17-94:2 and 103:19-114:2. Having reviewed the cited testimony, the Court finds no persuasive explanation of how the disclosure of the '196 Application would enable all of the compounds of claim 6. The entirety of the testimony on this specific question seems to be as follows:

> Q: How, if at all . . . does the lack of any specific in vivo data impact your opinion that the '196 application provides support for the claims in the '995 patent which you just identified[?]
> A: I think the claims of the '995 patent are supported by the data in the '196 application.
> Q: For the same reasons or different reasons?
> A: For the reasons I mentioned before. Because the data are present. Which know what the correlation between in vitro and in vivo is.

(Trial Trans. IV 109:14-23.) This falls far short of persuasively explaining how the disclosure of the '196 Application enables the full scope of claim 6.

The Federal Circuit has explained that the written description requirement and enablement requirement "usually rise and fall together." LizardTech Inc. v. Earth Resource Mapping, Inc., 424 F.3d 1336, 1346 (Fed. Cir. 2005). This case is

no exception.

> [A] recitation of how to make and use the invention across the full breadth of the claim is ordinarily sufficient to demonstrate that the inventor possesses the full scope of the invention, and vice versa. . . . Whether the flaw in the specification is regarded as a failure to demonstrate that the patentee possessed the full scope of the invention recited in claim [6 of the '995 Patent] or a failure to enable the full breadth of that claim, the specification provides inadequate support for the claim under section 112, paragraph one.

Id. In sum, the Court finds that the enablement requirement for claim 6 of the '995 Patent is not satisfied by the disclosure of the '196 Application.

iv. *The '196 Application Does Not Violate the Best Mode Requirement*

The final requirement of § 112 is that the application must "set forth the best mode contemplated by the inventor for carrying out his invention." 35 U.S.C. § 112. Pfizer contends that the "best mode requirement" is not met for claim 6 of the '995 Patent. Specifically, Pfizer argues that Merck identified Vioxx as the best mode of the invention, but failed to disclose the compound in the '196 Application.

The Court does not agree that the failure to disclose Vioxx in the '196 Application constitutes a violation of the best mode requirement. There is no evidence that Vioxx was the inventors' preferred embodiment at the time the '196

Application was filed. In the absence of a subjective preference *at that time*, there can be no best mode violation. See Go Med. Indus. PTY, Ltd. v. Inmed Corp., 471 F.3d 1264, 1270 (Fed. Cir. 2006).

v. *Summary of Claim 6*

In sum, the Court finds that claim 6 of the '995 patent was not fully supported by the disclosure of the '196 Application since neither the written description nor enablement requirements were satisfied by the disclosure.

(c) Claim 15 of the '995 Patent is Not Supported By the Disclosure of the '196 Application

Teva contends that claim 15 of the '995 Patent is fully supported by the disclosure of the '196 Application. As with claim 6, the parties do not dispute the relevant facts, only the legal conclusions to be derived therefrom.

i. *Undisputed Facts*

Claim 15 of the '995 Patent is a Markush claim that lists 36 compounds. (PTX 17, at col. 76.) The first two compounds of Markush claim 15 of the '995 Patent are the same as the compounds of examples 9 and 10 of the '196 Application. As explained above, the '196 Application also includes data and

synthesis methods for these two compounds. The other 34 compounds are not disclosed anywhere in the '196 Application. Teva claims that § 112 support for the first two compounds of Markush claim 15 is sufficient to describe and enable the entire claim. Pfizer disagrees and further argues that the '196 Application fails to provide adequate support for even those first two compounds.

ii. *Adequate Section 112 Support for Markush Claims*

"A Markush group is a listing of specified alternatives of a group in a patent claim." Abbott Labs. v. Baxter Pharm. Prods., 334 F.3d 1274, 1280 (Fed. Cir. 2003). Markush claims usually cover a family of compounds by defining the structure common to all members, as well as one or more alternatives selected from a set consisting of named chemical compounds. A letter, most often the letter "R," is typically used to represent the set of alternatives. Roger Schechter and John Thomas, Principles of Patent Law 217 (2d ed). For example: "A compound of the formula OH – CH – R, where R is selected from the group consisting of chlorine, bromime, and iodine." Id.

> Although this simple example neatly illustrates the Markush format, it may not fully convey the desirability of this type of claim. In this case, if the Markush format were unavailable an inventor could simply three draft claims individually reciting chlorine, bromime and iodine. But in the real world of chemistry

> the relevant alternatives often constitute chemical radicals that may themselves consist of hundreds of closely related compounds. Inventors in such fields as pharmacology . . . would be sorely pressed if required to draft dozens or hundreds of claims to define each and every member of the alternative group.

Id.

Teva claims that a Markush group is fully supported as long as there is adequate § 112 support for even one member of the Markush group. Pfizer vigorously disputes this proposition, and contends that Markush claims require support for each member of the Markush group. There is little caselaw on this question. Indeed, there is little caselaw on Markush claims in general. Given that over 1,000 patents with Markush claims issue in the United States every year,[18] one would expect this to be a common issue with a settled answer. However, this is not the case. Pfizer and Teva direct the Court to one case each. In an independent search of the caselaw, the Court was unable to find any other relevant cases and virtually no guidance in treatises or other texts.

Teva relies on Ex parte Ebata, 19 U.S.P.Q.2d 1952 (Bd. Pat. App. & Inf. 1991). Ebata filed a patent application on June 10, 1981. This application was

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[18] See Peter J. Dehlinger, A Not-so-Radical Proposal for Selecting Radical Substitutions in Markush Type Claims, 74 J. PAT. & TRADEMARK OFF. SOC'Y 463, 463 (1992). Although this article was written over a decade ago, it is likely that the number of patents with Markush claims has increased in that time as chemical innovation has accelerated.

followed by a series of CIP applications, the last of which—No. 07/045,775 (the "'775 Application")— was filed on April 29, 1987. The patent examiner rejected the application as obvious over several prior art references, including U.S. Patent No. 4,761,426 (the "Martin Patent"). Ebata appealed.

The Martin Patent also resulted from a series of continuation and continuation-in-part applications culminating with application No. 06/643,763 (the "'763 Application"), which was filed on August 24, 1984. The Martin Patent issued from the '763 Application on August 2, 1988. For the sake of clarity, the various applications that led to the Martin and Ebata Patents are listed in the chart below.

	Martin History	Ebata History
October 8, 1980	App. No. 06/196,722	
June 10, 1981		App. No. 06/272,387
August 7, 1981	CIP No. 06/291,134	
July 1, 1983		CIP No. 06/509,983
August 24, 1984	Cont. No. 06/643,763	
April 4, 1985		CIP No. 06/719,045
April 29, 1987		CIP No. 07/045,775 (rejected)
August 2, 1988	Martin Patent Issues	

The Board of Patent Appeals began its opinion by stating that "*if* the Martin

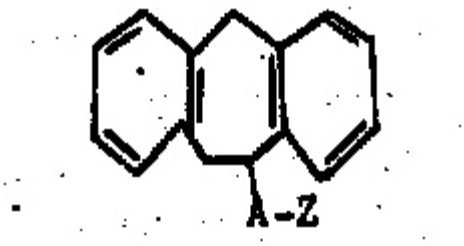
patent constitutes legally available prior art in this case, the relevant subject matter disclosed by Martin anticipated claim 23 within the meaning of 35 U.S.C. 102." Id. at 1954. The Board then turned to what it considered the "real question," "whether and to what extent Martin constitutes legally available prior art under 35 U.S.C. 102(e)." Id. In this regard, the Board had to determine whether the Martin Patent was entitled to claim priority to the October 8, 1980 filing date of its (grand)parent application. Only if it was entitled to that date would it be available as prior art. Id.

Claim 2 of the Martin Patent was a Markush claim covering four salt forms of lysocellin. The Board held that the Markush claim was full supported by the '722 Application, which disclosed one of the four salt forms. Id. at 1955 ("[T]he specific recitation of the manganese salt or complex is fully described within the meaning of 35 U.S.C. 112, first paragraph, in grandparent application Serial No. 06/196/722."). The Board explained its reasoning as follows:

> Bear in mind that the Markush group of claim 2 is merely an arbitrary subgenus covering four salt forms of lysocellin . . . . This is tantamount to claiming the administration of each salt form or embodiment separately in separate claims. It would elevate form over substance to hinge a legal conclusion, respecting availability of the Martin patent as a reference, on whether Martin set forth four separate claims directed to patentable salt forms or, as in claim 2 here, set forth a Markush group covering the four embodiments alternatively.

Id.

Pfizer, meanwhile, relies on In re Fouche, 439 F.2d 1237 (C.C.P.A. 1971), to support its position that all members of a Markush group must have adequate § 112 support. In Fouche, the inventors claimed "a class of compounds having pharmaceutical utility due to their antidepressant, neuroleptic and tranquilizing properties." Id. at 1238. The Patent Office rejected claims 1-3 of the application, and the Board of Patent Appeals affirmed the rejection. Claim 1 was a Markush claim covering a range of compounds:

> 1. A dibenzo [a, d] cycloheptadiene derivative of the formula:
>
> 
>
>
> and its acid addition salts and quaternary ammonium derivatives in which A is a divalent, saturated aliphatic hydrocarbon chain of 2 to 5 carbon atoms, such that at least 2 carbon atoms separate the radical Z from the dibenzocycloheptadiene ring, and Z is a member selected from the group consisting of amino, monoalkylamino, dialkylamino, in which the alkyl radicals contain 1 to 5 carbon atoms each, and 1-pyrrolidinyl, piperidino, morpholino, 1-piperazinyl, and 4-alkyl-1-piperazinyl in which the alkyl radical contains 1 to 5 carbon atoms, and such rings substituted by at least one alkyl radical of 1 to 5 carbon atoms each.

The Patent Examiner rejected this claim on the ground of insufficient disclosure under § 112. The Examiner noted that the definition of "Z" in the claim was by a Markush group including both aliphatic and heterocyclic members, and found that the specification did not enable use of compounds within the claim having heterocyclic moieties. Id. at 1242. None of the examples included compounds wherein Z was heterocyclic. Id. The Court agreed that the application failed to teach a person of ordinary skill how to use the heterocyclic members and affirmed the PTO's rejection of claim 1. The Court stated:

> It seems clear, and it is not disputed by appellant, that where an applicant undertakes to define his invention by the recitation of a Markush group, he must enable one of skill in the art to make and use at least one composition employing each member of the Markush group.

Id.

Both parties offer various interpretations of the cases and attempt to distinguish the unfavorable opinion on various grounds—none of which the Court finds particularly persuasive. The Court need not resolve this complicated question because the evidence does not establish that even the first two compounds of Markush claim 15 are fully supported by the disclosure of the '196 Application.

iii. *The '196 Application Does Not Enable the First Two Compounds of Claim 15 of the '995 Patent*

Since compounds 1 and 2 of claim 15 are expressly disclosed in the '196 Application, there can be no dispute that the written description requirement is met with respect to those specific compounds. The enablement requirement, however, if not satisfied even with respect to these two particular compounds. As discussed in detail in Section I.B.1(b), given the lack of in vivo data in the '196 Application, the person of ordinary skill would not know whether examples 9 and 10 (which are compounds 1 and 2 of claim 15) were anti-inflammatory. Since the Application fails to establish the practical utility of those compounds, it also fails to enable them under § 112. Thus, even under Teva's interpretation of the law, claim 15 of the '995 Patent is not fully supported by the disclosure of the '196 Application because the enablement requirement is not satisfied.

(d) Conclusion Regarding the '196 Application/'995 Patent

Since neither claim 6 nor claim 15 or the '995 Patent are fully supported by the disclosure of the '196 Application, the '995 Patent is not entitled to the June 24, 1993 filing date of the '196 Application. Accordingly, the '196 Application/ '995 Patent is not prior art to the patents-in-suit.

2. The '829 Application Is Prior Art to the Patents-in-Suit

The Fujisawa '829 Application was published on August 11, 1993. Pfizer initially argued that the '829 Application was not prior art to the patents-in-suit because celecoxib was invented on August 2, 1993—nine days prior to this reference date. As discussed above, Pfizer has abandoned this argument and the Court has established the invention date to be October 4, 1993. See *supra* Section I.A. Accordingly, the '829 Application is proper prior art.

C. The Level of Ordinary Skill in the Prior Art

The second Graham factor is the level of ordinary skill in the prior art. The obviousness analysis is conducted from the perspective of a person at that skill level. 35 U.S.C. § 103(a). This hypothetical person of ordinary skill is an objective legal construct who is presumed to be aware of all the relevant prior art. Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc., 807 F.2d 955, 962 (Fed. Cir. 1986).

While the person having ordinary skill knows all of the prior art, s/he is neither a genius nor an innovator. "A person of ordinary skill in the art is also presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate, whether by patient, and often

expensive, systematic research or by extraordinary insights, it makes no difference which." Standard Oil Co. v. Am. Cyanamid Co., 774 F.2d 448, 454 (Fed. Cir. 1985); see also Life Techs., Inc. v. Clontech Labs., Inc., 224 F.3d 1320, 1326 (Fed. Cir. 2000).

The parties in this case dispute the appropriate educational background of the person having ordinary skill in the art. Pfizer argues that such a person would have a bachelor's or master's degree in chemistry or a related science and several years of experience at a pharmaceutical or biotechnology company. Teva claims that the person of ordinary skill would have a PhD in chemistry or a related science plus several years of experience. "The dispute appears to be somewhat academic (so to speak)." Janssen Pharmaceutica N.V. v. Mylan Pharms., Inc., 456 F. Supp. 2d 644, 653 (D.N.J. 2006). Neither party contends that the educational background of the person of ordinary skill is determinative of whether the patents-in-suit are obvious or not. Additionally, neither party provided evidence on how specific prior art references in the record would have been viewed differently depending upon the educational background of the person of ordinary skill.

Furthermore, it appears that few courts conducting an obviousness analysis ever specify the exact level of ordinary skill in the art. In the opinion of one authority, this is because, "[i]n practice, the concept of 'a person of ordinary skill

in the art' seems more designed to remind judges to put themselves in the shoes of a skilled artisan, rather than to compel a specific factual finding." Roger Schechter & John Thomas, Principles of Patent Law, § 5.3.2.2 (2d ed. 2004).

To the extent that it matters, the Court agrees with Pfizer that the person of ordinary skill would have a bachelor's or master's degree in chemistry or a related science and several years experience working in the relevant field. Pfizer's expert in pharmaceutical chemistry so testified (Trial Trans. XVI 50:11-19), and one of the inventors of celecoxib testified that only half the people on the team that developed celecoxib had PhDs. The other half had a bachelor of science or master's degree in chemistry or a related science. (Id. XV 45:6-13.) Although both of Teva's chemistry experts testified that the person of ordinary skill would have had a PhD, the Court finds the combination of hypothetical and real world testimony presented by Pfizer's witnesses to be more persuasive.[19]

Pfizer also argues that Teva's person of ordinary skill is, contrary to law, someone who invents. Pfizer relies in part on the testimony of one of Teva's

[19] The Court stresses, however, that its ultimate ruling that the patents-in-suit are not invalid is not dependent upon this finding. The Court would find the patents-in-suit nonobvious even were it to hold that the person of ordinary skill possessed a doctorate degree. As noted above, the parties have neither argued not presented any evidence tending to show that particular pieces of prior art would have been viewed any differently if the person evaluating it had a bachelor's, master's, or doctorate degree.

expert witnesses, Dr. Baker, who stated that he derived the pharmacophore through the use of his own intuition. The Court does not find this to be persuasive evidence. "Intuition" is not synonymous with "invention." A comparison of the definitions of the two words is illustrative.

- "Intuition" is defined as "the act or process of coming to direct knowledge or certainty without reasoning or inferring," "immediate cognizance or conviction without rational thought," and "immediate apprehension or cognition." Webster's Third New International Dictionary 1187 (1993).

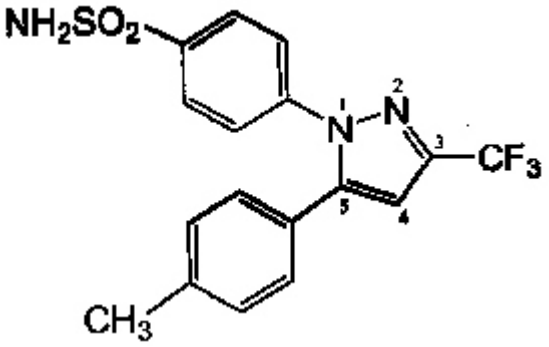
- "Invention," by contrast, is defined as "the power to conceive new ideas and relationships," "a faculty for creative selection of theme and imaginative treatment of design or content," and "a product of thought or mental synthesis." Id. at 1188.

Accordingly, the Court does not interpret Dr. Baker's statement regarding his use of intuition as a concession that Teva's person of ordinary skill is one who invents.

Pfizer also relies on testimony of Teva's experts that the person of ordinary skill is "trying to get a patent," and makes choices with the goal of avoiding prior art and creating a patentable invention. This issue is addressed below in the context of the specific choices—*i.e.*, steps in Teva's obviousness theory—that are predicated on that goal.

D. The Differences Between the Claimed Invention and the Prior Art

Assuming *arguendo* that the '196 Application/'995 Patent is prior art, Teva still has to prove that the claimed invention is obvious in light of this and other prior art references. As explained above, a *prima facie* case of obviousness exists with respect to a chemical compound if there is "structural similarity between claimed and prior art subject matter . . . [and] the prior art gives reason or motivation to make the claimed compositions." In re Dillon, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc). Here, the chemical compound at issue is celecoxib. The chemical structure of celecoxib can be pictorially depicted as follows:



Teva's theory of the obviousness of celecoxib involves many steps, all of which must be proven by clear and convincing evidence. See Takeda Chem. Indus., Ltd. v. Mylan Labs, Inc., 417 F.Supp.2d 341, 347 (S.D.N.Y. 2006) (stating that when a theory of obviousness "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*.") (emphasis added). Teva contends that on October 4, 1993, a person of ordinary skill would have taken all of the following steps: (1) selected the '196 Application as a starting point; (2) devised the hypothetical pharmacophore proposed by Teva's experts; and (3) combined the teachings of the '196 Application and the '142 Patent with a knowledge of pharmacological principles to arrive at the twelve allegedly obvious compounds. Each of these steps involves several sub-steps, all of which must also be proven by clear and convincing evidence for Teva to successfully establish a *prima facie* case of obviousness. If the person of ordinary skill would not have taken even one of the asserted steps, Teva's obviousness defense must fail. Although Teva proved some of these sub-steps, the Court finds that Teva's obviousness argument fails at every major crossroad.

The Court also notes at the outset that it found the testimony of Pfizer's expert witness, Dr. Jorgensen, to be more comprehensible, comprehensive, persuasive, and credible than the testimony of either of Teva's chemistry experts, Dr. Baker or Dr. Trummlitz. Although all three experts are eminently well-qualified, the Court found Dr. Jorgensen's testimony to be understandable, logical,

and compelling. Dr. Trummlitz's testimony, by contrast, was extremely difficult to follow. Both Drs. Baker and Trummlitz frequently hurried over complicated issues and—even after prodding from the Court—failed to provide detailed explanations of their opinions and the bases therefor.

Moreover, specific aspects of Drs. Baker and Trummlitz's testimony cast doubt on their credibility. As discussed in more detail herein, Dr. Baker provided internally inconsistent testimony with respect to the exclusion of a carbon, carbon double bond from the pharmacophore, see *infra* Section I.D.2(d), and offered post-hoc rationalizations to explain his failure to consider certain references, see *infra* Section I.D.1(c), n.19. Dr. Trummlitz testified that the person of ordinary skill would have made choices based on the excessive half-life of DuP 697 without any actual knowledge of whether that information was known in 1993, see *infra* Section I.D.3(d), and asserted that he made an error in his expert report when it became clear that the analysis laid out in his report could not have led to the development of celecoxib, see *infra* Section I.D.3(e). In addition to these examples, which are discussed in context below, Dr. Trummlitz supplemented the opinions articulated in his expert report in order to respond to issues raised in Dr.

Baker's cross-examination, which Dr. Trummlitz observed.[20] Finally, Dr. Trummlitz asserted at trial that the person of ordinary skill would not have attempted to innovate; however, when he was asked at his deposition whether the person of ordinary skill tried to innovate, his response was "Sure. That's why he is hired." (Trial Trans. VII 177:23-178:19.)

Based on all of these considerations, the Court finds Pfizer's chemistry expert to be more credible and more persuasive than Teva's chemistry experts. This finding colors the Court's view of the entire case, and underlies—even when not explicitly mentioned—many of the Court's impressions and decisions.

1. The Person of Ordinary Skill Would Not Choose the '196 Application/'995 Patent As the Starting Point for Developing New

[20] Pfizer objected to allowing Dr. Trummlitz to testify concerning the creation of the pharmacophore. Pfizer argued that Dr. Trummlitz, having listened to the cross examination of Dr. Baker, would be able to "clean up" whatever issues Pfizer's counsel had been able to raise during Dr. Baker's cross examination. The Court ruled that Dr. Trummlitz could testify on the creation of the pharmacophore, but that it would adversely affect his credibility if it appeared Dr. Trummlitz was altering or supplementing his testimony in order to respond to issues raised in Dr. Baker's cross. This is precisely what he did. For example, Dr. Trummlitz's expert report does not disclose that he excluded some examples from the '196 Application when creating the pharmacophore. Dr. Baker was cross examined extensively on his decisions to exclude certain examples. Having witnessed this exchange, Dr. Trummlitz, when he later testified, offered—for the first time—explanations as to why he chose to exclude the compounds from his pharmacophore. (Trial Trans. VII 47:24-49:20.)

NSAIDs

Even assuming *arguendo* that the '196 Application is prior art to the patents-in-suit, the Court finds that the person of ordinary skill would not select it as the starting point for his/her efforts. One thing the parties essentially agree on is that the problem to be solved was the development of a new NSAID without serious GI side effects. The parties disagree, however, about what the person of ordinary skill would have chosen as the starting point for solving this problem.

Teva argues that the person of ordinary skill would have searched the prior art for references that disclosed COX-2 selective compounds because s/he would have expected those compounds to be anti-inflammatory and gastric sparing. Among the references disclosing COX-2 selective compounds, the person of ordinary skill would have preferred those that included enough information to derive a pharmacophore. Teva contends that using these parameters, the person of ordinary skill would have selected the '196 Application as his/her starting point because it was the only reference that disclosed a series of COX-2 selective compounds from which a person of ordinary skill could have derived a pharmacophore for COX-2 selectivity.

Pfizer argues that the person of ordinary skill would not have limited his/her search to COX-2 related art, and even if s/he did so limit the search, would not

have selected the '196 Application as the starting point because flaws in the Application made it inferior to other potential leads. Specifically, Pfizer contends that the person of ordinary skill would not have reasonably expected the compounds of the '196 Application to be anti-inflammatory in vivo, and would have preferred to start with a compound (or group of compounds) with proven in vivo activity such as DuP 697 or NS-398.

For the reasons discussed below, the Court finds that Teva has failed to prove by clear and convincing evidence that the person of ordinary skill would have selected the '196 Application as the starting point for developing a new NSAID with reduced GI side effects.

(a) The Person of Ordinary Skill Would Not Have Limited the Search to COX-2 Selective Compounds

Pfizer first argues that the person of ordinary skill would not have limited his/her search to COX-2 selective inhibitors. Teva contends that the person of ordinary skill would have limited the search to such compounds because by 1993, s/he would have understood that COX-2 selective inhibition was the most promising approach to solving the problem at hand. In support of its position, Teva points out that Pfizer created an entire project devoted to identifying COX-2

selective NSAIDs.

While it is certainly true that Pfizer allocated significant resources to this project, Pfizer scientists pursued several other approaches during this time as well. For example, in the early 1990s, Pfizer scientists were investigating the possibility of developing a "steroid like drug" that would inhibit the conversion of genes to COX-2 enzymes—i.e., inhibit the synthesis of COX-2 entirely. (Trial Trans. XII 63:9-65:7; PTX 2400.) Although Pfizer shifted more resources into the COX-2 selective NSAID project following the Keystone Conference, it continued working on other approaches as well. Similarly, other companies looking for gastric-sparing anti-inflammatory compounds were also investigating several different pathways. (Id. at XVII 8:2-10:12; PTX 2501.) These approaches were still being actively pursued in 1993 because scientists were not confident that they would be able to develop a compound that selectively inhibited COX-2.

Accordingly, the Court finds that Teva has failed to prove that the person of ordinary skill would have focused his/her search exclusively on COX-2 selective compounds.

(b) Teva Has Not Established That the Person of Ordinary Skill Would Have Reasonably Expected the Compounds of the '196 Application to Be Anti-Inflammatory

Pfizer's next argument is that even if the person of ordinary skill searched only COX-2 related art, s/he would not have selected the '196 Application as the starting point because s/he would not have expected the compound to be anti-inflammatory. Pfizer contends that due to the lack of in vivo data in the '196 Application, the person of ordinary skill would not have known whether the compounds possessed the desired anti-inflammatory activity. Several of Pfizer's witnesses testified to this effect.[21] (See, e.g., Trial Trans. XVI 51:6-12; XII 74:5-16; XV 67:7-13; XVII 10:22-11:4; see also *supra* Section I.B.1(b).)

Teva vigorously disputes this assertion and contends that the person of ordinary skill would have concluded, based on the disclosure and teaching of the

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[21] Pfizer also argues that the person of ordinary skill would not have been certain that the compounds were even COX-2 selective in vitro. The Court is not persuaded by this argument. Pfizer points to Dr. Jorgensen's testimony that although the application claims 100-fold selectivity, neither the data provided in table III nor any other evidence in the document supports this statement. (Trial Trans. XVI 52:25-53:14.) Dr. Jorgensen also testified that there are "a lot of weaknesses" in table III. He stated that "there is a lot of sloth, scientific sloth, in the table that gives me little faith in the table." (Id. XVI 120:18-23.) For example, table III has several boxes with no data at all. This does not negate the essential fact that data provided in the '196 Application demonstrated COX-2 selectivity for numerous compounds disclosed therein. Even Dr. Jorgensen admitted as much. (Id. XVI 122:10-123:2.) Having considered all of the evidence and arguments, the Court finds that the person of ordinary skill would have reasonably expected the compounds disclosed in the '196 Application to be COX-2 selective—perhaps not quite as selective as claimed, but COX-2 selective nonetheless.

'196 Application, that the compounds disclosed therein were anti-inflammatory in vivo.[22] Specifically, Teva points to the fact that the application discloses the rat paw edema assay (a standard in vivo assay for determining anti-inflammatory activity), describes it in the past tense, and states that the compounds are anti-inflammatory. See DTX 302 at 10 ("The Compound of Formula I is useful for the relief of pain, fever and inflammation of a variety of conditions . . . ."); Id. at 44 ("Rat Paw Edema - Protocol").

With respect to the rat paw edema assay, the '196 Application states:

> Assays for Determining Biological Activity
>
> The compound of formula I can be tested using the following assays to determine their cyclooxygenase-2 inhibiting activity.
>
> Inhibition of Cyclooxygenase Activity
>
> Compounds were tested as inhibitors of cyclooxygenase activity in whole cell and microsomal cyclooxygenase assays. Both of these assays measures prostaglandin E_2 synthesis in response to arachidonic acid, using radioimmunoassay. . . .
>
> Rat Paw Edema Assay - Protocol

[22] Teva also contends that the fact that a small group of other diphenyl heterocycles with sulfone substituents had demonstrated in vivo activity would have given the person of ordinary skill even more reason to expect the diphenyl heterocycle compounds of the '196 Application to be anti-inflammatory. The Court is not persuaded by this argument. Given the unpredictability of the chemical field, the Court is not convinced that a person of ordinary skill would assume, simply because a few compounds were anti-inflammatory, that all structurally similar compounds would exhibit the same property.

> Male Sprague-Dawney rats (150-200 g) were fasted overnight and were given po either vehicle (1% methocel) or a test compound. One hr later, a line was drawn using a permanent marker at the level above the ankle in one hind paw to define the area of the paw to be monitored. The paw volume (V_0) was measured using a plethysmometer (Ugo-Basile, Italy) based on the principle of water displacement. The animals were then injected subplantarly with 50 µl of 1% carrageenan solution in saline (FMC Corp., Maine) into the paw using an insulin syringe with a 25-gauge needle (i.e. 500 µg carrageenan per paw). Three hr later, the paw volume (V_3) was measured and the increases in paw volume (V_3 - V_0) were calculated. The animals were sacrificed by CO_2 asphyxiation and the absence or presence of stomach lesions scored. Data were compared with the vehicle-control values and percent inhibition calculated. Since a maximum of 60-70% inhibition (paw edema) was obtained with standard NSAIDs, ED_{30} values were used for comparison. All treatment groups were coded to eliminate observer bias.

(DTX 302 at 44.) This section of the Application also includes "representative biological data" from the in vitro test to evaluate "inhibition of cyclooxygenase activity" referred to above. (Id. at 11, tbl. III.) As for the rat paw edema assay, there is no data, no summary of the results, no further discussion at all.

Mr. Smith, Teva's expert on Patent Office practice and procedure, testified that there is an understanding in the PTO that "applicants are not to use the past tense unless the work has already been done. In fact, if they use the past tense indicating that work had been done when in fact it was a prophetic example and work had not been done, that would be considered to be misleading [t]o the Patent

Office. It would be inappropriate." (Trial Trans. XI 69:13-22.) Thus, according to Teva, the description of the rat paw edema assay in the past tense shows that the test was done, and, coupled with the statement that the compounds are anti-inflammatory, would have led the person of ordinary skill to reasonably expect that the compounds were, in fact, anti-inflammatory in vivo.

Pfizer has several issues with Teva's theory. First, the description is captioned a "protocol," and does not mention any particular compounds being tested. Second, the description is in a section called "Assays for Determining Biological Activity," which begins with the general statement that "[t]he compound of Formula I *can be tested* using the following assays . . . ." (DTX 302 at 10 (emphasis added).) Third, when compounds were actually tested in an assay described in the section—as with the "Inhibition of Cyclooxygenase Activity" test—the inventors explicitly stated that "compounds were tested," and provided data on the results obtained.

The Court admits that it finds this issue hard to resolve. Both parties raise legitimate points with respect to the proper interpretation of the language of the "Rat Paw Edema Assay - Protocol." On the one hand, the use of the past tense certainly implies that the test was actually done, and it would be both odd and improper to phrase the section that way if the test were not done. On the other

hand, the use of the phrase "protocol," the lack of any data or results, and the differences between the description of the in vitro and in vivo tests (e.g., failure to state that "compounds were tested") imply—at best—that the test was not done. At worst, the person of ordinary skill could infer from lack of data that the test was done and the results did not support a finding that the compounds were anti-inflammatory.

Accordingly, the resolution of this issue turns on the burden of proof. It is Teva's burden to prove its assertion that the person of ordinary skill would have selected the '196 Application as the starting point for the development of new NSAIDs because s/he would have reasonably expected the compounds to be gastric sparing and anti-inflammatory. This Teva has not done. Especially in light of the existence of other possible leads (discussed in Section D.1(c), below) that were known to be both COX-2 selective and anti-inflammatory, the Court finds that Teva has failed to meet its burden of proof on this issue.

(c) Better Leads Were Available to the Person of Ordinary Skill to Begin Development of New NSAIDs

Pfizer has proffered several other potential starting points, namely DuP 697, NS-398, Merck Patent No. 5,604,260 (the "'260 Patent"), and Merck Patent No.

5,436,265 (the "'265 Patent"). The Court will discuss these potential leads in turn.

i. *'260 Patent and '265 Patent*

Pfizer argues that the person of ordinary skill could have started with the '260 Patent or the '265 Patent. The '260 Patent states that the disclosed compounds are COX-2 selective, and provides data and instructions for synthesizing the compounds. The '265 Patent contains a list of representative embodiments of the invention, which the Patent claims are COX-2 selective. Thus, they would appear to be promising leads.

However, the filing date for the '260 Patent was November 4, 1993 and the filing date for the '265 Patent was November 12, 1993. Since both of these dates are after the invention date for the patents-at-issue, which the Court has found to be October 4, 1993 (see *supra* Section I.A), neither the '260 nor the '265 Patents were available to the person of ordinary skill as of the date of invention and therefore cannot be considered for the purpose of determining whether the person of ordinary skill would have started with the '196 Application.[23]

[23] The testimony (or lack thereof) of Teva's experts with respect to the '260 and '265 Patents can be considered, however, for the purpose of evaluating their credibility. Despite the fact that both experts conducted their initial analysis from the perspective of a person of ordinary skill in the art on November 30, 1993 (when these two patents were available), neither of them mentioned these

ii. *DuP 697 and NS-398*

Pfizer also argues that the person of ordinary skill could have started with DuP 697 or NS-398. Teva concedes that the available literature in October 1993 identified DuP 697 and NS-398 as displaying COX-2 selectivity in vitro and having anti-inflammatory activity in vivo. However, both Dr. Baker and Dr. Trummlitz testified that the person of ordinary skill would have preferred to start with the '196 Application because neither DuP 697 nor NS-398 could provide as much information as the numerous examples disclosed in the '196 Application concerning which elements were important to achieving COX-2 selectivity. (Trial Trans. I 116:6-23; III 130:8-21; 124:12-125:5.) In other words, both experts said that the person of ordinary skill could build a better pharmacophore from the multiple examples of the '196 Application than from DuP 697 or NS-398.

Pfizer disputes the idea that the person of ordinary skill would have

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references in their expert reports or direct examination. That they apparently failed to consider these relevant references casts doubt on their credibility as independent experts. Moreover, Dr. Baker testified on cross examination that he could not recall if he ever saw the '265 Patent before. (Trans. II 41:14-15; II 42:2-4.) He then stated on re-direct that the person of ordinary skill would prefer the '196 Application to the '265 Patent, because the '265 Patent contains only two pieces of data. Given Dr. Baker's previous testimony, the explanation he offered on re-direct is clearly a post-hoc rationalization for rejecting the '265 patent in favor of the '196 Application. That he would engage in such rationalization casts further doubt on his credibility as an expert.

preferred to work from a pharmacophore rather than an individual lead compound. It cites Dr. Jorgensen's testimony that "most individuals practicing medicinal chemistry prefer to work from a lead compound." (Trial Trans. XVI 105:22-106:3.) Pfizer also argues that in a field where the COX-2 in vitro assays were new and less understood than well-established in vivo assays, the person of ordinary skill would have clearly preferred to start with a lead compound with demonstrated in vitro and in vivo activity, rather than to create a pharmacophore based solely on in vivo data. The Court finds the last point quite persuasive. Regardless of whether an inventor would generally prefer a single lead compound or a pharmacophore, it would be logical for the person of ordinary skill to prefer a single compound known to have all the desired properties over a pharmacophore derived from compounds that may or may not have those properties.

Furthermore, DuP 697 and NS-398 were both covered by patents that contained additional examples of compounds. Dr. Trummlitz testified that the person of ordinary skill could derive a pharmacophore from these patents, but that it would be different from the hypothetical pharmacophore proposed in this case and would not lead the person of ordinary skill to celecoxib. (Trial Trans. VII 71:7-73:20 (NS-398); VII 73:21-75:21 (DuP 697); see also PTX 913 (patent covering NS-398).)

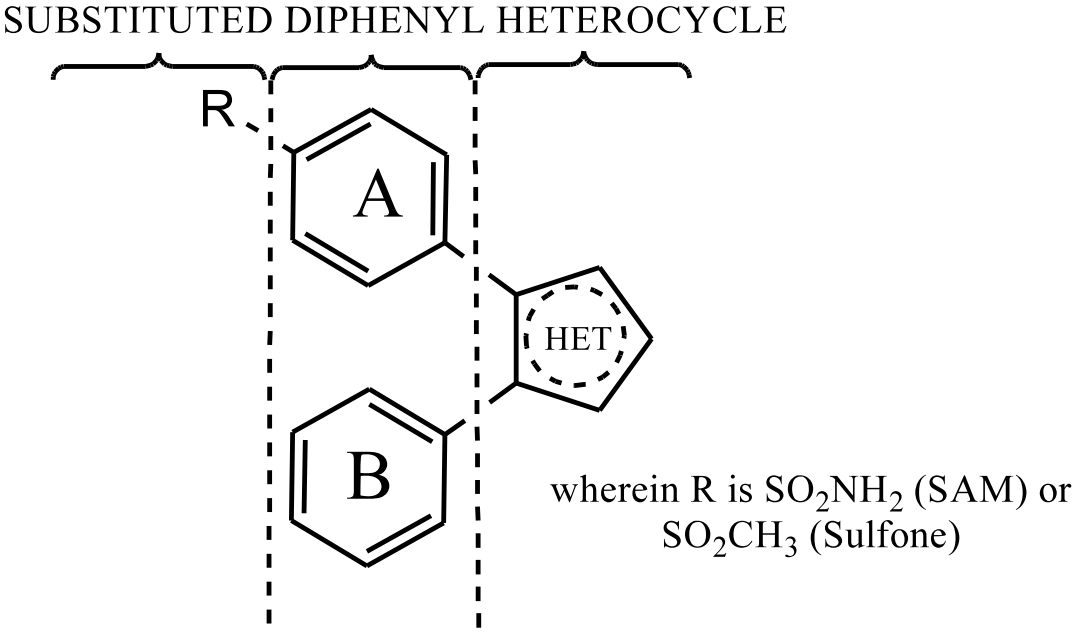
After being questioned about these two patents on cross examination, Dr. Trummlitz testified on re-direct that he did not use the patent covering NS-398 because it did not include COX-1 or COX-2 data. He offered no explanation as to why the person of ordinary skill would not use the patent covering DuP 697.

Taking all of this into consideration, the Court is not persuaded that it is "highly probable" that the person of ordinary skill would choose the '196 Application as the starting point for developing new NSAIDs. Buildex, Inc. v. Kason Indus., Inc., 849 F.2d 1461, 1463 (Fed. Cir. 1988). Accordingly, Teva has not met its burden of proving by clear and convincing evidence that the '196 Application was the appropriate starting point for the development of new NSAIDs.

2. The Person of Ordinary Skill Would Not Derive The Hypothetical Pharmacophore From the Teachings of the '196 Application

Even if the '196 Application/'995 Patent is prior art to the patents-in-suit and the person of ordinary skill would have selected it as the starting point, Teva has not proven that the person of ordinary skill would derive the hypothetical pharmacophore from the disclosure of the Application. A pharmacophore is a "core structure . . . drawn from a series of biological data . . . [which] summarizes

the basic features which might lead to [the desired activity.]" (Trial Trans. I 108:23-25.) Dr. Baker testified that pharmacophores are commonly used in the development of new pharmaceuticals. Both Dr. Baker and Dr. Trummlitz testified that the person of ordinary skill would have derived the following pharmacophore from the examples disclosed in tables 1 and 2 of the '196 Application, and would have reasonably expected compounds within the pharmacophore to be COX-2 selective:



Essentially, Teva argues that the person of ordinary skill would have derived this pharmacophore because almost all of the 71 example compounds in the '196 Application contain 5-membered heterocycles, have a methylsulfonyl or

sulfonamide substituent on the 4-position of one of the phenyl rings, and have two phenyls attached to the heterocycle in adjacent positions. (Trial Trans. I 114:12-22; I 116:6-23; III 124:12-126:1.) Pfizer vigorously disputes that the person of ordinary skill would have derived this pharmacophore. Pfizer argues that the pharmacophore is too broad in some respects, too narrow in others, and the result of impermissible hindsight. Specifically, Pfizer raises four arguments with respect to Teva's hypothetical pharmacophore: (1) the person of ordinary skill would not have focused exclusively on the examples; (2) Teva's experts ignored several examples in creating the pharmacophore; (3) the pharmacophore should not permit the use of any heterocycle; and (4) the pharmacophore should require the six membered rings to be attached to the heterocycle via a carbon, carbon double bond. The Court will address each of these arguments in turn.

(a) The Person of Ordinary Skill Would Focus on the Examples

Although Pfizer seems to have abandoned this argument, Pfizer initially argued that the person of ordinary skill would not have focused on the examples and representative compounds to the exclusion of the genus disclosed in the '196 Application. The Court disagrees. Dr. Baker and Dr. Trummlitz both testified that the person of ordinary skill would, in fact, focus primarily on the examples.

Moreover, Pfizer's own medicinal chemistry expert, Dr. Jorgensen, testified that in building a pharmacophore, the person of ordinary skill "would rely heavily on the examples in table one, the additional structures in table 2 and also be cognizant of the data that is in table three." (Trial Trans. XVI 56:1-4.)

Accordingly, the Court is persuaded that the person of ordinary skill would focus on the examples provided in the '196 Application, and not on the broader genus disclosed therein.

(b) Exclusion of Some Examples From the Pharmacophore Was Appropriate

Pfizer's second issue with the hypothetical pharmacophore is that Teva's experts ignored three of the fourteen examples with data in table 1 when deriving the pharmacophore. Example 7 used a non-heterocycle as the five-membered ring. Example 4 used a cyclohexane, rather than a phenyl ring, as one of the six-membered rings. Example 14 used an acylsulfonamide, rather than a sulfonamide or methylsulfone, as the A-phenyl substituent. Therefore, Pfizer argues, the pharmacophore is too narrow and should include heterocycles and non-heterocycles, phenyls and cyclohexanes, and acylsulfonamides.

Teva's experts offered two explanations for their failure to include these

examples in the pharmacophore. First, Teva's experts testified that it was unnecessary to include these variations in the pharmacophore because they were essentially the same as the elements that were included. As for examples 4 and 14, Dr. Baker testified that a cyclohexane is "quite equivalent to a phenyl group," (Trial Trans. II 96:20-97:4), and that an acylsulfonamide is a labile group, which will quickly form a "grouping equivalent to a sulfonamide group," (Id. at II 101:22-102:4).

Dr. Baker's explanation regarding example 7 is more complex, but essentially expresses the same idea: the non-heterocyclic example did not have to be included because it would act the same way as the heterocyclic examples. He explained his reasoning as follows. In both the heterocyclic and non-heterocyclic examples, the phenyl rings were situated on adjacent carbon atoms that were connected by a double bond. As the person of ordinary skill would have known, the carbon, carbon double bond in the heterocyclic examples would cause the central ring to be flat. This, in turn, would situate the phenyls in distinct and proper positions. Similarly, the person of ordinary skill would have known that in the non-heterocyclic example, the "double bond [would be] flat[,] exactly the same as th[e] heterocycle is flat. Therefore, the two phenyl groups situated on that double bond are in the same orientation as from the [heterocycle]." (Id. at II

100:9-12; II 97:3-100:12.)

In other words, Dr. Baker asserted that the carbon, carbon double bond was the essential feature that ensured the phenyl rings were placed in the correct orientation—whether the ring was heterocyclic or not. A non-heterocycle with a carbon, carbon double bond would act the same way as a heterocycle with a carbon, carbon double bond to position the phenyl rings in the appropriate position. "Therefore, although this molecule was not included in the pharmacophore, it really doesn't negate anything about the pharmacophore, and in fact a man skilled in the art would understand that this molecule would be within this pharmacophore if he needed to consider that in the future." (Id. at II 100:12-17.)

The Court is not persuaded by this explanation. In fact, this explanation seems to hurt Teva's case more than it helps it. If the excluded examples are the same as the included examples, and they are—as Dr. Baker asserted—implicitly within the pharmacophore, then there was no reason not to explicitly draw them into the figure, other than thinly-veiled hindsight and an attempt to narrow the options to arrive at celecoxib. Indeed, including them would benefit the person of ordinary skill by expanding the pool of possible options in which to pursue further development and testing.

Teva's second explanation is more persuasive. Teva's second explanation is that the inclusion of these examples would have meant including exceptions to the teachings of the '196 Application. According to Teva, the person of ordinary skill would not have included such "outliers." Rather, as a matter of standard practice, s/he would have looked for and included only the majority teaching of the Application. The Court agrees.

Dr. Baker testified that "when one examines a patent of this sort . . . one takes the main information one can gain." (Trial Trans. I 117:4-9.) Moreover, Dr. Talley, one of the inventors on the patents-in-suit, submitted a declaration to the PTO in connection with another patent application. In the declaration, he reviewed and analyzed the teachings of the Fujisawa '142 Patent. He concluded that the Patent taught the use of a 5,1 configuration, rather than a 1,5 configuration, because 199 of 204 compounds with a sulfur containing substituent had a 5,1 configuration. (DTX 32 at PFC 01561786-89.) Dr. Talley testified at trial that he believed this was an appropriate analysis of the '142 Patent and its teachings. (Trial Trans. XV 92:17-95:10.) This supports Teva's assertion that the person of ordinary skill would follow the majority teaching of a reference and

disregard "exceptions" to that general trend.[24]

Pfizer offered no contrary evidence indicating that all examples or available information must be included in a pharmacophore. Dr. Jorgensen did testify that all of the examples should have been included, but these conclusory statements are not sufficient to overcome the testimony of Dr. Baker and Dr. Talley relied on by Teva.

Accordingly, since only 2 of the 71 examples in the '196 Application included a non-heterocycle, only 4 of the examples include a non-phenyl, and only 1 of the examples uses a substituent other than a sulfonamide or methylsulfone, it was not inappropriate for Teva's experts to exclude these "outliers" from the hypothetical pharmacophore.

(c) Inclusion of Unlisted Heterocycles Was Not Appropriate

The hypothetical pharmacophore proposed by Teva's experts permits any

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[24] Dr. Trummlitz testified that he did not include the non-heterocyclic example in the pharmacophore because he wanted to "keep the types of heterocycles as easy as possible" and "not complicate things." (Trial Trans. III 132:14-18). He said that he did not include the non-phenyls "because it would make things a little bit too difficult . . . ." (Id. at VII 157:19-25.) These statements are, at best, a poor articulation of the idea discussed above. Applying a standard practice of following the majority teaching of a reference is a legitimate reason for excluding particular examples; "[t]rying to keep things simple" is not.

one of approximately fifty heterocycles to be used. Pfizer contends that this aspect of the pharmacophore is unduly broad. The examples of the '196 Application disclose only eight different heterocycles, and the genus claim explicitly states that the heterocycle should be selected from a list "consisting of" twenty-seven possible heterocycles. (PTX 34 at PFC 02019268-72.) "The phrase 'consisting of' is a term of art in patent law signifying restriction and exclusion." See Vehicular Techs. Corp. v. Titan Wheel Int'l, Inc., 212 F.3d 1377, 1382-83 (Fed. Cir. 2000). In other words, "consisting of" means these-and-only-these-options. See Norian Corp. v. Stryker Corp., 363 F.3d 1321, 1331 (Fed. Cir. 2004) ("'Consisting of' is a term of patent convention meaning that the claimed invention contains only what is expressly set forth in the claim."). Thus, Pfizer argues that the pharmacophore should be limited to those heterocycles actually listed in the '196 Application. Importantly, pyrazoles—the heterocycles used in celecoxib—are not among the possibilities listed or disclosed in the '196 Application. Therefore, if the pharmacophore were limited to the listed heterocycles, it would be impossible to arrive at celecoxib.

Pfizer's argument has significant intuitive appeal. Merck could have included a broader range of heterocycles in its '196 patent application. It did not. It selected specific heterocycles and excluded others. Common sense dictates that

the person of ordinary skill would have assumed that this choice was made for a reason, that the excluded heterocycles would not act in the same way, and that they should not be included in the pharmacophore.

Teva raises three points in opposition to this argument. The Court does not find any of them to be persuasive.

First, Teva argues that '196 Application does not "teach away" from pyrazoles or other unlisted heterocycles:

> Nothing in the Merck '196 application would have provided a disincentive to using a pyrazole. It is silent regarding pyrazoles. The law is clear that teaching away requires more than silence; it requires an express statement regarding the unadvisable or disadvantageous nature of a given element.

(Teva's Post-Trial Brief at 89.) This is a red herring. While it is true that the '196 Application does not teach away from unlisted heterocycles—*i.e.*, it does not include any teaching that pyrazoles or other heterocycles would *not* work—this is not the relevant test. The question is whether it would have been obvious to the person of ordinary skill that other unlisted heterocycles *would* work and should therefore be included in the pharmacophore. See Syntex (U.S.A.) LLC v. Apotex, Inc., 2006 U.S. Dist. LEXIS 36089, at *64-65 (N.D. Cal. June 2, 2006) (the question of whether a reference teaches away from a given use is separate and distinct from the question of whether there is motivation to combine the references

in the asserted way). Not saying something *will not* work is not the same as saying that it *will* work. Thus, the fact that the '196 Application does not teach away from unlisted heterocycles does not establish that these heterocycles should be included in the pharmacophore.

Next, Teva contends that the person of ordinary skill would have been aware of other diphenyl heterocycles that had anti-inflammatory activity, such as the compounds of the Fujisawa '142 Patent, and that this would have motivated him/her to include other heterocycles in the pharmacophore. This is a post-hoc rationalization put forth by Teva with no evidentiary support in the record. Neither of Teva's expert witnesses said that they considered the '142 Patent (or any other material) when building the pharmacophore. The experts clearly stated that they derived the pharmacophore from the teaching of the '196 Application alone. Accordingly, the Court is not persuaded by this argument.

Finally, Teva argues that the variety of heterocycles disclosed in the '196 Application would indicate to a person of ordinary skill that the heterocycle is merely a scaffold (to hold the phenyls in the proper place) and that the precise identity of the heterocycle is not important for achieving COX-2 selectivity. Thus, the person of ordinary skill would know that any heterocycle—not just the ones listed in the '196 Application—would work.

In support of this argument, Teva relies on the testimony of Dr. Baker and Dr. Trummlitz. Dr. Baker testified that "a man skilled in the art would clearly know that [unlisted heterocycles, including] a pyrazole could be included in the pharmacophore" because the '196 Application teaches that a pyrazole would work in the same way as the other heterocycles that were disclosed in the Application. (Trial Trans. II 103:6-104:5; II 104:20-25.) On cross-examination, however, Dr. Baker conceded that the person of ordinary skill might *not* assume this to be true:

> Q: [T]here is no express teaching in the '196 application that you can or should use other five-member'd rings. Correct?
> A: There is no express disclosure but a man skilled in the art might well assume that other five-member'd rings not mentioned might be active.
> . . .
> Q: Which also means he might not. True?
> A: I can't deny that.

(Id. at II 57:25-58:5.) This testimony—that a person of ordinary skill might or might not assume that unlisted heterocycles would work in the same way—falls far short of meeting the high burden of proving by clear and convincing evidence that it would be obvious to the person of ordinary skill to include these structures in the pharmacophore.

Moreover, the only evidence cited by Dr. Baker in support of his opinion is

an article by Merck scientists, written no earlier than 1999,[25] explaining what they learned from their experiments with DuP 697, namely that the thiophene ring (the heterocycle ring used in DuP 697) could be replaced with a wide variety of cyclic groups because the purpose of the ring was "simply to act as a template to anchor the two phenyls in a rigid conformation." (DTX 394.) This discussion by Merck scientists of what they learned from their own experiments with a specific compound is not relevant to determining what the person of ordinary skill would have known in 1993 from the disclosure of the '196 Application.[26, 27]

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[25] There is no date indicated on the copy of the article provided to the Court; however, the authors cite to references dated as late as 1999. Thus it is clear that this article was written no earlier than 1999, and possibly later.

[26] To the extent that this article is relevant, one would have to consider the entire paragraph cited by Teva, which states that it is acceptable to use any six-, five-, or four-membered ring. This would support Pfizer's argument, discussed *supra*, that the pharmacophore should permit the use of non-heterocycles.

[27] In its opposition to Pfizer's Rule 52 motion, Teva also cited to the deposition testimony of Dr. John Talley, one of the inventors of the patents-in-suit. Teva's reliance on Dr. Talley's deposition testimony is misplaced for similar reasons. Teva asserted that "Dr. Talley . . . testified that the purpose of the heterocycle was as a scaffold." (Teva's Memorandum of Law Opposing Plaintiff's Motion for Judgment as a Matter of Law at 16.) In fact, Dr. Talley testified that Pfizer scientists had concluded—based on extensive research on DuP 697—that one of the most important functions of the heterocycle was to act as a scaffold. This testimony does not illustrate that the person of ordinary skill would know, *based on the disclosure of the '196 Application*, that the purpose of the heterocycle is to act as a scaffold or that the identity of the heterocycle was unimportant. Accordingly, it is irrelevant to the issue at hand.

As for Dr. Trummlitz, Teva's counsel summarized his testimony on this issue as follows: "Dr. Trummlitz testified that the variety of heterocycles disclosed in the Tables I and II of the Merck '196 application would have indicated to a person of ordinary skill in the art that the heterocycle is merely a scaffold, and that the precise heterocycle is not important for purposes of achieving COX-2 selectivity." (Teva's Post Trial Brief at 89.) The Court is not certain that this is an accurate characterization of Dr. Trummlitz's testimony. The portion of the trial transcript that Teva cites in support of this summary reads as follows:

> Q: How did you arrive at that pharmacophore from the '196 application?
> A: I arrived, at this pharmacophore from an analysis of the '196 patent application. By analyzing the compounds I have taken the examples, especially the examples of table one, where we have different heterocycles included and therefore, it could exist in a more general way because the substitution of the heteroatoms might be in any position, and the function of the heterocycle is here to bring the two phenyl rings into the right position.
> . . .
> Q: What does a scaffold do?
> A: Okay. I mentioned it earlier. The function of this heterocycle is a scaffold because it has to connect the two groups in the right positions. If you would go to a different position with this substituent, would go up and therefore, you would not reach the goal. They have to go in this direction and in this direction, the scaffold, it is a function of the heterocycle is the scaffold.

(Trial Trans. III 125:6-15; III 132:2-9.) As was the case with much of Dr.

Trummlitz's testimony, this testimony was difficult to comprehend. Assuming, *arguendo*, that Teva's characterization of the testimony is accurate, this explanation for the inclusion of unlisted heterocycles is conclusory. Neither Dr. Trummlitz nor any other witness provided any evidence to support the proposition that the sole function of the heterocycle is to act as a scaffold and that changing the core structure would have no other effect on the activity of the compound.

Thus, even before considering the testimony of Pfizer's witnesses, the Court would conclude that Teva failed to establish by clear and convincing evidence that the person of ordinary skill would have included unlisted heterocycles, including pyrazoles, in the pharmacophore. The testimony of Pfizer's witnesses bolsters this conclusion. Pfizer's medicinal chemistry expert, Dr. Jorgensen, testified that Teva's assertion that the identity of the heterocycle is unimportant is "truly contrary to normal thought in medicinal chemistry." (Trial Trans. XVI 56:25-57:1.)

> In medicinal chemistry we are very sensitive to the differences between heterocycles and that they lead to different properties and different activity. So fundamentally, a suggestion that the nature of heterocycle, you know, broadly is unimportant, is just contrary to normal thought in medicinal chemistry.

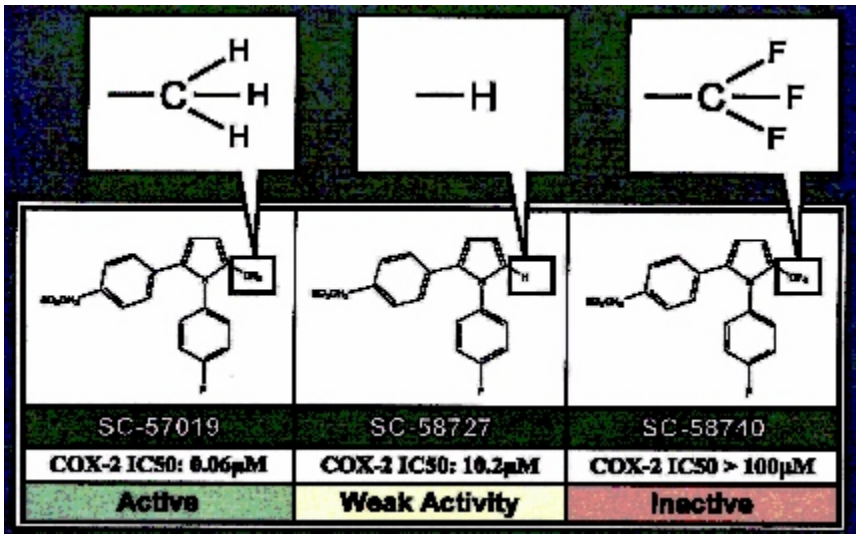
(Id. at XVI 57:1-6.) Dr. Jorgensen explained that the person of ordinary skill would have known in 1993 that different heterocycles had different attributes and

could affect the activity of the compound. (Id. at XVI 59:23-60:3.) He characterized it as "silly" to assume that the identity of the five membered ring would not impact the compound's ability to bind to an enzyme, and explained that there is—even today—no reason to think that any part of a molecule is irrelevant to the binding process. (Id. at XVI 61:5-25.) The Court finds Dr. Jorgensen's testimony to be more comprehensible, comprehensive, credible, and generally more persuasive than the testimony of Teva's expert witnesses with respect to this issue.[28]

Finally, the Court is persuaded by the testimony of Dr. Talley, who provided real world examples that support Dr. Jorgensen's expert opinion. Dr. Talley testified that during the process of developing celecoxib, Pfizer scientists created a plethora of different compounds. Three of those compounds were SC-57019, SC-58727, and SC-58740. All of these compounds had a pyrrole as the central ring, and were identical to each other except for the substituent in the position adjacent to the benzene ring. SC-57019 had a methyl (CH_3) substituent, and was a "very good inhibitor." SC-58727 used a hydrogen (H) substituent, and displayed "weak activity." SC-58740, which included a trifluoromethyl (CF_3) substituent, was

[28] As explained *supra*, see Section I.D., the Court finds Dr. Jorgensen to be generally more credible and persuasive than Dr. Baker or Dr. Trummlitz.

completely inactive. (See figure below.)



Dr. Talley explained that these results were "surprising" because structures with pyrazole rings at their core (rather than pyrrole rings) displayed "just the opposite kind of activity." (Trial Trans. XV 76:2-7; see also PTX 635 at 11.)

> [I]n the case of [pyrroles], the methyl is real good and the trifluoromethyl is not any good. If you switch them to the pyrazole series, it is just the opposite. So trifluoromethyl is very active, whereas methyl is not very active.

(Id. at XV 76:11-15.) In other words, changing the central ring dramatically altered the activity of the compound in surprising and unexpected ways. (See also id. at XV 84:8-11 ("[T]he nature of that central ring . . . really, really plays a big role in terms of, you know, making the compound, activ[e] in the various assays.").)

Accordingly, the Court finds that Teva's proposed pharmacophore is unduly broad in that it inappropriately includes heterocycles, including pyrazoles, that were not disclosed or listed in the '196 Application. Since pyrazoles are the central ring in celecoxib, this finding alone is sufficient to rule in favor of Pfizer on Teva's obviousness defense. Nevertheless, the Court will continue to address the other issues implicated by Teva's obviousness theory.

(d) The Pharmacophore Should Require Attachment of the Phenyls at a Carbon, Carbon Double Bond

Pfizer's final issue with Teva's proposed pharmacophore is that it does not require the phenyl rings to be attached to the heterocycle at a carbon, carbon double bond, and instead improperly allows the phenyl rings to be bound to any position on the heterocycle, including the heteroatom. All fourteen examples in table 1 of the '196 Application have the phenyls attached at adjacent carbon atoms connected by a double bond. The PTO examiner who reviewed (and rejected) the '196 Application found this element to be the "sole constant in the subject matter of the claim." (PTX 34 at PFC 02019555.) Even Teva's own expert, Dr. Baker, conceded that "if you took the unifying feature out of all fourteen examples, you would create a five member'd ring that included a carbon, carbon double bond."

(Trial Trans. II 70:2-71:10.) The pharmacophore, however, does not incorporate this feature.

Teva attempts to explain its failure to include a carbon, carbon double bond in the pharmacophore by arguing that the '196 Application teaches that a phenyl can be bound to a heteroatom without loss of COX-2 selectivity and without significantly affecting the shape of the structure. The Court is not convinced. Dr. Baker testified that the person of ordinary skill

> would know that replacing a carbon atom in a heterocyclic ring [with] a nitrogen doesn't change the shape of the heterocyclic ring, and therefore . . . a phenyl group which is bound to a nitrogen would be equivalent to if it were bound to a carbon in the compounds that we are dealing with here. So the heterocyclic ring is the same shape, whether the phenyl group is attached at a nitrogen or carbon.

(Trial Trans. II 102:21-103:3.)[29] This testimony/explanation directly contradicts

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[29] As best as the Court can tell, Dr. Trummlitz said essentially the same thing:

> There are two reasons [why your pharmacophore allows this phenyl to be bound to a nitrogen]. One reason is the position of the nitrogen atom within the five-member'd ring is open. It can be any position. Therefore, we are expecting not the action, versus nitrogen, interactive side, it is an enzyme. We do not see a relevance for the nitrogen atom to be there. It can also be a carbon atom. This is point one. We can exchange it because it is not necessary in a certain position. This is what is teached from '196. The second reason is we have the two phenyl groups, one going to the upper left and one to the upper right, and they have to be in the right position. And they get the position because they

Dr. Baker's own previous testimony. In explaining why the non-heterocycle of example 7 was not included in the pharmacophore, Dr. Baker testified that the carbon, carbon double bond—not the identity of the heterocycle—was the critical element to orient the phenyls in the correct positions and achieve COX-2 selective inhibition. See *supra* Section I.D.2(b). Dr. Baker also confirmed that in the context of this structural configuration, a double bond can only be a carbon, carbon double bond.[30] (Trial Trans. II 27:21.)

If, as Dr. Baker testified, the double bond was critical to achieving COX-2 selectivity, one could not replace one of the carbon atoms with a nitrogen.[31] Doing so would mean that the bond between the atoms where the two phenyls attach to

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> are, as they are coming from the five member'd ring, they are connected with this. And in order to come to the right positions out, it doesn't matter if you have a nitrogen in this position or a carbon atom because they are so close in this case, both are planar and both have the right angles to bring the phenyl groups into the right position.

(Trial Trans. VII 155:23-156:21; see also III 130:22-131:7; III 131:18-132:9.)

[30] The double bond can only be carbon, carbon based on the laws of covalence which permit four bonds to be attached to a carbon atom, but prohibit more than three bonds to attach to a nitrogen. (See generally Trial Trans. XVI 37:17-49:3.)

[31] Among oxygen, sulfur, and nitrogen heteroatoms used in the structures involved in this case, nitrogen is the only heteroatom to which a phenyl can be bound. (Trial Trans. XVI 66:4-6.)

the heterocycle would be a single bond, not a double bond. Thus, the phenyl groups would not necessarily orient to the correct position. Accordingly, Dr. Baker's testimony is internally inconsistent and one of his assertions must fail. The Court need not resolve which assertion is inaccurate, but the Court must assess the credibility of witness testimony. Given the inherent contradiction in Dr. Baker's testimony, the Court finds his testimony on this issue to lack credibility.

Teva makes several other arguments with respect to this issue, but none of them are any more persuasive. First, Teva argues that "the Merck '196 application never says that such a configuration [*i.e.*, attaching a phenyl to a nitrogen atom] would not work." (Teva's Post-Trial Brief at 97.) This is essentially the same "teaching away" argument that Teva asserted with respect to the use of unlisted heterocycles. See *supra* Section I.D.2(c). Once again—and for the same reasons—this argument is not persuasive. The relevant question here is whether it would have been obvious to the person of ordinary skill from the teaching of the '196 Application that s/he could attach a phenyl to a heteroatom. The fact that the '196 Application does not expressly say such a configuration would *not* work is not the same as teaching that it *would* work.

Moreover, this argument is disingenuous in light of Teva's earlier argument concerning the exclusion of examples 4, 7, and 14 from the pharmacophore. In

that context, Teva argued vehemently that a person of ordinary skill would follow the "majority teaching" and ignore the "exceptions"—even though the '196 Application explicitly taught that those exceptions would work. Here, Teva argues that the person of ordinary skill would completely ignore the majority teaching in favor of a configuration that the '196 Application does not disclose at all. Teva cannot have it both ways.

Teva next argues that the '196 discloses various isomers (compounds having the same structure but with the atoms arranged differently), which would have led the person of ordinary skill to understand that the position of the heteroatom relative to the phenyl is not important for the purposes of achieving COX-2 selective inhibition. The Court is not persuaded by this argument. None of the isomers disclosed in the '196 Application include a phenyl bound to a heteroatom. So while the isomers may teach that one could put a heteroatom in any "non-phenyl position," they do not teach that one could attach a phenyl to a heteroatom.

Finally, Teva argues that the person of ordinary skill would have been aware of the Fujisawa '142 Patent, which permits the placement of a phenyl on a heteroatom. As above, this can only be considered a post-hoc rationalization put forth by Teva since neither of Teva's expert witnesses said that they considered

the ‘142 Patent (or any other material) when building the pharmacophore.

Accordingly, the Court finds that Teva’s proposed pharmacophore is too broad in that it inappropriately permits the phenyl rings to be attached to heteroatoms and does not include a carbon, carbon double bond. The pharmacophore should require the phenyls to be attached to double bonded carbon atoms. Since celecoxib does not include this feature, but rather has a phenyl attached to a nitrogen heteroatom, the person of ordinary skill could not possibly derive celecoxib from the properly constructed pharmacophore. This, on its own, is an independent and sufficient ground to rule in favor of Pfizer on Teva’s obviousness defense.

(e) Summary

In summary, the Court finds that the pharmacophore should *not* permit the use of heterocycles that were not included in the ‘196 Application, should *not* permit a phenyl group to be attached to a heteroatom, and *should* include a carbon, carbon double bond. The person of ordinary skill would not have derived Teva’s hypothetical pharmacophore from the ‘196 Application, and the pharmacophore s/he would have derived could never lead to celecoxib. Indeed, neither celecoxib nor any of the other allegedly obvious compounds are within this proper

pharmacophore. Accordingly, Teva's obviousness attack must fail.

3. The Person of Ordinary Skill Would Not Make All of the Necessary Changes to Arrive at Twelve Obvious Compounds

Even if the Court were to find that the '196 Application/'995 Patent was prior art, and that the person of ordinary skill would derive Teva's proposed hypothetical pharmacophore from its teachings, Teva's obviousness attack would still fail because the pharmacophore does not teach the claimed invention.

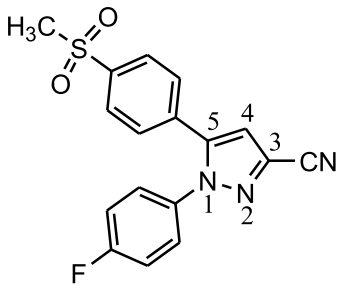
According to Teva, once in possession of the hypothetical pharmacophore, the person of ordinary skill would have conducted a search for anti-inflammatory compounds that were within the pharmacophore. This search would have led to the '142 Patent and the '829 Application.[32] Teva initially indicated that the '829

[32] Neither party presented much evidence or argument on the issue of whether the person of ordinary skill would have even considered the '142 Patent and '829 Application. Teva's expert stated that the person of ordinary skill would have selected the'142 Patent and '829 Application because those references teach numerous examples that are within the pharmacophore but outside the explicit disclosure of the '196 Application, contain a considerable amount of data indicating that the compounds are anti-inflammatory, and the compounds contained therein are easy to synthesize. (Trial Trans. I 111:15-121:24; see also III 142:20-143:11; III 145:4-12.) Pfizer's expert, on the other hand, testified that the person of ordinary skill would not select the '142 Patent because the preamble of the Patent states that the compounds display antithrombotic activity, which is associated with COX-1 inhibition. Thus, the person of ordinary skill would have been concerned that the compounds of the '142 Patent would inhibit both COX-1 and COX-2. (Trial Trans. XVI 76:19-77:14.)

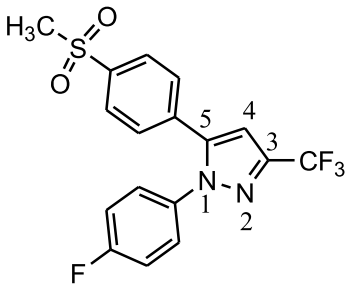
Application was a critical reference. However, at trial Teva referred to the '829 Application only in passing, and instead relied almost exclusively on the '142 Patent.

The '142 Patent provides data obtained in five different tests for one or more of 11 compounds. (DTX 34 at col. 21-22.) Of the 11 compounds, the Patent provides data for three compounds, examples 6, 11-3, and 24, that were tested in three or more assays. Of these three compounds, only examples 6 and 11-3 (shown below) are within the pharmacophore.

Compound 6



Compound 11-3



Neither party provided any further details or supporting references. Because of the paucity of testimony and evidence, and because resolution of this question is not dispositive, the Court will assume for purposes of this analysis that the person of ordinary skill would consider the '142 Patent.

Teva argues that it would be obvious to the person of ordinary skill—based on the combined teachings of the '196 Application and the '142 Patent, as well as a general knowledge of pharmacological principles—to take all of the following steps: (a) selecting a pyrazole as the five-membered heterocyclic ring; (b) selecting a sulfonamide as the substituent on the A-phenyl; (c) attaching a phenyl to a nitrogen atom in a 1,5 configuration; (d) adding an F, CH_3, or OCH_3 as a substituent on the B-Phenyl; and (e) adding a CF or CN_3 on the 3-position of the pyrazole. Teva contends that these steps would inexorably lead to twelve compounds, one of which is celecoxib, all of which are within the scope of at least one of the claims of each of the patents-in-suit, and all of which would have been reasonably expected to be COX-2 selective.

The Court finds that Teva has failed to carry its burden of proving many of these individual steps, let alone the entire complex combination. Accordingly, Teva's theory of obviousness fails at this stage of the analysis as well.

(a) Selecting a Pyrazole

Teva's pharmacophore permits the use of any heterocycle. Teva argues that the combined teachings of the '196 Application and '142 Patent would have motivated the person of ordinary skill to specifically select a pyrazole. See In re

Kahn, 441 F.3d 977, 986 (Fed. Cir. 2006) (explaining that a *prima facie* case of obviousness requires the party to "explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious.") (internal quotations omitted).

Both of the compounds disclosed in the '142 Patent that fit within Teva's pharmacophore (*i.e.*, examples 6 and 11-3, reproduced above) use pyrazoles as the central heterocyclic ring. (DTX 34.) The '196 Application discloses several other heterocycles, but not pyrazoles. Teva argues that the person of ordinary skill would have selected pyrazoles, rather than any of the heterocycles included in the '196 Application, precisely because the '196 does not expressly disclose them. Teva relies on Dr. Trummlitz's testimony to support this position.

Dr. Trummlitz testified that, in his opinion, the person of ordinary skill in 1993 was trying to get a patent. (Trial Trans. VII 29:22-25 ("Q: In your opinion, [the person of ordinary skill in the art in 1993] is trying to get a patent. Correct? A: Yes."); VII 30:15 ("He is trying to get a patent, that is one aspect.").) He also said that a "[m]edicinal chemist has to take into account several of the patent aspects. And he should not infringe a patent of a competitor company, that is one important point. The other point is from his compounds, *it is preferred that they are patentable*." (Id. at IV 42:24-43:3 (emphasis added).) Thus, he concluded that

the person of ordinary skill looking at the '196 Application and the '142 Patent would have been motivated to select a pyrazole in order to obtain compounds that were not covered by an existing patent and to "avoid any patent problems." (Trial Trans. IV 32:21-33:2.)

This testimony could be interpreted two ways: that the person of ordinary skill would have been motivated by a desire to avoid infringing someone else's patent, or that s/he would have been motivated by a desire to get his/her own patent. There is a subtle but potentially important distinction between these two concepts. The problem with desire to get a patent as a motivating factor is well-illustrated by the following excerpt from Dr. Trummlitz's cross examination:

> A. [The person of ordinary skill] is trying to get a patent, that is one aspect.
> Q. And since he is trying to get a patent, he wants to do things that are not obvious. Correct?
> A. Yes. That is included.
> Q. So the person of ordinary skill in the art is trying to invent, he wants to do things that are patentable and not obvious, and in your mind he comes to Celebrex, correct?
> . . .
> A. Yes, that's correct.
> . . .
> Q. . . . . A person skilled in the art, in your opinion, knows that to get patents his work has to be non-obvious, correct?
> A. Yes.
> Q. So the person of ordinary skill in the art, according to your definition of the person, wants to do something that is not obvious, correct.

A. He wants to do it, yes.

(Trial Trans. VII 30:15-31:19.) In other words, if the person of ordinary skill is trying to get a patent, s/he must invent something new and non-obvious. However, under Federal Circuit caselaw, the person of ordinary skill is not permitted to invent. See, e.g., Standard Oil Co. v. Am. Cyanamid Co., 774 F.2d 448, 454 (Fed. Cir. 1985) ("A person of ordinary skill in the art is also presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate . . . ."); see also Life Techs., Inc. v. Clontech Labs., Inc., 224 F.3d 1320, 1326 (Fed. Cir. 2000). S/he is supposed to undertake to do only what is obvious from the existing prior art. Thus, desire to make a patentable non-obvious compound cannot be a proper motivation for selecting a pyrazole over the myriad of other heterocycles disclosed in the prior art.

Perhaps recognizing this pitfall, Teva argues that the person of ordinary skill would select a pyrazole, not in order to get a patent, but to avoid infringing other patents. In one submission, Teva even denied that Dr. Trummlitz ever testified that the person of ordinary skill's goal is to develop patentable compounds. (Teva's Memorandum of Law Opposing Plaintiff's Motion for Judgment as a Matter of Law at 26.) Although this is clearly inaccurate, the Court will accept *arguendo* Teva's characterization of Dr. Trummlitz's testimony—*i.e.*

that the person of ordinary skill would have been motivated to select a pyrazole by a desire to avoid patent infringement.

Notably, the legitimacy of this motivation is also uncertain. Pfizer claims it is not a proper motivation. Teva claims that it is. Pfizer cites a case from the Southern District of New York, Takeda Chem. Indus. v. Mylan Labs, Inc., 417 F. Supp.2d 341, 377-78 (S.D.N.Y. 2006). Teva cites a case from the District of Delaware, Kao Corp. v. Unilever United States, Inc., 344 F.Supp. 2d 527, 558 (D. Del. 2004). In the absence of binding authority on the issue, the Court is inclined to believe that there may be circumstances wherein a desire to design around the prior art and avoid infringing other patents is a valid motivation for the person of ordinary skill to pursue a specific course of action. However, the Court need not definitively resolve this issue or determine whether the facts presented here constitute such a circumstance. Since the Court does not agree that the person of ordinary skill would attach a phenyl to a nitrogen atom in a 1,5 configuration; add an F, CH_3, or OCH_3 as to the B-Phenyl; or add a CF or CN_3 to the heterocycle, whether s/he would select a pyrazole as the central ring is not dispositive in deciding the case, or even determining whether the pharmacophore would lead him/her to the twelve allegedly obvious compounds.

(b) Selecting a Sulfonamide

As with the pyrazole, Teva argues that the person of ordinary skill would have selected a sulfonamide as the substituent on the A-phenyl because none of the prior art expressly said to do so—*i.e.*, because a pyrazole/sulfonamide combination was not covered by an existing patent. Accordingly, the same concerns discussed in the previous section apply in this section with equal force. However, unlike with the selection of a pyrazole, Teva offers another unrelated reason why the person of ordinary skill would be motivated to select a sulfonamide rather than a methylsulfone: to decrease the lipophilicity of the compound.

Lipophilility refers to a compound's solubility in fat as compared to water. A compound that is highly lipophilic is very soluble in fat. Dr. Trummlitz testified that diphenyl heterocycles in general are very lipophilic (very soluble in fat). Since a certain amount of solubility in water is necessary to ensure that a drug is absorbed into the body, high lipophilicity can create a bioavailability problem. Thus, according to Dr. Trummlitz, sulfonamides were the obvious choice because the person of ordinary skill would have known that they have a lower lipophilicity profile than methylsulfones and would lower the overall lipophilicity of the compound and improve bioavailability. (Trial Trans. IV 34:25-35:3.)

Pfizer's expert, Dr. Jorgensen, asserted that this was not a valid reason to prefer sulfonamides because "[t]here was no indication that there was a problem of bioavailability." (Id. at XVI 83:12-14.) He also testified that if even there was a bioavailability issue, using a sulfonamide instead of a methylsulfone "might hurt you in terms of bioavailability. It is not a guarantee." (Id. at XVI 83:18-19.) Finally, he noted that it was well known in 1993 that drugs containing sulfonamides carried a risk of causing sulfa allergies, whereas drugs containing methylsulfones did not. This, he said, was "another reason not to go with the [sulfonamide]." (Id. at XVI 83:20-84:3.) For all of these reasons, Dr. Jorgensen stated that: "In my lab we would not be going with [sulfonamide]." (Id. at XVI 83:22-23.)

Neither expert cited any authority to support their respective positions. Given the conflicting testimony and the lack of authority, the Court does not find clear and convincing evidence that bioavailability concerns would have motivated the person of ordinary skill to select a sulfonamide over a methylsulfone. Accordingly, the Court is left with only the desire to avoid existing prior art as a possible motivation. For the same reasons discussed above, see *supra* Section I.D.3(a), the Court need not decide whether that motivation is sufficient here.

(c) Attaching a Phenyl to a Nitrogen Atom in a 1,5 Configuration

Teva's pharmacophore permits a phenyl ring to be attached at any position, including the heteroatom. All twelve of Teva's allegedly obvious compounds have a phenyl attached to a nitrogen atom in a 1,5 or 5,1 configuration.[33] Thus, the relevant question here is whether the person of ordinary skill would have been motivated to exclusively create compounds with a phenyl attached to a heteroatom, and if so, whether s/he would have employed both 1,5 and 5,1 configurations.

The compounds of the '142 Patent all have a phenyl group bound to a nitrogen atom, but none of the compounds of the '196 Application do. In the '196 Application all of the examples have the phenyl groups attached to carbon atoms. Teva offers no explanation at all for why the person of ordinary skill would have chosen to follow the teaching of the '142 Patent and not the '196 Application. Teva does not claim that compounds akin to those in the '142 Patent (with a phenyl bound to a nitrogen atom) are better, cheaper, easier to synthesize, or in any other way preferable to compounds of the variety disclosed in the '196 Application. Teva simply states that the '196 Application teaches that a phenyl

[33] In celecoxib, a phenyl group is attached to a nitrogen in a 1,5 configuration.

can be bound to a heteroatom without loss of COX-2 selectivity,[34] and that this—combined with the teaching of the '142 Patent—constitutes sufficient motivation. It does not. Just because one could do something does not necessarily mean that s/he would.

In the absence of any evidence that the person of ordinary skill would have understood that attaching a phenyl to a heteroatom was the preferable way to structure a compound, the Court finds that there would have been no reason—other than impermissible hindsight—for the person of ordinary skill to ignore the teaching of the '196 Application and only create structures according to the teaching of the '142 Patent with a phenyl attached to a nitrogen atom.

Moreover, even if the person of ordinary skill would have exclusively created compounds with a phenyl bound to a heteroatom, s/he would have created compounds with a 5,1 configuration—not the 1,5 configuration that is used in celecoxib. In a 1,5 configuration, the phenyl with the SO_2 group is attached to the nitrogen atom. If the other phenyl (without the SO_2 group) is attached to the nitrogen atom it is known as a 5,1 configuration. (See figure below.) These are fundamentally different structures with substantially different shapes. (Trial

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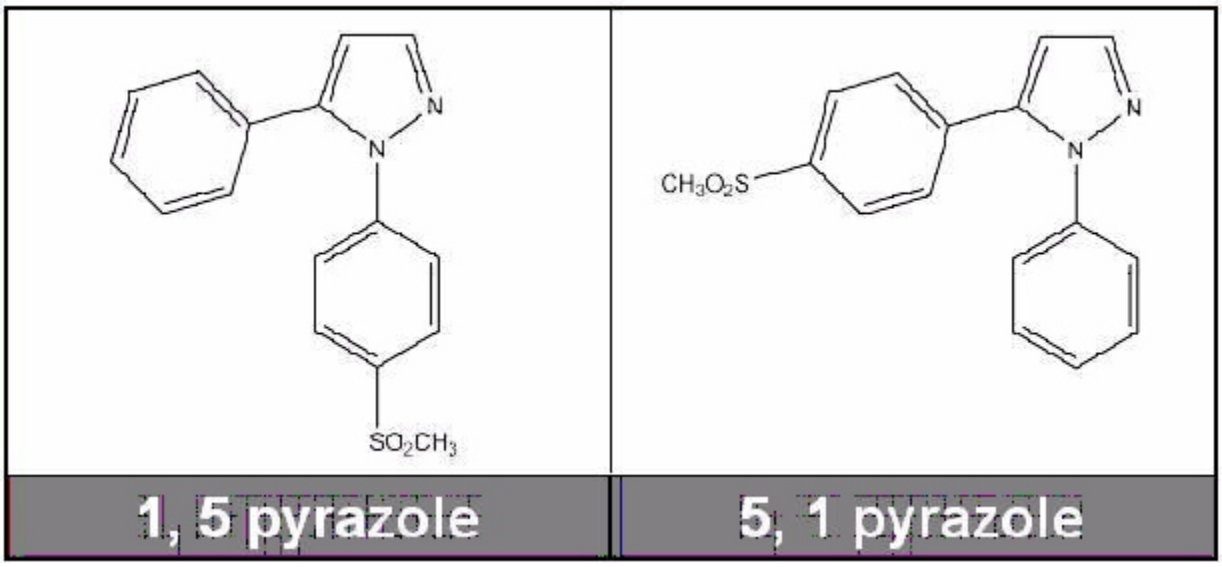
[34] The Court has already rejected this argument. See *supra* Section I.D.2(d). However, for purposes of this discussion, the Court will accept the proposition as true.

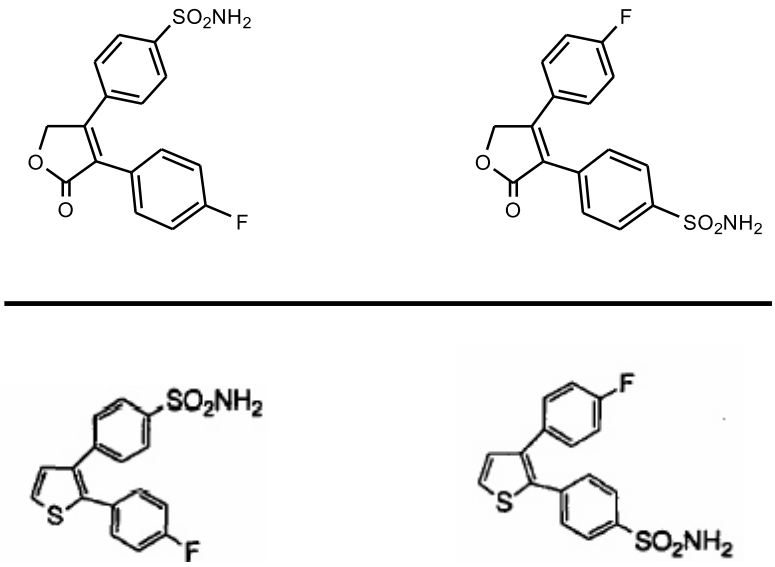
Trans. XVI 79:10-15.)



Teva argues that the person of ordinary skill would have created both 1,5 pyrazoles and 5,1 pyrazoles based on the combined teachings of the '196 Application and '142 Patent. According to Teva, (1) the '196 Application teaches that both 1,5 and 5,1 configurations can be used without affecting COX-2 selectivity, and (2) the '142 Patent "has an example of a 1,5-diphenyl pyrazole with Sulfone substitution, and numerous examples with 5,1 configurations thereby teaching use of a 1,5 or 5,1 configuration." (Teva's Post-Trial Brief at 114.) The Court disagrees with Teva's characterization of both references and with the ultimate conclusion Teva draws therefrom.

(i) *Teaching of the '196 Application*

The ‘196 Application does not include a single 1,5 pyrazole or 5,1 pyrazole. Nevertheless, Teva claims that the ‘196 Application teaches that both of these configurations should work. Teva bases this assertion on the fact that the ‘196 Application discloses several sets of isomers wherein the compounds differ only in the position of the SO_2 group relative to a heteroatom or another feature of the heterocycle. This is illustrated by the examples reproduced below.



Teva completely ignores the fact that none of these compounds have a phenyl bound to a heteroatom. These isomers may show that when placement on a heteroatom is not involved, phenyls can be “flipped” without affecting selectivity. However, Teva has offered no evidence to show that the same is true when one of the phenyls is placed on a heteroatom. In the absence of such evidence, the Court

cannot blindly accept Teva's teaching-by-analogy argument. Accordingly, the Court is not convinced that the '196 Application teaches the interchangeability of 5,1 and 1,5 pyrazoles.

(ii) *Teaching of the '142 Patent*

Even if the '196 Application did teach that both 1,5 and 5,1 configurations would work, the person of ordinary skill would not have been motivated to create 1,5 pyrazoles. Contrary to Teva's assertion, the '142 Patent does not "teach[] use of a 1,5 or 5,1 configuration." It teaches a 5,1 configuration. The overwhelming majority of compounds in the '142 Patent that fall within the pharmacophore are 5,1 pyrazoles. (Trial Trans. XVI 79:24:80:23.) Dr. Trummlitz admitted as much. (Id. at VII 82:13-83:24.) When arguing in support of its hypothetical pharmacophore, Teva argued that the person of ordinary skill would follow the majority teaching of the prior art reference and ignore "exceptions." Here, Teva claims that the person of ordinary skill would include such exceptions. This is another example of Teva attempting to make inconsistent arguments. To support its "majority teaching argument," Teva relied on an affidavit by Dr. Talley. In that affidavit, Dr. Talley reviewed and analyzed the teaching of a patent. He concluded that it taught the use of a particular feature because the vast majority of

compounds disclosed in the reference included that particular feature. Teva used this affidavit as proof that the person of ordinary skill would follow the majority teaching of a reference and disregard "exceptions" to that general trend. The reference Dr. Talley was discussing in the affidavit was the '142 Patent. The particular preferred feature he said it taught was the use of a 5,1 pyrazole. The "exception" was the use of a 1,5 pyrazole.

Thus, based in part on the arguments and references used by Teva itself, the Court finds that the person of ordinary skill would not have been motivated to attach a phenyl to a nitrogen atom in a 1,5 configuration. Since celecoxib is a 1,5 pyrazole, the person of ordinary skill never would have arrived at that compound.

(d) Adding an F, CH_3, or OCH_3 to the B-Phenyl

Next, Teva argues that the person of ordinary skill would have been motivated to use a flourine (F), methyl (CH_3), or methoxy (OCH_3) as the substituent on the B-phenyl (the phenyl without the SO_2 group).[35] There is no dispute that the prior art teaches the use of a flourine substituent on the B-phenyl. It is by far the most widely used substituent in both the '196 Application and the '142 Patent. Indeed, Dr. Trummlitz conceded that if the person of ordinary skill

[35] Celecoxib uses a methyl as the B-Phenyl substituent.

were to follow the preferences of these two references, s/he would simply keep the flourine. (Trial Trans. VII 94:1-11.) Dr. Trummlitz also conceded that there is nothing in the '196 Application or '142 Patent that discourages use of a flourine. (Id. at VII 95:14-96:7.) Nevertheless, Teva contends that the person of ordinary skill would not have felt limited to flourine substituents, and would have found it obvious, based on the teachings of the '142 Patent and '196 Application and on his/her general knowledge of half-life and biochemistry, to use two additional groups in this position, namely methyl (CH_3) and methoxy (OCH_3).[36]

Specifically, Teva claims the person of ordinary skill would have known that diphenyl pyrazoles with sulfonamide and flourine substituents tended to have unacceptably long half-lives. (Id. at IV 51:24-52:1 (the person of ordinary skill would have known that "these drugs have a certain tendency to accumulate in the body [and] [t]herefore you have to speed up the metabolism of the drug.").) Therefore, Teva contends, the person of ordinary skill would have been motivated to search for ways to reduce the half-life of the compounds. Because the '196 Application teaches that the flourine is not critical for achieving COX-2 selectivity

[36] The Court notes that this is yet another example of Teva playing both sides of the coin and contradicting its earlier argument that the person of ordinary skill would follow the majority teaching of the prior art. See *supra* Section I.D.2(b).

and because the person of ordinary skill would have known that flourine is not easily metabolized, s/he would have concluded that the best solution would be to replace the flourine substituent with a different group that was easier to metabolize (a "metabolizable" or "metabolic handle"). To select a replacement, the person of ordinary skill would have looked to the teachings of the '196 Application and '142 Patent. S/he would have selected methoxy (OCH_3) because it was known to be a metabolizable handle, and was the only non-halogen containing substituent used in both references. S/he would have selected methyl (CH_3) because it is another commonly used metabolic handle, and was used in the examples of the '142 Patent.

There are several problems with this argument. Initially, the Court is not convinced that the person of ordinary skill would have been motivated to replace the flourine. Furthermore, even if s/he would have been so inclined, the Court is not convinced that methyl and methoxy were the obvious replacements.

i. *The Person of Ordinary Skill Would Not Have Replaced the Flourine*

Dr. Trummlitz asserted that the person of ordinary skill would have been motivated to replace the flourine based on a desire to decrease the half-life of the drug, but his testimony on this issue lacks credibility. The only evidence he cited

in support of the critical idea that the person of ordinary skill would even be concerned about half-life is that "it was known [in 1993] that DuP 697 has a very long, a very long half life. [It was] withdrawn from . . . development because in humans the half life was above 200 hours." (Trial Trans. VII 173:25-174:3.) On cross-examination, however, Dr. Trummlitz admitted that he did not actually know whether it was known in 1993 that the half-life of DuP 697 was over 200 hours in humans. (Id. at VII 174:23-176:13.)

Indeed, later testimony confirmed that this information was *not* known in 1993. Dr. William Galbraith, who gave the DuP 697 presentation at the Keystone conference, testified at trial. He stated that he did not present any human half-life data for DuP 697 at the Keystone conference, or at any other conference, and that such data was not published until 1996.[37] (Trial Trans. XVII 19:11-16; XVII 20:21-21:4.) He explained that he did present half-life data for animals, but that the animal half-life data did not lead him or anyone else at DuPont to expect DuP 697 to have an unduly long half-life in humans. (Id. at XVII 19:17-20:4.) DuPont scientists had no idea that human half-life would be a problem until they took the drug into human clinical trials. (Id. at XVII 20:5-11.)

[37] A paper published in 1994 contained one figure showing the data for one subject, but did not calculate the actual half-life. (Trial Trans. XVII 20:21-21:2.)

Moreover, Dr. Jorgensen testified that the person of ordinary skill would not have been able to predict the half-life of the compound without conducting experiments. The half-life of a compound, he said, "was not predictable then [and] is not predictable today with any kind of quantitative reliability." (Trial Trans. XVI 89:7-9.)

> Half-life . . . potentially involves many different processes, metabolic processes, again, absorption of the compounds, binding to other proteins that are in your blood. It is a very complicated issue. And nobody can predict it with any quantitative reliability.

(Trial Trans. XVI 89:9-14; see also id. at XII 84:20-85:16 (Dr. Seibert addressing the unpredictability of half-life).)

Accordingly, Teva has not proven by clear and convincing evidence that the person of ordinary skill would have been concerned over the half-life of the compounds or been motivated to seek out ways to reduce it.[38] Additionally, even if the person of ordinary skill would have had concerns about half-life, the Court is not convinced that s/he would have looked to replace the flourine in order to solve

[38] In addition to Dr. Trummlitz's testimony, Teva also cites other evidence in support of its argument that the person of ordinary skill would have had concerns over the half-life; however, the Court finds that they suffer from the same infirmity discussed above. For example, Teva cites the slide from the Keystone conference disclosing the half-life for DuP 697 and its metabolite in rats and dogs. However, as discussed above, there is no evidence that these figures were unusually long or that they would translate into a lengthy half-life in humans. Indeed, Dr. Galbraith's testimony is exactly to the contrary.

the problem.

Teva argues that replacing the flourine would have been the obvious solution because the '196 Application teaches that the flourine is not critical for achieving COX-2 selectivity. However, this assertion is contradicted by testimony given by Dr. Baker in an unrelated proceeding. Dr. Baker, Teva's expert, admitted that he previously testified in a case in the United Kingdom that the person of reasonable skill would have known that both the methylsulfonyl group *and the flourine* were critical for achieving COX-2 selectivity. Although he asserted that this would not "be entirely [his] view at this moment," Dr. Baker's previous testimony was that "the flourine may well give you that selectivity together with the methylsulphonyl and thereafter you may not be able to separate the two away from each other." (Trial Trans. II 82:11-83:8.)

Accordingly, the Court is not convinced that the person of ordinary skill would have been motivated to ignore the majority teaching of both the '196 Application and the '142 Patent and replace the flourine in order to reduce the half-life of the resulting compounds.

ii. *The Person of Ordinary Skill Would Not Select Methyl and Methoxy as the Replacements*

Even if Teva is correct that the person of ordinary skill would have been motivated by concern over half-life to replace the flourine, the Court is not convinced that s/he would have selected methyl and methoxy as the obvious replacements. Teva has offered no real explanation for focusing exclusively on these groups and ignoring the myriad of other possible substituents included in the '142 Patent and '196 Application, such as:

- CO_2H (carboxylic acid) (See, e.g., PTX 34 at PFC 02019235);
- OH (hydroxide) (See, e.g., id. at PFC 02019240); and
- SCH_3 (methylthio) (See, e.g., DTX 34 at col. 26, ln. 6).

Teva does explain that methyl and methoxy would be superior to chlorine (and presumably bromine) because chlorine and bromine are halogens, which were also known to be hard to metabolize, but it says nothing about the other possible alternatives.

Further, the explanation Teva does offer for the decision to select methyl and methoxy is not persuasive. Teva claims that the person of ordinary skill would select methoxy because it is the only group (other than chlorine and flourine) that is used in both the '196 Application and '142 Patent. The Court fails to see why this fact is important. Moreover, methyl is not used in both references, only in the '142 Patent. Teva's explanation for selecting methyl is simply that

methyl "is another very commonly used metabolic handle." (Teva's Post-Trial Brief at 118.) In support of this assertion, Teva cites the trial and deposition testimony of several scientists who agreed that methyl and methoxy are easier to metabolize than flourine. The Court does not dispute the truth of this assertion, but given the complete lack of information about the other substituents disclosed in the references, the Court has no reason to believe that those groups are not equally good metabolic handles.

Finally, the Court notes that Dr. Jorgensen testified that even if the person of ordinary skill were to move away from the flourine, s/he would not necessarily select a CH_3 or OCH_3 group as the replacement, and would not know what effect those groups would have on the half-life of the compound. (Trial Trans. XVI 89:15-90:20 ("[Y]ou don't know exactly what will happen. You can make the change there. You may get something where the half-life is two minutes. That doesn't do you any good.").)

Having considered all of this evidence, the Court finds that Teva has failed to meet its burden of proving that the person of ordinary skill would have substituted the flourine on the B-Phenyl for a methyl or methoxy group. This finding is an adequate and independent ground to rule against Teva on its obviousness attack.

(e) Adding a CN or CF_3 on the 3-Position of the Pyrazole

As the next and final step in Teva's theory of obviousness, Teva contends that the person of ordinary skill would have been motivated to make compounds with a cyano (CN) or trifluoromethyl (CF_3) on the three position of the pyrazole.[39] Dr. Trummlitz testified on direct examination that the person of ordinary skill would have considered this obvious because these two groups dominate the examples of the '142 Patent with the most data:

> The most widely used substituents, and this means the substituents for compounds for which are the most detailed data are available, or the compounds, biological data, two groups are dominating. One is the CN group, and the other one is the CF 3 group. And this is the reason for the selection of these two groups which are connected to a heterocycle, we discussed before, which is the pyrazole.

(Trial Trans. IV 49:22-50:3.)

On cross examination, however, counsel for Pfizer confronted Dr. Trummlitz with his expert report, in which he wrote that the person of ordinary skill would have been motivated to use either a CN or CF_3 group "based on the *in vitro* biological data given in the Fujisawa references." (Dr. Trummlitz Expert Report, at ¶ 86 (emphasis added); see also Trial Trans. VII 85:14-23 .) Example 6

[39] Celecoxib has a trifluoromethyl in this position.

of the '142 Patent is the only example with in vitro data. Upon further questioning, Dr. Trummlitz refined his previous testimony and explicitly conceded that he had based his opinion on the heterocycle substituent in example 6:

> Q: [Paragraph 86 of your expert report] says you would be motivated to use a CF 3 or a CN based on the in vitro biological data in the Fujisawa references, right that is what you said, right?
> A: Yes.
> Q: That is example 6, right?
> A: Yes.
> Q: [There] is no other in vitro data, right?
> A: No other in vitro, yes.
> Q: So I am correct that in this section of your expert report, even though you don't say it, you say you are looking at the in vitro data and that has to be example 6, right?
> A: Yes.
> Q: That's correct?
> A: Yes.

(Trial Trans. VII 85:20-86:8.) Example 6 uses a CN group as the substituent—it says nothing about CF_3. Accordingly, relying only on example 6 would not have led the person of ordinary skill to make a compound with CF_3 as the heterocycle substituent.

On re-direct, Dr. Trummlitz testified that he meant to write "biological data" in his expert report, not "in vitro biological data." This testimony hurts Teva's case at least as much as it helps. At best, Dr. Trummlitz was not accurate in his expert report and not truthful when he conceded on cross examination that he

based his opinion on example 6. This would cast doubt on his credibility. At worst, Dr. Trummlitz derived a false post-hoc rationalization to avoid statements in his expert report that damaged Teva's case. This would also cast serious doubt on his credibility. Accordingly, the Court is not inclined to give significant weight to Dr. Trummlitz's testimony on the subject of the CN/CF_3 substituent.

Putting aside Dr. Trummlitz's testimony, the fact remains that there are seven examples in the '142 Patent that use a sulfonamide substituent and have biological data included. Of these seven, four have cyano as the heterocycle substituent, two have trifluoromethyl, and one is unsubstituted. (DTX 34, examples 6, 11-3, 15-6, 17-1, 36, 37-2, and 45-8.) Teva argues that this is sufficient to show that the person of ordinary skill would have been motivated to make compounds using cyano and trifluoromethyl as the substituent. Teva concedes that the '142 Patent includes examples without data that use other heterocycle substituents, but contends that the person of ordinary skill would have given preference to the examples with data.

Even assuming that this is correct, Teva failed to offer any explanation for ignoring the examples *with data* in the '196 Application. There are five examples in the '196 Application that use a sulfonamide substituent and have biological data. Of those five, not a single one uses a CN or CF_3 as the heterocycle

substituent. Three are unsubstituted, one has a hydroxide as the heterocycle substituent, and one has a methyl. (PTX 34 at PFC 02019235-37.) Thus, the majority teaching of the '196 Application is to have no substituent at all on the heterocycle.[40] Teva offers no explanation for ignoring this teaching or discarding methyl and hydroxide as possible substituents.

Moreover, Dr. Jorgensen testified that the person of ordinary skill would have been disinclined to use cyano or trifluoromethyl because of significant problems with those groups that were well known in the field in 1993. (Trial Trans. XVI 84:21-85:7.) As for trifluoromethyl, Dr. Jorgensen also explained that it is an "extremely lipophilic group."[41] (Id. at XVI 85:24.) It is incongruous for Teva to argue that the person of ordinary skill would select a sulfonamide to reduce the lipophilicity of the compound (see *supra* Section I.D.3(b)), and then turn around and argue that the s/he would select an "extremely lipophilic group" as the substituent on the pyrazole. (See Trial Trans. XVI 87:7-11 ("[I]f there was a concern for bioavailability as suggested by the Teva experts, then you certainly would want to avoid a CF 3 group. That is a very well known, you know,

[40] Of the 71 examples with and without data, 49 have no substituent on the heterocycle.

[41] For an explanation of lipophilicity, see *supra* Section I.D.3(b).

lipophilic group that would make your compounds less water soluble and less bioavailable.").)

Accordingly, Teva has not shown by clear and convincing evidence that the person of ordinary skill would have been motivated to use a cyano (CN) or trifluoromethyl (CF_3) as the heterocycle substituent. This is another adequate and independent ground to rule against Teva on its obviousness defense.

4. Pfizer's Actual Efforts Belie Obviousness

Drs. Talley and Seibert both offered detailed testimony about the extensive efforts undertaken by Pfizer scientists in relation to the development of celecoxib.[42] Dr. Talley, a chemistry group leader, testified that dozens of scientists spent thousands of hours for many years working on the development of a new

[42] Teva moved in limine to preclude evidence concerning Pfizer's efforts to develop a COX-2 selective inhibitor. Teva argued that the efforts of the actual inventors are irrelevant to the obviousness inquiry because obviousness is determined from the point of view of a hypothetical person having ordinary skill in the art—not the actual inventor. The Court denied the motion. See Opinion on Teva's Motion in Limine No. 2 (Oct. 13, 2006). The "Federal Circuit has frequently focused on the unsuccessful attempts of the patentee in its obviousness analyses," and other courts have followed suit. Syntex LLC v. Apotex, Inc., No. 01-2214, 2006 U.S. Dist LEXIS 36089, at *78 (N.D. Cal. June 2, 2006); see also Micro Chem, Inc. v. Great Plains Chem. Co., 103 F.3d 1538, 1547 (Fed. Cir. 1997); In re Dow Chemical Co., 837 F.2d 469, 473 (Fed. Cir. 1988). Accordingly, the Court reiterates its position that this evidence is probative of the non-obviousness of the patents-in-suit.

NSAID. They screened over 200,000 compounds looking for potential leads,[43] and scoured the relevant scientific literature. They ultimately selected five lead compounds. They created thousands of analogs based around these leads—approximately 2000 in 1992-1993—but despite their extensive efforts were often unable to determine how to optimize the compounds for COX-2 selectivity or which structural features affected the potency of the series.[44] Many of the analogs displayed good in vitro activity against COX-2 but failed to display good anti-inflammatory activity in vivo.

Dr. Seibert, a biology group leader, provided additional testimony about the extensive efforts that went into the creation of celecoxib. She described the various levels of testing that compounds were put through in order to evaluate their efficacy and safety. She explained that of the thousands of compounds developed and tested over the course of the project, only two ever made it to the last level of testing—clinical trials—and only one of these was proven to be safe

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[43] Pharmaceutical companies store small samples of test molecules that can be screened against a new target when scientists want to create a new drug. (Trial Trans. XV 48:20-49:1.)

[44] Structure Activity Relationship ("SAR") testing is one way that scientists investigate new compounds. SAR analysis involves changing individual parts of a molecule to see how the changes affect the activity of the compound. The resulting compounds with individual changes are known as analogs.

and effective in humans.

The extensive efforts that preceded the creation of celecoxib is "entitled to fair evidentiary weight," and weighs against a finding of obviousness. In re Dow Chemical Co., 837 F.2d 469, 473 (Fed. Cir. 1988) (stating that "the five to six years of research that preceded the claimed invention" was "entitled to fair evidentiary weight.").

5. Summary

In sum, Teva falls far short of satisfying its burden of showing a *prima facie* case of obviousness by clear and convincing evidence. The Court rejects Teva's argument on each of the following adequate and independent grounds: (1) the '196 Application/'995 Patent is not prior art to the patents-in-suit; (2) even if it were prior art, the person of ordinary skill would not use it as the starting point; (3) even if the person of ordinary skill did start with the '196 application, s/he would not derive Teva's proposed hypothetical pharmacophore because (a) s/he would not include unlisted heterocycles, and (b) s/he would require the phenyl rings to be attached to adjacent carbon atoms connected by a double bond; (4) even if the person of ordinary skill did derive the pharmacophore, s/he would not arrive at the twelve allegedly obvious compounds because (a) s/he would not attach a phenyl to

a nitrogen atom in a 1,5 configuration, (b) s/he would not add a cyano (CN) or trifluoromethyl (CF_3) as a substituent on the heterocycle, and (c) s/he would not add a methyl (CH_3), or methoxy (OCH_3) as a substituent on the B-phenyl. Accordingly, the Court finds for Pfizer with respect to Teva's obviousness defense.[45]

II. INEQUITABLE CONDUCT

Teva next argues that the patents-in-suit are unenforceable due to inequitable conduct by Pfizer during prosecution of the patents. "Patent applicants and those substantively involved in the preparation or prosecution of a patent application owe a 'duty of candor and good faith' to the PTO." M. Eagles Tool Warehouse, Inc. v. Fisher Tooling Co., 439 F.3d 1335, 1339 (Fed. Cir. 2006) (quoting 37 C.F.R. § 1.56(a) (2004)). Breaching this duty can constitute inequitable conduct, which renders the patent unenforceable. Id. at 1340.

An inequitable conduct analysis involves three steps. See Hoffmann-La Roche, Inc. v. Promega Corp., 323 F.3d 1354, 1359 (Fed Cir. 2003). First, there must have been a "misrepresentation or omission of a material fact." Id. Second,

[45] Because Teva did not show even a *prima facie* case for obviousness, this Court has considered, but need not separately address, the objective evidence of non-obviousness.

the misrepresentation or omission must have been made "with an intent to deceive the PTO." Id. Materiality and intent to deceive must be shown by clear and convincing evidence. Id. Third, assuming the first two requirements have been met, "the district court must determine whether the equities warrant a conclusion that the patentee has engaged in inequitable conduct." Id. (citing Molins PLC v. Textron, Inc., 48 F.3d 1172, 1178 (Fed. Cir. 1995); See also Kemin Foods, L.C. v. Pigmentos Vegetales Del Centro, 464 F.3d 1339, 1346 (Fed. Cir. 2006) ("Even when a court finds that the patentee failed to disclose material information to the PTO and acted with deceptive intent, the court retains discretion to decide whether the patentee's conduct is sufficiently culpable to render the patent unenforceable.").

Here, Teva argues that Pfizer committed inequitable conduct by failing to disclose International Application No. WO 95/00501 (the "'501 Application") during prosecution of the '823 Patent, and failing to disclose the '501 Application and the '995 Patent during prosecution of the '068 and '165 Patents. The following dates are critical to understanding and evaluating Teva's inequitable conduct argument:

- June 24, 1993: Merck filed the '196 Application (discussed at length above);

- Nov. 30, 1993: Pfizer filed the '594 Application that ultimately issued as the '823 Patent;
- Jan. 10, 1994: Merck abandoned the '196 Application;
- Feb. 22, 1994: Merck filed the '467 Application as a continuation-in-part of the '196 Application;
- 1993 or 1994: Merck filed the '501 Application, an international application which claimed priority to the '196 and '467 Applications;
- Jan. 5, 1995: The '501 Application was published;
- Nov. 14, 1995: The '823 Patent-in-Suit issued;
- Dec. 12, 1995: The '995 Patent issued from the '467 Application;
- August 8, 1996: The '165 Patent-in-Suit issued;
- June 2, 1998: The '068 Patent-in-Suit issued.

Teva's argument with respect to the '823 Patent is addressed below in Section (A). Teva's additional arguments with respect to the '068 and '165 Patents are addressed in Section (B).

A. The '823 Patent

As noted above, Teva contends that the '823 Patent is unenforceable because Pfizer committed inequitable conduct during prosecution of the Patent by

failing to disclose the '501 Application to the PTO. For Teva to succeed in this argument, it must prove by clear and convincing evidence (1) that the '501 Application was material and (2) that Pfizer omitted this reference with an intent to deceive the PTO.

1. Materiality of the '501 Application

At the time the patents-in-suit were filed, the standard for materiality was the "reasonable examiner" standard: A reference is material if a reasonable examiner would have considered it important in deciding whether the proposed claims were patentable. See Digital Control, Inc. v. Charles Machine Works, 437 F.3d 1309, 1314 (Fed. Cir. 2006). Under this standard, a reference need not necessarily present a *prima facie* case of unpatentability to be considered material. Id. at 1315; Agfa Corp. v. Creo Prods., 451 F.3d 1366, 1373 (Fed. Cir. 2006).

As best as the Court can tell, Teva does not claim that the '501 Application is material due to the compounds or teachings expressly disclosed therein.[46]

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[46] Even if the Court is misinterpreting Teva's position, and Teva does in fact contend that the compounds and teachings of the '501 Application render the document material, the argument would fail for the same reasons discussed herein since it is undisputed that the '501 Application is not prior art to the patents-in-suit. (Trial Trans. XI 28:18-22.)

The Court also notes that its difficulty understanding Teva's argument is due to a lack of clarity in Teva's explication of its inequitable conduct theory.

Rather, Teva argues that if Pfizer had disclosed the '501 Application to the PTO, the Patent Examiner could have obtained a copy of the '196 and '467 Applications, and reviewed them to determine whether the content of the '196 Application that was carried forward into the '467 Application was prior art that could have formed the basis of an obviousness rejection.[47] According to Teva, the Examiner would have found this common content important because it taught the interchangeability of sulfonamides and methylsulfones. Thus, the examiner could have held Pfizer's '594 Application in abeyance until the '467 Application issued as a patent and then issued a rejection of Pfizer's claims. (See Teva's Post-Trial Reply Brief at 57-58.)

The Court agrees that if the '501 Application had been disclosed to the PTO, it would have revealed the existence of the '196 and '467 Applications to the Patent Examiner. These Applications are clearly listed as priority documents on the face of the published '501 Application. (See PTX 66.) The Court also agrees

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Since it is Teva's burden to prove inequitable conduct by clear and convincing evidence, a lack of clarity in its argument is a potentially significant fault in its defense.

[47] Only disclosures that are "carried forward" from a parent application to the final patent can ever be considered invalidating prior art. See In re Lund, 376 F.2d 982 (C.C.P.A. 1966). For the remainder of this Section, the content of the '196 Application that was carried forward to the '467 Application (and ultimately to the '995 Patent) will be referred to as the "common content."

that after learning about them from the '501 Application, the Examiner could have obtained a copy of the Applications and reviewed them. Mr. Smith, Teva's expert on Patent Office practice and procedure, so testified and this testimony is not disputed.[48] (Trial Trans. XI 28:25-29:7.) Finally, the Court agrees that the examiner could have held the '594 Application in abeyance until the '467 Application issued as a patent, and then rejected Pfizer's claims—if he found that the common content was prior art that rendered Pfizer's claims obvious. The MPEP clearly provides for such a procedure. (DTX 692 at 800-12.)

However, the Court does not agree with one crucial element of Teva's argument. The Court does not agree that the Examiner would have found the common content to be prior art that rendered Pfizer's claims obvious. Therefore, the Examiner would not have considered the '501 Application to be important when evaluating the patentability of Pfizer's claims.

(a) The '196 Application Cannot Affect Patentability Because It Is Not Prior Art

The Court has already determined that the common content of the '196 Application and '995 Patent is not prior art to the patents-in-suit because the

[48] Mr. Wiseman, Pfizer's expert on Patent Office practice and procedure, testified that this is not routinely done, but did not dispute the fact that it could be.

claims of the '995 Patent were not fully supported by the disclosure of the '196 Application. (See supra Section I.B.1.) Thus, it could not have figured into an obviousness rejection. Teva argues that this is irrelevant because "[m]ateriality is not limited to prior art but instead embraces *any* information that a reasonable examiner would be substantially likely to consider important in deciding whether the allow an application to issue as a patent." GFI, Inc. v. Franklin Corp., 265 F.3d 1268, 1274 (Fed. Cir. 2001). There is no doubt that this is an accurate statement of the law. See, e.g., Liquid Dynamics Corp. v. Vaughan Co., 449 F.3d 1209, 1226-27 (Fed. Cir. 2006) (quoting Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., 326 F.3d 1226, 1234 (Fed. Cir. 2003)); Akron Polymer Container Corp. v. Exxel Container, Inc., 148 F.3d 1380, 1382 (Fed. Cir. 1998) ("With regard to the issue of inequitable conduct, we noted that both the parties and the district court appear to have assumed, quite incorrectly, that only prior art can be a material reference.") (internal quotation marks omitted). By definition, however, information is only material if it is likely that a reasonable examiner would consider it important to patentability for some reason, and Teva has offered no explanation of how the common content could possibly be relevant to patentability if it is not prior art.

In other cases where non-prior art was deemed potentially material, the

references could have served as the basis of a rejection on some ground other than obviousness. In Akron Polymer, for example, the Federal Circuit held that a reference was "highly material," despite the fact that it was not prior art, "because it could have served as the basis of a double patenting rejection." Akron Polymer Container Corp., 148 F.3d at 1382. Similarly, in GFI, Inc., the Federal Circuit agreed that a reference was material, even though it was not prior art, because the reference at issue raised a "potential priority conflict." GFI, Inc., 265 F.3d at 1274. Here, by contrast, there appears to be no reason that a reasonable examiner would have considered the '196 Application at all in deciding whether or not to allow Pfizer's application to issue as a patent. It could not have served as the basis for a rejection on obviousness grounds, double patenting grounds, or on any other ground that the Court can envision. In such circumstances, the reference cannot be considered material. See, e.g., Northern Telecom, Inc. v. Datapoint Corp., 908 F.2d 931, 940 (Fed. Cir. 1990) ("Since the Viatron 21 device was not prior art, it was not material to patentability."); Environmental Designs, Ltd. v. Union Oil co., 713 F.2d 693, 698 (Fed. Cir, 1983) ("The disclosure not being prior art, it would not have been material to the patentability of the Beavon process.").

Accordingly, the Court finds that a reasonable examiner would not have been likely to consider the common content important in deciding whether to

allow the '594 Application to issue as a patent. Thus, the '501 Application is not material, and Pfizer's failure to disclose it cannot constitute inequitable conduct.

(b) If the Common Content is Prior Art Then the '501 Application is Material

The Court has already held that the disclosure of the '196 Application does not render the claims of the '823 Patent obvious. As previously noted, however, a reference need not present a *prima facie* case of unpatentability in order to be considered material for purposes of an inequitable conduct analysis. Indeed, "[i]nformation concealed from the PTO may be material even though it would not invalidate the patent. . . . As stated, the test for materiality is whether a reasonable examiner would have considered the information important, not whether the information would conclusively decide the issue of patentability." The Li Second Family Ltd. P'ship v. Toshiba Corp., 231 F.3d 1373, 1380 (Fed. Cir. 2000); see also A.B. Dick Co. v. Burroughs Corp., 798 F.2d 1392, 1397 (Fed. Cir. 1986) ("The test for materiality is *not* whether there is anticipation or obviousness but, rather, what a reasonable examiner would consider . . . important in deciding whether to allow the application to issue as a patent.") (internal quotation marks omitted). The Court agrees that the '501 Application would be material under this

standard if the common content were prior art.

There is substantial evidence indicating that Pfizer believed use of a sulfonamide substituent was critical to the patentability of their invention over the prior art. Indeed, Dr. Talley conceded that Pfizer scientists were concerned that their initial pyrazole compounds, which used methylsulfone substituents, were not patentable over Fujisawa references that disclosed diphenyl heterocycles with methylsulfone substituents. (Trial Trans. XV at 101:20-103:1.) The evidence also shows that it was considered a "pivotal discovery" when Dr. Khanna, another inventor on the patents-in-suit, discovered that the methylsulfone could be replaced with a sulfonamide in pyrrole compounds without affecting the compounds' activity. (DTX 8 at PFC 01218943; see also Inventor Penning Dep. at 145:4-146:9 (Nov. 4, 2005).) Pfizer believed that the discovery was equally applicable to compounds with heterocyclic cores other than pyrroles (DTX 8 at PFC 01218943), and that this could solve the "patent issue" with their initial pyrazole compounds (see, e.g., DTX 62 at 00322023).[49]

[49] See also DTX 214 at PFC 00289843 ("Initial data suggest that we can replace $MeSO_2$ [methylsulfone] in the diaryl series with NH_2SO_2 [sulfonamide], a finding that has important patent ramifications.") Id. at 00289859("Emerging data indicate that in vitro potency is maintained, if not improved, when $MeSO_2$ is replaced by NH_2SO_2. This discovery should be applicable to other heterocyclic series and has important patent ramifications.").

The common content discloses the possibility of using either a methylsulfone or sulfonamide as the substituent on one of the phenyls of a diphenyl heterocycle. It includes 55 diphenyl heterocycles with a sulfonamide substituent and 12 diphenyl heterocycles with a methylsulfone group. Thus, Teva argues that a reasonable examiner would have considered it important. Pfizer contends that it is irrelevant to the patentability of the '594 Application because none of the structures disclosed by the common content use pyrazoles as the heterocycle, so it does not teach the interchangeability of a methylsulfone and sulfonamide *on pyrazole compounds*. While it is true that the teaching of the common content does not expressly include pyrazoles, the Court does not agree that this would necessarily make it irrelevant in the eyes of a reasonable examiner.

Thus, the Court finds that if the common content were prior art, a reasonable examiner would likely have considered it important when evaluating the patentability of Pfizer's claims since it purported to solve the same problem as the '823 Patent and disclosed diphenyl heterocyclic anti-inflammatory compounds with both sulfonamide and methylsulfone substituents. Accordingly, the '501 Application would be material. Nevertheless, Teva's inequitable conduct defense would still fail because, as explained below, Teva has not established that Pfizer acted with the requisite intent to deceive the PTO when it failed to disclose the

‘501 Application.

2. Intent to Deceive

“To satisfy the requirement of the intent to deceive element of inequitable conduct, ‘the involved conduct, viewed in light of all the evidence, including evidence of good faith, must indicate sufficient culpability to require a finding of intent to deceive.’” M. Eagles Tool Warehouse, 439 F.3d at 1341. The ‘501 Application was published while the ‘823 Application was still pending, and it is undisputed that Dr. Talley and Mr. Bulock (the attorney who prosecuted the patents-in-suit) were aware of the ‘501 Application during that time. However, knowledge of an omitted reference is not sufficient to support a finding of intent. Indeed, even “a finding that particular conduct amounts to ‘gross negligence’ does not of itself justify an inference of intent to deceive.” See, e.g., Kingsdown Medical Consultants, Ltd. v. Hollister, Inc., 863 F.2d 867, 876 (Fed. Cir. 1988).

Intent can rarely be proven by direct evidence. See Merck & Co. v. Danbury Pharmacal Inc., 873 F.2d 1418, 1422 (Fed. Cir. 1989). Thus, “[i]ntent is generally inferred from the facts and circumstances surrounding the applicant’s overall conduct, especially where there is no good faith explanation for nondisclosure.” M. Eagles Tool Warehouse, 439 F.3d at 1341.

Here, Teva argues that actual intent can and should be inferred from both (a) the lack of a credible explanation for Pfizer's failure to disclose the '501 Application and (b) Pfizer's pattern of alleged misconduct. The Court disagrees.

(a) Pfizer Has Offered a Good Faith Explanation for Failing to Disclose the '501 Application

A good faith explanation for failure to disclose a material reference can refute an inference of intent. Id. The inverse proposition is also true: "the absence of such an explanation can constitute evidence to support a finding of intent." Id. Thus, the parties vigorously dispute whether Pfizer has offered a good faith explanation for its failure to disclose the '501 Application. Pfizer says it has—namely, that nobody at Pfizer believed the '501 Application was relevant to the claims of the '594 Application because the '501 did not include pyrazoles. Teva contends that this is an incredible, litigation-driven rationalization—not a good faith explanation.

Pfizer cites a significant amount of strong evidence to support the legitimacy of its explanation. First, Teva cites the trial testimony of Dr. Talley.[50] Dr. Talley testified that he first saw the '501 Application around February 1995

[50] As previously noted, Dr. Talley is one of the inventors of celecoxib named on the patents-in-suit.

when he received a copy of it from a patent alerting service. Upon receipt, he and his colleagues "studied it and tried to get . . . and understanding of what Merck had done." (Trial Trans. XV 80:25-81:5.) They concluded that the Application was directed to a series of furanone derivatives. The inventors were concerned by this because they had also done work with furanones. In fact, they found that there were compounds in the '501 Application that they had synthesized in their labs and had included in a pending patent application, U.S. Application No. 08/004,822 (the "'822 Application"). Accordingly, Pfizer declared an interference over the overlapping subject matter in the '501 and '822 Applications.[51] Dr.

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[51] Dr. Talley also noted that the celecoxib related patents never came up during the lengthy interference proceedings regarding the '501 and '822 Applications:

> There was never any question that, you know, those – the celecoxib series of patents, was in any way related to the ['501] PCT application, they are different compounds and Merck scientists never contended that that patent would relate to the one that you have just seen for Merck.

(Trial Trans. XV 85:2-8.) Teva argues that the fact that celecoxib was never raised during the interference is irrelevant because there is nothing in the record about the scope of the interference:

> Interferences are priority contests as to conception of claimed subject matter. There is nothing in the record to indicate that Merck ever presented any patent claims broad enough to include celecoxib. But even if Merck did not, that does not mean that the disclosure (as opposed to the claims) is not material and invalidating prior art . . . .

(Teva's Post-Trial Reply Brief at 70-71.) The Court agrees with Teva's argument, but still finds it somewhat relevant that Pfizer's work with celecoxib was never

Talley testified that it never occurred to him that the compounds disclosed in the '501 Application were relevant to any other application, including the '594 Application, or to or his work with celecoxib because the '501 Application did not include pyrazoles:

> Q: Now, did you, when you read the Merck ['501] application, did it come into your mind that it was relevant to any other patent application?
> A: No, that didn't dawn on me. . . .
> . . .
> Q. And did you have any understanding of whether or not that list related to your Celecoxib work?
> . . .
> A: There is no pyrazole described in [the '501] application.
> Q: So what? What does that matter?
> A: Well, because, you know, from my way of thinking then that ['501] application, it is not relevant to the class of compounds that we had discovered. Because there is no pyrazole in there at all.
> Q: Why does it matter what the ring is? I guess that is, that seems to be what you are talking about. Why does it matter?
> A: Well, it makes, you know, I think what you have seen this morning is that, you know, changing the nature of the substituents about the ring can have a real big effect on both in vitro and in vivo activities, and so the nature of that central ring is really, really plays a big role in terms of, you know, making the compound, activity in the various assays.

(Trial Trans. XV 83:7-84:11.)

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raised at all. Accordingly, this fact has been afforded only minimal weight in the Court's analysis.

Dr. Talley's testimony regarding Pfizer's understanding of the relevance—or lack thereof—of the '501 Application is corroborated by other record evidence. For example, Mr. Bulock, who prosecuted the patents-in-suit, also prosecuted several other patent applications that included claims with heterocyclic structures. (Trial Trans. XIV at 90:21-25.) None of these other applications were directed solely to pyrazoles. Each one contained claims that depicted heterocycles which were disclosed in the '501 Application. Mr. Bulock disclosed the '501 Application during prosecution of all these applications. Accordingly, the record reflects a consistent practice by Mr. Bulock of considering the heterocyclic core and disclosing the '501 Application to the PTO when the application being prosecuted had claims depicting compounds with the same heterocyclic core as compounds disclosed in the '501 Application. This confirms that Pfizer's practice was to make distinctions and disclosures based on the heterocycle.

Moreover, Patent Office practice confirms the reasonableness of focusing on the heterocyclic core in determining the relevancy of a reference. The record indicates that examiners normally design prior art search parameters based on the identity of the heterocyclic core when examining claims involving heterocyclic compounds. For example, when examining the '594 Application, which is limited

to pyrazoles, the Patent Examiner "presented a core structure which he wanted the search technician to look for. And that structure has a pyrazole . . . . " (Trial Trans. XIV 74:18-25.) Similarly, the Examiner responsible for the '995 claims, which include structures with a furnanone heterocyclic core, directed the search to furanones. (Id. at 75:22-76:3; PTX 2446; PTX 37 at PFC 02025397; see also Trial Trans. XIV 73:24-74:16.)

Accordingly, the Court finds that Pfizer has offered credible and compelling evidence of a good faith explanation for failing to disclose the '501 Application. Teva contends, however, that Pfizer's explanation is not credible and is simply a post-hoc litigation-driven rationalization for its intentional concealment of the reference. Although Teva makes several arguments in support of this position, the Court does not find any of them to be persuasive.

To counter Pfizer's argument that Mr. Bulock's standard practice was to disclose references with the same heterocyclic core as the application being prosecuted, Teva points out that Mr. Bulock disclosed an oxazole reference when prosecuting U.S. Patent 5,616,601—an imidazole patent. (PTX 48 at PFC 02017878-79.) Teva argues that this disclosure discredits the idea that it was Pfizer's practice to make distinctions and disclosures based on the heterocycle. However, by focusing on this single disclosure, Teva ignores the record which

reflects a highly consistent pattern of disclosing references that have the same heterocyclic core as the patent application in which the disclosure was made. Of the non-pyrazole patent applications that Mr. Bulock prosecuted, Teva has pointed to only one out of approximately 190 disclosures that is not directed to the same heterocycle claimed by the respective applications. (See PTX 24-31, references listed on patent cover.) Of both the pyrazole and non-pyrazole applications that Mr. Bulock prosecuted, Teva pointed to only that same single reference out of approximately 380 disclosures. (See PTX 1, PTX 3, PTX 5, PTX 19-31, references listed on patent cover.) Accordingly, the Court is not convinced that this single disclosure of an oxazole reference during prosecution of an imidazole patent discredits Pfizer's assertion that its practice was to make distinctions and disclosures based on the identity of the heterocycle.

Teva also relies on Attorney Bulock's deposition testimony that his absolute understanding as to why the '501 Application was not disclosed was unclear, (Bullock Dep. Vol. 1 at 230:25-231:5 (Jan 27, 1006)), and asserts that "[s]uch a failure of memory is not accepted as a credible explanation." (Teva's Post-Trial Reply Brief at 60-61.) In order to evaluate this argument and the import of Mr. Bulock's testimony, it is necessary to put Mr. Bulock's statement in context. After stating that his "absolute understanding" was "not clear," Mr. Bulock went on to

say:

> What is clear, looking at the ['501 Application] now, is that it does not teach [p]yrazoles. And even though it may teach some diaryl compounds, they don't ever connect to a [heteroatom]. So they're quite far removed, in my mind, looking at it at this time, and not pertinent to the pyrazole application-at-suit.

(Bullock Dep. Vol. 1 at 230:5-11.) Taken in its complete context, the Court does not view Mr. Bulock's testimony as evidence that Pfizer's explanation for omitting the '501 application is not legitimate.

Next, Teva contends that Dr. Talley is not credible. Teva relies heavily on the existence of an error in the '594 Application, namely the inclusion of a methylsulfone group rather than a sulfonamide group in formula II of the Application. Teva points out that each of the eleven inventors of the patents-in-suit, including Dr. Talley, signed an oath and declaration associated with the '594 Application, which states: "I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims . . . ." Teva argues that the fact that Dr. Talley signed the declaration—despite the error in formula II—shows that he did not read the specification and claims as he swore he did. This, Teva contends, demonstrates that Dr. Talley had a "cavalier attitude" toward his obligation to the PTO and calls his credibility into question. The Court is completely unconvinced by this argument. All of the record evidence indicates

that the error was a mere oversight—a typographical error. (See, e.g., Trial Trans. XI 103:4-17.) The Court fails to see how the fact that Dr. Talley overlooked a typographical error among hundreds of pages of chemical compounds affects his credibility.

Teva also attempts to cast doubt on Dr. Talley's credibility by arguing that his trial testimony was inconsistent with deposition testimony he gave several years ago in un unrelated litigation. Teva contends that "Dr. Talley testified in 2000 in litigation against Merck that he believed the '501 application was relevant to all heterocycles." (Teva's Post-Trial Reply Brief at 67.) However, the Court has reviewed the deposition testimony, and does not agree with Teva's characterization of Dr. Talley's statements. The Court finds no inconsistency between the testimony Dr. Talley gave in this trial and the earlier deposition.

With respect to credibility, Teva also argues that although Pfizer could have called several inventors to testify as to their reasons for failing to disclose the '501 Application, Pfizer "chose not to give the Court an opportunity to evaluate, live, the credibility of any of these inventors. Instead, Plaintiffs brought only Dr. Talley to testify." (Teva's Post-Trial Brief at 64; see also Teva's Post-Trial Reply Brief at 69.) The Court is completely unpersuaded by this argument as well. The fact that Pfizer selected one inventor to testify on this issue, rather than presenting

cumulative evidence from each inventor, affects neither the credibility of Pfizer's selected witness nor the overall credibility of Pfizer's explanation.

Finally, Teva points out that although learning of Merck's COX-2 research was a "landmark event" at Pfizer, there is no documentary evidence demonstrating that anyone at Pfizer thought the '501 Application was not relevant to the patents-in-suit. This argument is spurious. As an initial matter, Teva tries to create the impression that learning about the '501 Application was a major event at Pfizer because Pfizer was deeply concerned about whether the '501 Application would interfere with the celecoxib patent applications. This is misleading. As Dr. Talley explained, Pfizer was concerned about the '501 Application because of the overlap between that and the '822 Application, which was also directed to furanone compounds—not because of potential problems with their work on celecoxib or the celecoxib related patents.

Furthermore, the absence of documents showing that the inventors did not perceive the '501 Application as material to the '594 Application simply does not establish that they believed the document was important. It is illogical to assume that anyone would prepare documents regarding the immateriality of a reference. If anything, one would expect there to be documents discussing the reference if the inventors believed that it was material. Accordingly, the complete lack of

documentary evidence concerning the '501 Application actually favors Pfizer's position that the inventors did not believe the '501 Application was relevant to the '594 Application.

Accordingly, given the totality of the evidence, the Court finds Pfizer's explanation for its failure to disclose the '501 Application to be credible and made in good faith.[52] This weighs strongly against a finding of intent to deceive the PTO, and ultimately against a finding of inequitable conduct.

Moreover, even if the Court were convinced that there was no good faith explanation for Pfizer's failure to disclose the '501 Application, the lack of an explanation would not, on its own, be sufficient to support an inference of intent. See M. Eagles Tool Warehouse, 439 F.3d at 1341 ("Failure to disclose a prior art device to the PTO, where the only evidence of intent is a lack of a good faith explanation for the nondisclosure, cannot constitute clear and convincing evidence to support a determination of culpable intent."). Accordingly, Teva argues that Pfizer engaged in a pattern of conduct that provides additional inferential support for a finding of intent. As detailed below, the Court does not agree that Pfizer's

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[52] Notably, even if Pfizer were wrong in its assumption that the '501 Application was not material, "[i]t is not inequitable conduct to omit telling the patent examiner information that the applicant in good faith believes is not material to patentability." Allied Colloids, Inc. v. Am. Cyanamid Co., 64 F.3d 1570, 1578 (Fed. Cir. 1995).

conduct is indicative of intent to deceive the PTO. Therefore, the Court would find that Teva has failed to prove intent by clear and convincing evidence even if it believed that there was no good faith explanation for Pfizer's omission of the reference.

(b) Teva Has Not Proven a Pattern of Culpable Conduct By Pfizer

Teva argues that Pfizer engaged in a pattern of conduct that indicates its intent to conceal material evidence from the PTO. Specifically, Teva alleges that Pfizer: (1) intentionally prevented the PTO from effectively considering the '829 Application; (2) failed to disclose DuP697; and (3) cited only non-analogous benzenesulfonamide art.[53]

i. *The '829 Application*

As discussed above, the Fujisawa '829 Application includes several compounds that are structurally similar to celecoxib as well as a considerable

[53] In its Post-Trial Reply Brief, Teva also contends that the fact that the Canadian counterpart to the patents-in-suit has been adjudged unenforceable under Canadian law further reflects Pfizer's pattern of misconduct. Teva concedes that the omissions at issue in the Canadian litigation did not occur during prosecution of the patents-in-suit. Moreover, Teva provides no information concerning the relevant Canadian law or how it compares to American law on inequitable conduct. Accordingly, the Court finds that the Canadian adjudication is irrelevant to the instant case.

amount of data indicating that the compounds are anti-inflammatory. It is undisputed that Pfizer submitted the '829 Application to the PTO during prosecution of the '823 Patent. Teva claims that the manner and timing of the submission was calculated to prevent the PTO from effectively considering the Application, and that this is indicative of Pfizer's general intent to conceal relevant information from the PTO. The relevant facts are not in dispute, and are outlined below.

- September 1993: At least one of the inventors of the '823 Patent was aware of the '829 Application.
- Nov. 30, 1993: The '594 Application was filed. It did not disclose the '829 Application.
- 1993 or 1994: Pfizer filed an international continuation-in-part application to the patents-in-suit (the "PCT '720 Application").
- March 23, 1995: The International Searching Authority issued an International Search Report ("ISR") that identified the '829 Application as a relevant reference. Under PTO procedure as set forth in the MPEP, an applicant must disclose any reference identified in an ISR to the PTO within three months. (See Trial Trans. XII 27:4-16.)
- April 18, 1995: The claims of the '594 Application were allowed. Once claims are allowed, an applicant must petition to have additional references considered by the Patent Examiner.
- May 16, 1995: Pfizer disclosed the '829 Application to the PTO in a Supplemental Information Disclosure Statement ("IDS")

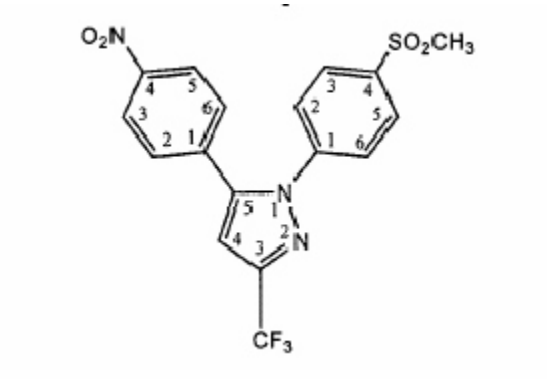
and petitioned to have the reference considered. The evidence indicates that no grant of petition was ever received and the '829 Application was not actually considered by the Examiner.

- August 7, 1995: The '594 Application issued as the '823 Patent.

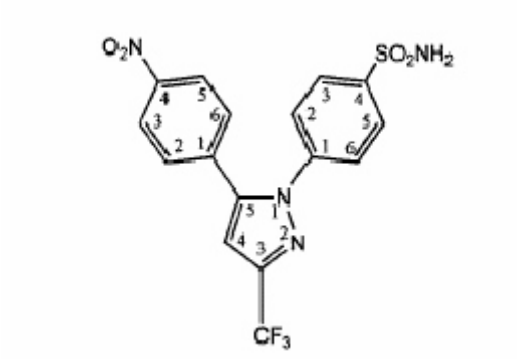
Teva contends that Pfizer intentionally waited to disclose the '829 Application until it was most likely that the Examiner would not actually review it. Pfizer responds that it did not disclose the '829 Application initially because the Application was cumulative to references already disclosed, namely the '142 Patent, and that it properly disclosed the Application when required to do so because of the International Search Report. Pfizer argues that "[p]roper disclosure of a reference that was entirely cumulative to references already in the record cannot possibly be evidence of intent to deceive the PTO." (Pfizer's Post-Trial Reply Brief at 33.) Teva claims that Pfizer's explanation is incredible because the '829 Application was not cumulative, and that foreign prosecution activity emphasizes Pfizer's deceitful intent by demonstrating the materiality of the reference.

As to cumulativeness, Teva claims the '829 Application cannot be cumulative to the '142 Patent because the '829 discloses at least one compound, example 29-3, that is structurally more similar to the compounds claimed in the

patents-in-suit than those disclosed in the '142 Patent. As shown in the picture below, example 29-3 differs from claim 11 of the '823 Patent only in the use of a methylsulfone rather than a sulfonamide substituent.



Fujisawa EP '829
Example 29-3



Pfizer '823 Patent
Claim 11 compound

Teva's position on the question of cumulativeness is undercut by its own trial strategy and the testimony of its own witness, Dr. Trummlitz. Teva originally planned to rely on the '829 Application as a crucial component in its obviousness analysis. (See Memoradum in Support of Teva's In Limine Motion No. 1.) When it became clear that Pfizer intended to challenge the prior art status of the '829 Application, Teva all but abandoned the '829 Application in favor of the '142 Patent. Teva's witnesses testified that the '196 Application in conjunction with the '142 Patent (rather than the '829 Application) rendered the claimed inventions

obvious. When asked how the '829 Application would affect his obviousness analysis, Dr. Trummlitz stated that the person of ordinary skill would consider the '829 Application relevant to the issue of choosing a substitutent to use on the B-phenyl of the chemical compound. He did not mention any other issue. Moreover, he conceded that the '829 Application does not actually include any additional information on the B-phenyl substituents beyond that which was disclosed in the '142 Patent—it merely provides additional examples of compounds using the same susbstituents taught by the '142 Patent:

> Q. How would the '829 application figure in to your analysis which you did?
> . . .
> A. . . . There are additional points just as the '829, the '829 is about 80 examples, the '142 has 250 examples. So in principal, the '829 handles a lower amount of substituents, it handles less information, but I have to, okay, I use one information regarding the OCH 3, but it would not change the analysis.
> . . .
> Q. Did the '829 application include some additional information from what was in the '142?
> A. No. As far as I know there are no structural information, no new substituents, it is reduction to a lower amount of substituents.

(Trial Trans. IV 56:1-57:10.) This testimony supports Pfizer's position that the '829 Application is cumulative to the '142 Patent, which was disclosed to the PTO.

Turning to the foreign patent prosecution activity, Teva's first argument is that the prosecution history of the PCT '720 Application suggests that Mr. Bulock was aware of the significance of the '829 Application. The Court disagrees. On August 7, 2005, the International Preliminary Examining Authority ("IPEA") issued a written opinion regarding the patentability of the claims in the PCT '720 Application. The IPEA rejected several claims of the '720 Application over, *inter alia*, the '829 Application and Fujisawa European Application No. 418845. Pfizer's foreign patent attorney responded to the written opinion on November 3, 1995. (DTX 551.) Teva states that this response was "presumably [written] with advice from the prosecuting attorney Bulock, suggesting that Bulock was aware of the pertinence of the Fujisawa '829 application to the claims of the Searle '594 application." (Teva's Post-Trial Brief at 71.) Thus, Teva's entire argument with respect to the PCT '720 Application rests on speculation that the foreign patent attorney discussed the IPEA's rejection of the claims with Mr. Bulock. The Court will not engage in such speculation. Teva cites no evidence that such a consultation occurred, and in the absence of such evidence the Court will not infer that Mr. Bulock was aware of the alleged pertinence of the '829 Application.

Teva's second argument with respect to foreign patent prosecution histories is that Pfizer made statements to other patent offices around the world in which it

distinguished similar claims over the '829 Application based on Pfizer's use of a sulfonamide substituent. Teva contends that these statements "emphasize the knowing omission of material references from which intent to deceive the PTO can be inferred." (Teva's Post-Trial Brief at 72.) Teva cites the prosecution history of European Patent Application 95902444 (EP '444) as its one and only example.[54]

On April 3, 1997, the European Patent Office rejected the claims of EP '444 over the Fujisawa '829 Application (D2) and '845 Application (D1). The European Patent Office explained:

> The present compounds (like the compounds described in D1 and D2) are 1,5-diaryl-substitued pyrazoles and differ from the known compounds in that in one phenyl group an akylsulfonyl [methylsulfone] or alkylsulfinyl group is replaced by an aminosulfonyl [sulfonamide] group. . . . this structural modification is prima facie obvious for a skilled person when looking for further anti-inflammatory agents.

(DTX 522.) On May 14, 1997, Pfizer's foreign agent, Dr. Hans C. Beil, sent a response in which he wrote: "All references related to the present antiinflammatory area require a sulfonyl substituent. Thus, one skilled in the art would not know to substitute sulfonamide or alkylsulfonyl." (Id.) Teva contends

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[54] EP '444 is a European patent awarded to the Pfizer inventors that was filed as a national stage of the PCT '720 Application. It claims priority to the '594 Application.

that Dr. Biel's response was written "at the direction of Mr. Bulock." (Teva's Post-Trial Brief at 72.) Teva cites Mr. Bulock's deposition testimony in support of this assertion, but the cited testimony does not establish that Mr. Bulock had any role in drafting this response. Mr. Bulock testified that he was "responsible for directing foreign agents in the prosecution of EP 794," but said nothing about the prosecution of EP '444. (Bulock Depo. 241:15-17 (Jan. 27, 2006).) Moreover, Mr. Bulock expressly stated that he probably would *not* have seen a letter submitted to the European Patent Office in response to an Office Action:

> Q: In the normal course, would you approve of the response to [the Office Action] before it was filed? . . .
> A: Again, probably I would not have seen this exact -- every word, every claim, change. There would have been some communications and some instructions as to *general approaches* to the -- to any outstanding examination report.

(Id. at 241:18-25 (emphasis added).) This testimony does not support an inference that Dr. Beil was acting at the direction of Mr. Bulock when Dr. Beil wrote that all of the existing anti-inflammatory references require a methylsulfone substituent Accordingly, whatever this letter may demonstrate with respect to Dr. Beil's knowledge or intent is irrelevant to the instant case because Dr. Beil was not involved in the prosecution of the patents-in-suit—and his knowledge and intent cannot be imputed to anyone who was.

Furthermore, even if the Court were to find that Mr. Bulock was in control of the prosecution of EP '444, the Court would still not be convinced that this letter evidences the materiality of the '829 Application, demonstrates Pfizer's awareness of the alleged materiality of the reference, or "emphasize[s] the knowing omission of material references from which intent to conceal from the PTO may be inferred." (Teva's Post-Trial Brief at 72.)

Accordingly, the Court is not convinced that Pfizer intentionally prevented the PTO from effectively considering the '829 Application, or that Pfizer's actions surrounding the '829 Application evidence a pattern of conduct from which intent to deceive can be inferred.

ii. *DuP 697*

It is undisputed that Pfizer did not disclose DuP 697 to the Patent Office during prosecution of the '823 Patent. Teva argues that this omission is further evidence of Pfizer's intent to deceive the patent office by withholding material prior art. The Court disagrees. Teva's own expert, Dr. Baker, conceded that DuP 697 is less relevant than the '142 Patent, which Pfizer disclosed:

> Q: But in fact, the compound like DuP697, but even closer, was disclosed through the Matsuo reference [the '142 Patent, correct?

A: '142, yes. Was in the '823 reference to the patent, yes.
Q: And that compound is even closer to what is claimed by [Pfizer] than DuP 697. Correct?
A: It has to be closer because they are both pyrazoles.

(Trial Trans. II 76:3-8.)

Nevertheless, Teva argues that DuP 697 is not cumulative because DuPont furnished in vivo data for a compound similar to one disclosed in the '196 Application. While true, this does not make DuP 697 more pertinent than the '142 Patent because the '142 Patent also discloses in vivo data.

Accordingly, the Court does not find Pfizer's omission of DuP 697 to evidence a pattern of conduct from which intent to deceive can be inferred.

iii. *Non-analogous Art*

Finally, Teva argues that Pfizer demonstrated an intent to deceive the PTO by disclosing primarily non-analogous art. Teva notes that Pfizer disclosed 27 references during prosecution of the patents-in-suit, but only four of those are described as disclosing anti-inflammatory agents, and none of those four disclose benzenesulfonamides. Pfizer characterizes its disclosure differently. Pfizer notes that it accurately described references that disclosed compounds consisting of pyrazoles and sulfonamides and explained that—unlike the pyrazole/sulfonamide

compounds claimed by the patents-in-suit—the prior art compounds were not known to possess any anti-inflammatory activity.

"Analogous art is that which is from the same field of endeavor or, if not within the field of endeavor, is still reasonably pertinent to the particular problem with which the inventor is involved." Janssen Pharmaceutica N.V. v. Mylan Pharms., Inc., 456 F. Supp.2d 644, 652 (D.N.J. 2006). Under this definition, the analogous art in this case would not be limited to anti-inflammatories. The prior art compounds containing pyrazoles and sulfonamides are also analogous because they are structurally similar to the compounds claimed in the '594 Application and are therefore "reasonably pertinent to the particular problem with which the inventor is involved."

Accordingly, Pfizer's prior art disclosures are not indicative of an intent to deceive the PTO.

B. The '165 Patent and '068 Patent

The '995 Patent issued while the '165 and '068 Patents were still pending. Thus, Teva argues that Pfizer committed inequitable conduct during prosecution of these patents by failing to disclose both the '501 Application and the '995 Patent. As to the materiality requirement, the materiality analysis set forth above

is equally applicable here. In other words, neither the '501 Application nor the '995 is material because neither reference is prior art; however, both would be material if they were prior art.

As to the intent requirement, the only difference from the previous analysis involves Pfizer's disclosure of the '829 Application and the inferences—if any—to be drawn therefrom. Teva does not dispute that the Examiner received and reviewed the '829 Application during prosecution of the '165 and '068 Patents. However, Teva argues that Pfizer's intent to conceal material information from the PTO can be inferred from the fact that Pfizer did not provide a description of the '829 Application on the Information Disclosure Statement on which it was disclosed. It is true that Pfizer did not provide a description of the document, but Teva's own expert witness conceded that no description was required by the PTO's rules. (Trial Trans. XI 90:17-19; see also PTX 880 at 600-82 ("The requirement for a concise explanation of relevance is limited to information that is not in the English language.").) Accordingly, the Court does not agree that any inference of intent to conceal information or deceive the PTO can be drawn from the omission of a description of the '829 Application.

C. Conclusion

In summary, Teva has not established that the '501 Application or the '995 Patent were material. Nor has Teva established that Pfizer acted with intent to deceive the PTO. Pfizer has offered a good faith explanation for the omission, and Teva has not proven that Pfizer engaged in a pattern of misconduct indicative of an intent to prevent consideration of material references.[55] Accordingly, the Court finds that the patents-in-suit are not unenforceable due to inequitable conduct.

III. BEST MODE

Teva also challenges the validity of the '823 patent and '165 Patent based on an alleged violation of the best mode requirement. Under 35 U.S.C. § 112, all patents must disclose the best mode of carrying out the claimed invention contemplated by the inventor at the time of filing. See 35 U.S.C. § 112. "The purpose of the best mode requirement is to ensure that the public, in exchange for the rights given the inventor under the patent laws, obtains from the inventor a full disclosure of the preferred embodiment of the invention." Dana Corp. v. IPC Ltd. P'ship, 860 F.2d 415, 418 (Fed. Cir. 1988); see also Herbert F. Schwartz, Patent

[55] Teva raised several other arguments in addition to those discussed in this opinion. The Court has considered all of these arguments but need not address them all because it finds them to be irrelevant or unpersuasive. The Court also notes that some of these arguments were expressly raised for the first time in Teva's 167 page Post-Trial Reply Brief.

Law and Practice 110 (5th ed. 2006) ("The purpose of the best mode requirement is to keep an inventor from concealing from the public preferred embodiments that the inventor has conceived."). The Federal Circuit has established a two-part test for evaluating compliance with the best mode requirement:

> First, the factfinder must determine whether, at the time of filing the application, the inventor possessed a best mode for practicing the invention. [This] prong . . . is highly subjective and focuses on the inventor's state of mind as of the date of filing the application. Second, if the inventor subjectively considered one mode to be preferred over all others, then the second inquiry is whether the inventor's disclosure is adequate to enable one of ordinary skill in the art to practice the best mode of the invention. This inquiry is objective and depends upon the scope of the claimed invention and the level of skill in the relevant art.

Bayer AG & Bayer Corp. v. Schein Pharms., Inc., 301 F.3d 1306, 1320 (Fed. Cir. 2002) (internal quotation marks and citations omitted); see also Old Town Canoe Co. v. Confluence Holdings Corp., 448 F.3d 1309, 1320 (Fed. Cir. 2006).

Teva argues that the inventors of the patents-in-suit had a best mode—they preferred COX-2 selective compounds and compounds that met specified performance criteria in in vivo assays—but failed to disclose this preference in the '823 or '165 Patent. Teva does not allege that the inventors preferred any particular compound or composition. Indeed, Teva's own witnesses testified that the inventors had not identified a "best compound" as of the filing date of the

application (Trial Trans. XV 56:22-57:11), and deposition testimony introduced by Teva establishes that the inventors actually expected all of the covered compounds to be COX-2 selective (Inventor Penning Dep. at 191:19-22 (Nov. 4, 2005)). Rather, Teva's position is essentially that the inventors' failure to disclose their method and criteria for selecting the best compound/composition from the numerous options covered by the patents constituted a violation of the best mode requirement.

As best as the Court can tell, Pfizer does not dispute that the inventors preferred compounds with a high COX-2 selectivity ratio or that they had criteria for selecting the most promising candidates for development. Pfizer argues, however, that this does not constitute a "best mode" within the meaning of § 112, and that failure to disclose it cannot be considered a violation of the best mode requirement.

Unfortunately, "the term 'mode' and the phrase 'carrying out the invention' are not definable with precision" and are not clearly defined by the statute or the relevant caselaw. Wahl Instruments, Inc. v. Acvious, Inc., 950 F.2d 1575, 1579 (Fed. Cir. 1991). However, the Federal Circuit's recent discussion of the best mode requirement in Bayer AG v. Schein Pharmaceuticals is instructive. There, the Federal Circuit noted that "[i]n the history of this court and our predecessor

courts, we have held claims invalid for failure to satisfy the best mode requirement on only seven occasions." Bayer AG, 301 F.3d at 1316. The Court then reviewed the facts and holdings of those seven cases, and determined that all of them involved one of two situations:

> [W]e have held a patent invalid for failure to satisfy the best mode requirement in two situations. First, we have invalidated patents when they do not adequately disclose a preferred embodiment of the invention. . . . Consequently, if an inventor fails to disclose the preferred embodiment of the invention, the best mode requirement is not satisfied.
>
> Second, we have invalidated patents when the patentee failed to disclose aspects of making or using the claimed invention and the undisclosed matter materially affected the properties of the claimed invention.

Id. at 1319.

Since Bayer AG, the Federal Circuit has addressed the best mode requirement on a handful of occasions—but has found a best mode violation only once. In one other case, Old Town Canoe Co. v. Confluence Holdings Corp., 448 F.3d 1309 (Fed. Cir. 2006), the Federal Circuit vacated a district court's grant of judgment as a matter of law to the plaintiff on the ground of no best mode violation, but did not affirmatively determine that a violation had in fact occurred. Id. at 1320-21. The decisions in all of these cases are consistent with the Federal Circuit's analysis and opinion in Bayer AG. Accordingly, the two categories of

cases identified in Bayer AG continue to be instructive in guiding this Court's best mode analysis. Because the situation here does not fit into either category, the Court finds that Teva has failed to establish a best mode violation with respect to the '823 or '165 Patents.

The instant situation does not fall within the first category (failure to disclose the preferred embodiment of the invention) because the preferred embodiment of a claim covering numerous compounds is a particular compound—not a process or criteria for selecting the best compound. Similarly, the preferred embodiment of a claim covering numerous compositions is a composition—not a process or criteria for selecting the best composition. Since Teva does not allege that the inventors preferred any particular compound or composition, this category is clearly inapplicable here.

Nor does the instant situation fall within the second category (failure to disclose a material aspect of making or using the invention). The data and criteria at issue are irrelevant to the process of making (*i.e.*, synthesizing) the compounds and compositions of the patents-in-suit. Teva does not claim otherwise. However, Teva argues that the information is necessary to using the compounds and compositions. (See, e.g., Teva's Memorandum of Law Opposing Plaintiff's Motion for Judgment as a Matter of Law at 68) ("Here, the issue is failure to

disclose preferences that materially affect *using* the claimed invention in the best mode, not *making* the invention."). Specifically, Teva states that:

> Without disclosure of at least the inventor preferences to achieve COX-2 selectivity, a person of ordinary skill in the art would not know which of the multitude of compounds covered by the '823 or the '165 patents the inventors believed had the best characteristics for their intended use as anti-inflammatories to achieve the additional benefit of significantly less harmful side effects. The person of ordinary skill in the art would also lack information critical to using the compounds in the best way contemplated by the inventors, in a manner that achieved COX-2 selectivity. This is improper.

(Teva's Post-Trial Brief at 21.)

Although Teva's argument has some intuitive appeal, this is not the situation contemplated by the Federal Circuit's "aspect-of-using-the-claimed-invention" jurisprudence. A closer look at the cases where the Federal Circuit found that inventors violated the best mode requirement by failing to disclose subjective preferences related to the use of the invention is instructive. In Bayer AG, the Federal Circuit identified only two cases that fell within this category: Dana Corp. and Great Northern Corp.. (Bayer AG, 301 F.3d at 1319.

In Great Northern, the Federal Circuit considered the validity of a patent claiming a molded pulp stacker for supporting rolls of material. Great Northern Corp. v. Henry Molded Prods., Inc., 94 F.3d 1569 (Fed. Cir. 1996). The patent did

not disclose the inventors' preference for placing diamond shaped indentations on the stackers. "The diamond indentations were crucial to producing a usable version of the invention because without diamonds the stacker simply collapsed under the weight of the rolls it was supposed to hold." Bayer AG, 301 F.3d at 1318. Accordingly, the Court found that the diamond indentations "relate[d] to the nature and quality of the invention," and materially affected the properties of the claimed invention. Thus, the inventors' failure to disclose them constituted a violation of the best mode requirement. Great Northern, 94 F.3d at 1571-72.

In Dana, the patent at issue claimed an internal combustion engine with a special seal between the valve stem and valve guide. Dana Corp. v. IPC Ltd. P'ship, 860 F.2d 415 (Fed. Cir. 1988). The inventor was aware approximately seven months before filing the patent application that a 60-second flouride surface treatment was "necessary to satisfactory performance of the seal." Id. at 418. The inventor knew that the seal would leak without the flouride treatment, yet he did not disclose this information in the patent specification. Because the treatment had a material affect on the properties of the invention, the Federal Circuit held the patent invalid for failure to disclose the best mode of carrying out the invention.

Id. at 418-20.[56]

In these cases, the non-disclosed information involved something one had to do to the invention in order to make it work. The stacker would collapse without the diamond indentations. The seal would leak without the flouride treatment. The Court understands this to be the meaning of "aspects of . . . using the claimed invention [that] materially affect[] the properties of the claimed invention." Bayer AG, 301 F.3d at 1319; see also Eli Lilly & Co. v. Barr Labs., Inc., 251 F.3d 955, 965 (Fed. Cir. 2001) (holding that disclosure of the inventor's preference for a particular method for synthesizing a starting material was not required because the

[56] Old Town Canoe Co. v. Confluence Holdings Corp., 448 F.3d 1309 (Fed. Cir. 2006), which was decided after the Court's decision in Bayer AG, may also involve a failure to disclose subjective preferences related to the use of the invention. The patent at issue in that case was directed to a method of making multilayered plastic laminate boat hulls by rotational molding. Confluence, the alleged infringer, challenged the validity of the patent on grounds, *inter alia*, of failure to satisfy the best mode requirement. Confluence argued that "at the time of filing of the patent application, the inventor had a *preferred way of using the invention* that included . . . optimal timing periods for coalescence and cooling." Id. at 1320 (emphasis added). At the close of Confluence's case-in-chief, the District Court "summarily concluded, without explanation" that there was insufficient evidence to meet the clear and convincing standard, and granted judgment as a matter of law in favor of the Patent holder, Old Town. Id. at 1313. The Federal Circuit vacated the District Court's grant of judgment as a matter of law, but did not affirmatively determine that a violation had in fact occurred. Id. at 1320-21. Although the Court did not explicitly characterize it as an "aspect-of-using-the-claimed-invention" case, Confluence phrased its argument in those terms, and the Court found that the "evidence suggest[ed] that Old Town did not disclose the details of the best mode of the invention." Id. at 1321.

method was "not linked to the *intrinsic quality* of [the claimed invention], which is the thrust of the best mode requirement."). The non-disclosed preferences in the instant case do not fall into this category.

The inventors' preferences for COX-2 selective compounds and compounds that met performance criteria in specific assays would assist an individual in selecting a preferred embodiment of the compound, but do not affect the intrinsic properties of the claimed invention or teach anything that must be done to the compounds or compositions in order to make them work. The claimed compositions and compounds of the patents-in-suit would work (or not) regardless of whether the inventors' preferences and selection criteria were disclosed. Therefore, Pfizer's criteria for selecting a preferred embodiment is not an aspect of using the claimed compounds or compositions that materially affects the properties of the claimed inventions.

Accordingly, and because the instant situation does not fit within either category of cases wherein the Federal Circuit has held a patent invalid for failure to satisfy the best mode requirement, the Court finds that Teva has failed to establish that the '823 or '165 Patents are invalid for failure to satisfy the best mode requirement.

IV. OBVIOUSNESS-TYPE DOUBLE PATENTING

The double patenting doctrine generally prevents a patentee from receiving two patents for the same invention.

> The proscription against double patenting takes two forms: statutory and non-statutory. Statutory, or "same invention," double patenting is based on the language in § 101 of the Patent Act mandating "a patent" for any new and useful invention. 35 U.S.C. § 101 (2000); In re Goodman, 11 F.3d 1046, 1052 (Fed. Cir. 1993) ("If the claimed inventions are identical in scope, the proper rejection is under 35 U.S.C. § 101 because an inventor is entitled to a single patent for an invention.") (citations omitted). Non-statutory, or "obviousness-type," double patenting is a judicially created doctrine adopted to prevent claims in separate applications or patents that do not recite the "same" invention, but nonetheless claim inventions so alike that granting both exclusive rights would effectively extend the life of patent protection. Gerber Garment Tech., Inc. v. Lectra Sys., Inc., 916 F.2d 683, 686 (Fed. Cir. 1990) (citing In re Thorington, 57 C.C.P.A. 759, 418 F.2d 528, 534 (CCPA 1969)).

Perricone v. Medicis Pharm. Corp., 432 F.3d 1368, 1372-1373 (Fed. Cir. 2005)

This case involves double patenting in this latter category. Specifically, Teva alleges that the '068 Patent (covering methods of use) is invalid for obviousness-type double patenting over the '165 Patent (covering compositions). Pfizer attacks this assertion on two fronts. First, Pfizer argues that the "safe harbor" provision of § 121 precludes reliance on any claims of the '165 Patent to support a double patenting rejection of the '068 Patent. Second, Pfizer argues that

even if the safe harbor provision is inapplicable here, the asserted claims of the '068 Patent are not so akin to the claims of the '165 Patent that "granting both exclusive rights would effectively extend the life of patent protection." Id.

A. Standard of Review

Double patenting is an affirmative defense. Symbol Technologies, Inc. v. Opticon, Inc., 935 F.2d 1569, 1580 (Fed. Cir. 1991). Accordingly, Teva must prove invalidity due to double patenting by clear and convincing evidence, a "heavy and unshifting burden." Id.; see also Carman Indus., Inc. v. Wahl, 724 F.2d 932, 940 (Fed. Cir. 1983) ("[T]here is a heavy burden of proof on one seeking to show double patenting"). The burden is on Pfizer, however, as the party seeking to invoke the protection of § 121, to prove that the section applies. See Regents of the Univ. of Cal. v. Dakocytomation Cal., Inc., No. 05-03955, 2006 U.S. Dist. LEXIS 31756 (N.D. Cal. May 17, 2006) ("The burden is on the patent holder to prove that section 121 applies.") (citing Geneva Pharms., Inc. v. GlaxoSmithKline PLC, 349 F.3d 1373, 1382 (Fed. Cir. 2003). If Pfizer is not successful in proving the applicability of § 121, the burden of proving invalidity of the patent remains with Teva as the party asserting invalidity. See Geneva Pharms., Inc. v. Glaxosmithkline PLC, 189 F. Supp. 2d 377, 382 (D. Va. 2002).

B. Pfizer Is Entitled to the Safe Harbor of Section 121

Section 121 of the Patent Act provides, in pertinent part, as follows:

> A patent issuing on an application with respect to which a requirement for restriction under this section has been made, or an application filed as a result of such a requirement, shall not be used as a reference either in the Patent and Trademark Office or in the courts against a divisional application or against the original application or any patent issued on either of them, if the divisional application is filed before the issuance of the patent on the other application.

35 U.S.C. § 121. Put simply, § 121 prohibits using one patent as a double patenting reference against another when the applications were filed pursuant to a restriction requirement. There is, however, a caveat to this safe harbor provision—the divisional application and the resulting patent must be "consonant" with the restriction requirement. The applicant cannot cross "the line of demarcation between the 'independent and distinct inventions' that prompted the restriction requirement." Geneva Pharms., Inc., 349 F.3d at 1381 (quoting Gerber Garment Tech., Inc. v. Lectra Sys., Inc., 916 F.2d 683, 688 (Fed. Cir. 1990)); see also MPEP § 804.01 (stating that § 121 does not apply if "[t]he claims of the different applications or patents are not consonant with the restriction requirement made by the examiner," and that "[i]n order for consonance to exist, the line of demarcation between the independent and distinct inventions identified by the

examiner in the requirement for restriction must be maintained").

Accordingly, as § 121 has been interpreted by the Federal Circuit, Pfizer is entitled to invoke the statutory prohibition against the use of the '165 Patent as a reference against the '068 Patent if, and only if: (1) the application resulting in the '165 Patent was filed as a result of a restriction requirement, and (2) the Application was consonant with that restriction requirement. See Bristol-Myers Squibb Co. v. Pharmachemie B.V., 361 F.3d 1343, 1348 (Fed. Cir. 2004); Geneva Pharms., 349 F.3d at 1378, 1381; Gerber Garment Tech., 916 F.2d at 687.

There is no question that the first element is met here. The divisional application that gave rise to the '165 Patent was undisputedly filed in response to a restriction requirement imposed by Patent Examiner Ramsuer. Thus, whether Pfizer is entitled to § 121 protection turns on whether the application is consonant with that restriction requirement. Teva claims it is not. Specifically, Teva asserts that the application is out of consonance with the restriction requirement because it crossed a line of demarcation set forth by the Examiner during prosecution of the '823 Patent. The Court disagrees. For the reasons explained herein, the Court finds that consonance was maintained and that Pfizer is entitled to the statutory safe harbor of § 121.

1. Detailed Prosecution History of the Patents-in-Suit

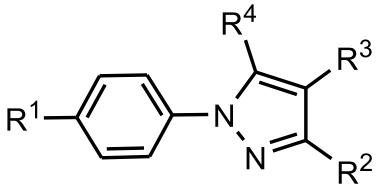
In order to understand and evaluate the parties' double patenting arguments, it is important to review the prosecution history of the patents-in-suit in some detail.[57] Pfizer filed the '594 Application on November 30, 1993. As filed, the '594 Application covered: (I) a broad range of chemical compounds, (II) pharmaceutical compositions utilizing the compounds, and (III) methods of treatment. On July 12, 1994, the Patent Examiner issued an office action, which stated as follows:

> Restriction to one of the following inventions is required under 35 U.S.C. 121:
>
> I. Claims 1-20, compounds.
> II. Claims 21-26, compositions.
> III. Claims 27-37, methods of use.
>
> The above groups are identified as general areas. Accordingly, as groups they are independent or distinct as the compounds of Group I would differ in scope from the compositions of Group II, the products would be capable of more than one use and separate search considerations are involved.
>
> The above groups themselves are inclusive of patentably distinct subject matter. Accordingly, along with the election of one of the above groups the following action is also taken.
>
> Claims 1, 16 [compound claim], 21 [composition claim] and 27 [method claim] are generic to a plurality of disclosed patentably distinct species comprising for example, the

[57] Some of this information is covered in Part II of the Background Section, *supra*. It is restated here with more relevant detail.

> compounds of (1) Example 1, (2) Example 3, (4) [sic] Example 4, (5) Example 16, etc., the method of treating fever using (5) the compound of Example 1, etc. Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species, even though this requirement is traversed. . . .
>
> Upon the election of a single disclosed species a generic concept inclusive of the elected species will be identified by the Examiner for examination along with the elected species.

(PTX 863, Paper 6, at PFC 02027226-28.) The species of Examples 1, 3, 4, and 16 differ with respect to their R^2 and R^4 substituents as identified on the generic structure below:



On September 15, 1995, Pfizer submitted a response to this office action entitled, "Amendment and Response to Restriction and Election Requirement." (Id., Paper 7, at PFC 02027233-55.) That document, in relevant part, provides as follows:

> Restriction has been imposed among the following groups of claims:
>
> I: Claims 1-20, compounds;
>
> II: Claims 21-26, pharmaceutical compositions;
>
> III: Claims 27-37, methods of use.
>
> Applicants elect, with traverse, to prosecute Group I,

> Claims 1-20.
>
> Applicants further elect, with traverse, the compound of new species Claim 40, which is shown as Example #1c at page 41, lines 5-8 of the specification.

(Id. at PFC 02027248-49.) Example 1c is celecoxib. It is one of eleven examples (Examples 1 and 1a-j) that make up Example 1. In all of these examples, R^2 is a haloalkyl group, and R^4 is a substituted aryl group.

In a subsequent office action dated January 12, 1995, the Examiner defined a generic concept for examination along with the elected species and withdrew the non-elected subject matter:

> In response to the restriction requirement of Paper No. 6 applicant has elected Group I and the species of claim 40 with travserse. The generic concept as depicted in claims 2-14, 16, 17, 38, and 39 wherein R^1 is a sulfonyl group, R^2 is haloalkyl, R^3 is H, or alkyl and R^4 is cycloalkyl, cycloalkenyl, or aryl, is identified for examination along with the elected embodiment. The remaining subject matter of claims 2-14, 16, 17, 38, 39, and the subject matter of claims 22, 23, 25, 26, 28, 29, 31-37, and 41-46 stands withdrawn from consideration under 37 CFR 1.142(b) as constituting other patentably distinct inventions.
>
> The withdrawn subject matter of claims 2-14, 16, 17, 38, and 39 is properly restricted as said subject matter differs in structure and element from the elected subject matter so as to be patentably distinct therefrom, . . .
>
> Accordingly, the claims are drawn to more than a single invention and restriction as has been required is proper 37 CFR 1.142(a).

(Id., Paper 12, at PFC 02027291.)

The ’594 Application, as narrowed, was approved and ultimately issued as the ’823 Patent. Pfizer filed several divisional applications directed to the compounds that were not covered by the ’823 Patent. These patents were issued, but are not relevant here. Pfizer also filed a divisional application to pursue the unelected composition claims. This Application issued as the ’165 Patent on August 8, 1996. Importantly for present purposes, at least one issued claim of the ‘165 Patent includes more than one of the species mentioned in the July 12, 1994 office action. For example, Claim 5 is a Markush claim directed to a pharmaceutical composition containing a therapeutically effective amount of a compound selected from a listed group of compounds. That listed group includes compounds like Example 1 and compounds like Example 4, which use a different substituent in the R^2 position.

Finally, Pfizer also filed international application PCT12720, which entered the national stage as the ’113 Application. The ‘113 Application ultimately issued as the ’068 Patent, which covers methods of use.

2. Pfizer Maintained Consonance With the Applicable Restriction Requirement

With this understanding of the relevant prosecution history, the Court will

now turn to an analysis of the parties' respective positions on the question of entitlement to the safe harbor of § 121. Teva does not dispute that the '165 Patent complied with the compound/composition/method restriction, but argues that consonance is nonetheless violated because Pfizer did not comply with what it characterizes as a second element of the restriction requirement—the election of species requirement set forth in the July 12, 1994 office action. According to Teva, the election of species requirement imposed restriction between several patentably distinct species (e.g., the compounds of Example 1, the compounds of Example 4, etc.). Teva argues that this restriction requirement to separate out the different species applied to all claim types (*i.e.*, compound claims, composition claims, and method claims), and that Pfizer crossed this line of demarcation by including composition claims in the '165 Patent application that encompassed compounds that were representative of more than one of the species identified by the Examiner as distinct. Teva points to claim 5, which includes compounds like Example 1 and Example 4, as its one and only example.

Pfizer vigorously disputes Teva's characterization of the restriction requirement. Pfizer contends that the election of species requirement was *not* a restriction requirement. According to Pfizer, the Examiner simply used the election of species requirement to identify a compound around which to create a

generic concept. This generic concept, Pfizer argues—and not the species—became the restriction. Finally, Pfizer asserts that this "generic concept restriction" applied only to the elected compound claims and not to the non-elected composition and method claims.

The availability of § 121's safe harbor protection depends on which interpretation of the restriction requirement is accurate. If Pfizer's characterization is accurate, the only requirement that applied to the composition claims in the '165 Patent was the compound/composition/method restriction. Since the '165 Patent, which includes only composition claims, complies with this requirement, it would be consonant with the restriction requirement, would fall within the safe harbor of § 121, and would not be available as a reference against the '068 Patent. If, on the other hand, Teva's characterization is correct, then Pfizer crossed the line of demarcation by including composition claims in the '165 Patent (e.g., Claim 5) that encompass more than one species the Examiner identified as distinct. In this case, the '165 Patent would be available as a double patenting reference.

The Court finds the Federal Circuit's recent decision in Geneva Pharmaceuticals, Inc. v. GlaxoSmithKline PLC, 349 F.3d 1373 (Fed. Cir. 2003), to be helpful in resolving this dispute and determining whether the election of

species language presented here qualifies as a restriction requirement. In Geneva, a patent holder facing a double patenting challenge sought to invoke the statutory protection of § 121. The Federal Circuit held that

> § 121 only applies to a restriction requirement that is documented by the PTO in enough clarity and detail to show consonance. . . . The restriction documentation must identify the scope of the distinct inventions that the PTO has restricted, and must do so with sufficient clarity to show that a particular claim falls within the scope of the distinct inventions.

Id. at 1382. Since the Examiner's statements did not meet this standard, the Federal Circuit found that § 121 was not implicated and that the divisional application could be used as a double patenting reference.

Certainly, the factual situation in Geneva differs significantly from the situation presented in the instant case. There, the patent holder was trying to establish that a particular statement *was* a restriction requirement in order to bring itself within § 121's safe harbor. Here, the patent holder is trying to show that a particular statement *was not* a restriction requirement in order to invoke the safe harbor provision. This appears to be a unique situation. Nevertheless, the Court finds the Federal Circuit's discussion of restriction requirements to be generally applicable and instructive in the instant case.

The Court reads Geneva to stand for the proposition that an examiner must

clearly define the scope of the distinct inventions in order for his/her statements to constitute a restriction requirement. The election of species language in the July 12, 1994 office action does not do so. Although Examiner Ramsuer did note that the different claim types were "themselves inclusive of patentably distinct subject matter," he did not set forth with precision the identity of these distinct inventions. He stated:

> Claims 1, 16 [compound claim], 21 [composition claim] and 27 [method claim] are generic to a plurality of disclosed patentably distinct species comprising for example, the compounds of (1) Example 1, (2) Example 3, (4) [sic] Example 4, (5) Example 16, etc., the method of treating fever using (5) the compound of Example 1, etc.

This language is markedly different from the language concerning the claim types, which clearly identified and defined three distinct inventions—(I) compounds, (II) compositions, and (III) methods—and explained why they were independent and distinct from each other. (See PTX 863, Paper 6, at PFC 02027226-28.) The election of species language, by contrast, is much less clear and simply identifies some examples of distinct subject matter. It does not clearly define the boundaries of distinct inventions.

Indeed, the Examiner explicitly left the boundaries unsettled by stating his intention to identify "a generic concept inclusive of the elected species . . . for

examination along with the elected species" after Pfizer elected the individual species it wished to pursue. The precise boundaries could not possibly have been known as of July 12, 1994, since the Examiner stated that they would not be set until after an individual species had been elected.

Accordingly, under Geneva, if Pfizer had submitted several divisional applications covering compositions and methods that were broken down along the lines suggested by Teva, § 112 would not be implicated and Pfizer would be vulnerable to a double patenting challenge. If the election of species requirement could not have been used defensively by Pfizer to justify separate applications, it cannot be used offensively by Teva to attack inclusion of the subject matter in a single application.

In short, the Court agrees with Pfizer's position that the election of species requirement set forth in the July 12, 1994 office action was not a restriction requirement. In that office action, the Examiner required Pfizer to select a single species for examination, but did not restrict the claims to that particular species or set forth a clear line of demarcation between patentably distinct inventions. Since there was no line of demarcation at that time, there was no consonance to be maintained—or violated. See MPEP § 804.01 (defining consonance as respecting the "line of demarcation between the independent and distinct inventions

identified by the examiner"). The line of demarcation between subject matter was not set forth with precision until the examiner created the generic concept that clearly defined which subject matter Pfizer could pursue in the pending application. Thus, it is the generic concept, if anything, that constitutes the restriction requirement with respect to species types.

The Court also agrees with Pfizer's argument that this species-type generic concept restriction requirement applied only to the elected compound claims. As an initial matter, the generic concept defines a genus of compounds without even alluding to compositions or methods. Therefore, by its own terms, the generic concept does not apply to the non-elected compositions or methods, but only to the pending compounds claims. Moreover, the Court finds this to be the most sensible interpretation of the Examiner's statements and intentions.

Although it is easy to lose the forest for the trees and get caught up in the factual and legal intricacies of this issue, resolution of the § 121 question ultimately depends simply on what Examiner Ramsuer intended to do in the July 12, 1994 office action. Having considered all of the documents and testimony, as well as the context of his statements, the Court finds that his intent was to require Pfizer to select either compounds, compositions, or methods and to elect a single example *within that group*, which he would use to create a generic concept to be

pursued in the pending application. The Court does not believe that he intended to impose a formal species-type restriction requirement to be applied to the non-elected composition and method claims.

Having so concluded, the Court emphasizes what it is *not* holding. The Court is not holding that an election of species requirement can never be a restriction requirement. Indeed, the MPEP expressly states that it can be. Section 802.02 of the MPEP provides a definition of "restriction," which includes election of species:

> Restriction, a generic term, includes that practice of requiring an election between distinct inventions, for example, election between combination and subcombination inventions, and the practice relating to an election between independent inventions, for example, *and election of species*.

MPEP § 802.02 (emphasis added). The Code of Federal Regulations ("CFR") is in agreement. Section 1.146 of the CFR states:

> In the first action on an application containing a generic claim to a generic invention (genus) and claims to more than one patentably distinct species embraced thereby, the examiner may require the applicant in the reply to that action to elect a species of his or her invention to which his or her claim will be restricted if no claim to the genus is found to be allowable.

C.F.R. § 1.146.

In this situation, however, where the election of species requirement failed

to precisely set forth the scope of identified separate inventions, and an allowable generic concept was defined by the examiner subsequent to the election of a single species, the Court finds that the initial election of species language did not constitute a formal restriction requirement.

Accordingly, the court finds that Pfizer has met its burden of proving the applicability of § 121. Pfizer maintained consonance with the only applicable restriction requirement when it filed the application for the '165 Patent, and is therefore entitled to invoke the statutory prohibition against use of that patent as a reference against the '068 Patent.

3. The Court Will Not Consider Teva's Argument That Section 121 Is Not Applicable to the '068 Patent

Teva makes an additional argument that the § 121 safe harbor provision does not apply to the '068 Patent because the '068 Patent was filed as a continuation-in-part application. Teva claims that § 121 prohibits use of a divisional application against another divisional application, the original application, or any patent issued on either application—but that it does not apply to continuation-in-part applications filed as new applications.

Teva raised this argument for the first time in its post-trial brief. It was

never raised, or even alluded to, at trial or in the Pretrial Order. Pfizer contends that consideration of this entirely new argument would be unduly prejudicial to its case. According to Pfizer, if Teva had raised this argument earlier—either in the Pretrial Order or at trial—Pfizer "could have put in additional evidence to demonstrate the non-obviousness of particular claims." (Pfizer's Post-Trial Reply Brief at 16.) Pfizer claims that Teva is "seek[ing] to exploit an unfair withholding of its position." (Id. at 17.) The Court agrees.

In Mannarino v. Morgan Township, 64 Fed. Appx. 844 (3d Cir. 2003) (not precedential opinion), the Third Circuit reviewed, *inter alia*, a district court's dismissal of a statute of limitations defense that was omitted from the Pretrial Order and raised for the first time during closing arguments. The Third Circuit noted that "'the finality of the pretrial order contributes substantially to the orderly and efficient trial of a case,'" and affirmed the dismissal. Id. at 847 (quoting Petree v. Victor Fluid Power, Inc., 831 F.2d 1191, 1194 (3d Cir. 1987)); see also Daniels v. Board of Educ., 805 F.2d 203, 210 (6th Cir. 1986) (holding that a district court did not abuse its discretion by failing to consider a new theory raised for the first time after trial). Here, as in Mannarino, allowing Teva to raise an entirely new argument in its post trial reply brief "would constitute undue prejudice." Mannarino, 64 Fed. Appx. at 847. Accordingly, the Court will not

consider this argument.[58]

C. The Asserted Claims of the '165 and '068 Patents Are Not Patentably Distinct

If Pfizer were not entitled to the statutory protection of § 121, however, the asserted claims of the '068 Patent would be invalid for obviousness-type double patenting over claim 5 of the '165 Patent. As explained above, claim 5 of the '165 Patent is a Markush claim directed to a pharmaceutical composition containing a therapeutically effective amount of a compound selected from a group of listed compounds, including celecoxib. The asserted claims of the '068 Patent claim "a method of treating inflammation or an inflammation disorder in a subject, said method comprising administering to the subject . . . a therapeutically effective amount of [celecoxib]."

The Federal Circuit has endorsed and adopted the view of its predecessor court that "a claim to a method of using a composition is not patentably distinct from an earlier claim to the identical composition in a patent disclosing the

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[58] The Court notes that were it to consider Teva's argument, it would find that § 121 does apply to the '068 Patent. The Federal Circuit has applied § 121 to continuation-in-part applications on several occasions. See, e.g., Geneva Pharms., Inc., 349 F.3d at 1378; Gerber Garment Tech. v. Lectra Sys., Inc., 916 F.2d 683, 688-689 (Fed. Cir. 1990); SKG v. Northern Petrochemical Co., 784 F.2d 351, 355-56 (Fed. Cir. 1986).

identical use." Geneva Pharms., Inc., 349 F.3d at 1385-86. The Federal Circuit explained that:

> "[i]t would shock one's sense of justice if an inventor could receive a patent upon a composition of matter, setting out at length in the specification the useful purposes of such composition, manufacture and sell it to the public, and then prevent the public from making any beneficial use of such product by securing patents upon each of the uses to which it may be adapted."

Id. at 1386 (quoting In re Byck, 48 F.2d 665, 666 (CCPA 1931)). Pfizer does not appear to dispute that the asserted claims of the '068 Patent claim a method of using a composition and that claim 5 of the '165 Patent claims "the identical composition in a patent disclosing the identical use." Pfizer argues, however, that one would only know of the identical utility if one were to read the specification of the '823 or '165 Patent, and that reference to the specification is not permitted in a double patenting analysis. The Court disagrees.

As an initial matter, one may refer to a patent's specification in the course of a double patenting analysis in order to determine the meaning and scope of the claims at issue. The Federal Circuit has said so, and done so:

> The challenge of a double patenting analysis . . . is to understand the scope of the compared claims. In this case, for instance, claim 1 of the '720 patent is drawn to a compound having a certain physical property. Standing alone, that claim does not adequately disclose the patentable bounds of the

> invention. Therefore, *this court examines the specifications of both patents* to ascertain any overlap in the claim scope for the double patenting comparison.

Id. at 1385 (emphasis added). Moreover, reliance on the specification is not even necessary for one to glean the common utility in this case. The parties have stipulated that the term "therapeutically effective amount" in the asserted claims of the '165 and '068 Patents means the same thing—an amount of active ingredient that would elicit an anti-inflammatory or analgesic response in the rat footpad edema test or analgesia test as described in the Patents. (Revised Pretrial Order at p.12, ¶ 45.) Based on this stipulation, the use of the compositions to treat pain and inflammation (the same method disclosed in the '068 Patent) would be readily discernable to a person of ordinary skill from the claims of the '165 Patent, without having to resort to the specification.

In sum, the '165 Patent describes pharmaceutical compositions with a particular use. The asserted claims of the '068 Patent claim "nothing more than [the '165 Patent's] disclosed utility as a method of using the [compositions]. Thus, the claims of the ['165 and '068] patents are not patentably distinct." Geneva Pharms., Inc., 349 F.3d at 1386. Accordingly, the Court finds that the asserted claims of the '068 Patent would be invalid for obviousness-type double patenting over the '165 Patent if the '165 Patent were available as a reference.

D. Summary of Double Patenting

As explained above, the asserted claims of the '068 Patent are not patentably distinct from claim 5 of the '165 Patent. Ordinarily, this would render the patent invalid under the double patenting doctrine. Here, however, the '165 Patent cannot be used as a reference against the '068 Patent pursuant to the statutory safe harbor of § 121. Accordingly, the Court finds that the '068 Patent is not invalid for obviousness-type double patenting.

V. CONCLUSION

For the foregoing reasons, the Court finds that Teva has failed to prove by clear and convincing evidence that the patents-in-suit are obvious, that Pfizer engaged in inequitable conduct, that Pfizer violated the best mode requirement, or that the '068 Patent is invalid for obviousness-type double patenting over the '165 Patent. Thus, the patents-in-suit are neither invalid nor unenforceable. Teva has infringed those patents under 35 U.S.C. § 271(e)(2).

/s/ John C. Lifland, U.S.D.J.

Dated: March 20, 2007