United States District Court,
S.D. New York.

In re BUSPIRONE PATENT LITIGATION.

In re Buspirone Antitrust Litigatio,
In re Buspirone Antitrust Litigation.

Feb. 14, 2002.

Owner of patent for antianxiety drug sued competitors for infringement. On competitors motion for summary judgment, the District Court, Koeltl, J., held that patent calling for administration of dosage of metabolized form of antianxiety drug did not cover use of underlying prodrug.

Motion granted.

6,150,365. Construed; Not Infringed.

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Opinion and Order No. 18

KOELTL**, District Judge.**

(Motion For Summary Judgment on Patent Infringement Claims)

On August 15, 2001, the Judicial Panel on Multidistrict Litigation consolidated for pre-trial purposes before this Court four patent actions, which had been consolidated under MDL-1410, and twenty-two antitrust actions, which had been consolidated under MDL-1413. All of these cases involve disputes among the various parties over the propriety of the manufacture, use, sale or allegedly anticompetitive conduct related to the use and sale of the drug buspirone FN1 to treat anxiety. Since that time, the Panel has also transferred twelve tag-along cases to this Court.

FN1. Buspirone hydrochloride is a pharmaceutically acceptable acid addition salt of buspirone. The distinction between buspirone and buspirone hydrochloride is not relevant to the legal issues in this motion, and the term "buspirone" will be used to refer to either or both in this opinion.

Bristol-Myers Squibb Company ("Bristol-Myers" or "BMS") is the plaintiff in three of the four patent actions. In 1980, Bristol-Myers obtained a patent (the " '763 Patent") covering, among other things, a method of treating anxiety by the use of a non-toxic anxiolytically-effective dose of buspirone. In 1986, after obtaining approval from the Food and Drug Administration (the "FDA") for the manufacture and sale of buspirone in accordance with a specific set of labeling instructions, Bristol-Myers began selling buspirone tablets under the name Buspar(R). Just before the '763 Patent was set to expire at the end of the day on November 21, 2001, Bristol-Myers obtained another patent (the "'365 Patent"), which, on its face, claims a process for ameliorating anxiety by the systemic administration of an effective but non-toxic anxiolytic dose of 6-hydroxy -8-[4-[4-(2-pyrimidinyl)-piperazinyl]-butyl]-8-azaspiro[4.5]-7,9-dione (the "6-hydroxy-metabolite" or "BMY 28674"), one of the metabolites that buspirone naturally produces in the human body. In all of the pending patent actions, as well as a number of the pending antitrust actions, Bristol-Myers has filed claims or cross-claims, or has asserted defenses, arguing that the manufacture or sale of generic buspirone by a competitor for use in accordance with the FDA-approved labeling instructions for Buspar(R) violates, or would violate, the new '365 Patent.

Danbury Pharmacal, Inc. and Watson Pharmaceuticals, Inc. (collectively "Watson") and Mylan Pharmaceuticals, Inc., Mylan Laboratories Inc. and Mylan Technologies Inc. (collectively "Mylan") are competitors of Bristol-Myers, who have been seeking to produce or sell generic buspirone tablets for use in accordance with the approved FDA-labeling instructions for Buspar(R). To that end, they have each filed Abbreviated New Drug Applications ("ANDAs") with the FDA, seeking approval of their respective products. After obtaining the ' 365 Patent, however, Bristol-Myers listed it with the FDA in the book entitled the "Approved Drug Products with Therapeutic Equivalence Evaluations," or the "Orange Book," as covering the uses of buspirone in question, thereby triggering an automatic forty-five-day period in which Bristol-Myers could bring patent infringement suits against its generic competitors before they could sue for a declaratory judgment action. Bristol-Myers then filed suits for patent infringement against Mylan and Watson within this forty-five day period, alleging that they infringed the '365 Patent by filing their ANDAs and certifying that their respective products do not violate the '365 Patent. These lawsuits triggered an automatic stay of the FDA's approval of Mylan's and Watson's products for up to the earlier of thirty months or until the relevant patent disputes were decided. *See* 21 U.S.C. 355(j)(5)(B)(iii).

Mylan and Watson move pursuant to Rule 56 of the Federal Rules of Civil Procedure for summary judgment on the patent infringement claims based on a finding that these generic competitors' manufacture, promotion and sale of generic buspirone tablets in accordance with the current FDA-approved labeling instructions for Buspar(R) would not infringe the '365 Patent, or, in the alternative, that the '365 Patent is invalid. Bristol-Myers opposes this motion, or, in the alternative, moves for a *Markman* hearing in which to produce evidence concerning claim construction. *See* Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed.Cir.1995) (en banc), *aff'd,* 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996).FN2

FN2. Bristol-Myers has also moved pursuant to Rule 12(b)(6) of the Federal Rules of Civil Procedure to dismiss a number of claims raised by the antitrust plaintiffs under the Sherman Act and analogous state law provisions. The Court has decided this motion in a separate companion opinion, issued today. *See In re*

Buspirone, MDL No. 1410, slip op. (S.D.N.Y. Feb. 14, 2002) (Opinion and Order No. 19) (Motion to Dismiss Antitrust and Related State Law Claims).

I.

The standard for granting summary judgment is well established. Summary judgment may not be granted unless "the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving part[ies are] entitled to a judgment as a matter of law." Fed.R.Civ.P. 56(c); *see also* Celotex Corp. v. Catrett, 477 U.S. 317, 106 S.Ct. 2548, 91 L.Ed.2d 265 (1986); Gallo v. Prudential Residential Servs. L.P., 22 F.3d 1219, 1223 (2d Cir.1994); Local 819, Int'l Bhd. of Teamsters, AFL-CIO v. Textile Deliveries, Inc., No. 99 Civ. 1726, 2000 WL 1357494, at (S.D.N.Y. Sep. 20, 2000). "The trial court's task at the summary judgment motion stage of the litigation is carefully limited to discerning whether there are genuine issues of material fact to be tried, not to deciding them. Its duty, in short, is confined at this point to issue-finding; it does not extend to issue resolution." Gallo, 22 F.3d at 1224. The moving parties, Mylan and Watson in this case, bear the initial burden of "informing the district court of the basis for [their] motion" and identifying the matters that they "believe[ ] demonstrate the absence of a genuine issue of material fact." Celotex, 477 U.S. at 323, 106 S.Ct. 2548. The substantive law governing the case will determine those facts that are material and "only disputes over facts that might affect the outcome of the suit under the governing law will properly preclude the entry of summary judgment." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248, 106 S.Ct. 2505, 91 L.Ed.2d 202 (1986).

In determining whether summary judgment is appropriate, the Court must resolve all ambiguities and draw all reasonable inferences against the moving parties. *See* Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 587, 106 S.Ct. 1348, 89 L.Ed.2d 538 (1986) (citing United States v. Diebold, Inc., 369 U.S. 654, 655, 82 S.Ct. 993, 8 L.Ed.2d 176 (1962)); *see also* Gallo, 22 F.3d at 1223. If the moving parties meet their burden, the burden shifts to the nonmoving party, Bristol-Myers in this case, to come forward with "specific facts showing that there is a genuine issue for trial." Fed.R.Civ.P. 56(e). With respect to the issues on which summary judgment is sought, if there is any evidence in the record from any source from which a reasonable inference could be drawn in favor of the nonmoving party, summary judgment is improper. *See* Chambers v. TRM Copy Ctrs. Corp., 43 F.3d 29, 37 (2d Cir.1994).

II.

The following facts are either undisputed, are matters of public record or are part of the prosecution history of the '365 Patent.

A.

Buspirone is a drug that can help treat anxiety and the symptoms of anxiety in humans, when used appropriately. *See* United States Patent No. 6,150,365 ("'365 Patent"), at col. 1 (issued Nov. 21, 2000), attached as Ex. 1 to Declaration of Daniel G. Brown dated November 7, 2001 ("Brown Decl."). Buspirone has the chemical formula of 8-[4-[4-(2-pyrimidinyl)-1-piperazinyl]-butyl]-8-azaspiro[4.5]decane-7,9-dione and exerts these so-called "anxiolytic" effects through human serotonin 1A (5-HT1A) receptors located in neurons throughout the human brain. *See* id. Once ingested, buspirone is naturally metabolized to produce a number of metabolites in the human body, including one of import to this case, which has the chemical formula of 6-hydroxy-8-[4-[4-(2-pyrimidinyl)-piperazinyl]-butyl]-8-azaspiro[4.5]-7,9-dione and is

commonly referred to as the "6-hydroxy-metabolite" or "BMY 28674" (the "metabolite"). Id. at cols. 1-2.

In 1980, shortly after the discovery of buspirone's anxiolytic potential, Bristol-Myers obtained a patent (the "'763 Patent") that claimed, among other things:

1. A method for the palliative treatment of neurosis in which anxiety symptoms are prominent which comprises administering a non-toxic anxiolytically effective dose of buspirone or a pharmaceutically acceptable acid addition salt thereof to a neurotic patient.

U.S. Patent No. 4,182,763, at col. 7 (the "'763 Patent") (issued Jan. 8, 1980), attached as Ex. 14 to Brown Decl. The Patent also claimed "[t]he method of claim 1 wherein buspirone hydrochloride is employed, and dosage is by the oral route." Id. In order to sell such a new medication, a pioneer drug company must obtain approval of a New Drug Application ("NDA") from the FDA, and, as part of this process, the pioneer drug company must conduct research establishing that the drug is safe and effective in use. *See* 21 U.S.C. s. 355(b)(1). Bristol-Myers conducted further testing of buspirone and, on September 29, 1986, obtained approval from the Department of Health and Human Services ("DOHHS") for the use and sale of the drug in accordance with a proposed set of labeling instructions reflecting its research. *See* Letter from DOHH to Bristol-Myers dated September 29, 1986 ("DOHH Approval Letter"), attached as Ex. 2 to Brown Decl. The FDA approval included the approved labeling instructions (the "Final Printed Buspar(R) Labeling"). *See* id. at 2-13.

In 1984, Congress passed the Hatch-Waxman Amendments, also known as the Drug Price Competition and Patent Term Restoration Act, Pub.L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. s. 355 and 35 U.S.C. s. 271(e)), which amended the Federal Food, Drug, and Cosmetic Act ("FDCA"), Pub.L. No. 52-675, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. s.s. 301-397), to permit the competitors of pioneer drug companies to obtain expedited and cost-efficient approval of generic versions of bioequivalents of drugs that have already obtained prior FDA approval by filing an "Abbreviated New Drug Application" ("ANDA") and relying in part on the safety and effectiveness findings supporting the original NDA for the drug. *See* Bayer AG v. Elan Pharm. Research Corp., 212 F.3d 1241, 1244 (Fed.Cir.2000). Under these provisions, pioneer drug companies filing an NDA must include information on any patent that "claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. s. 355(b)(1). If a pioneer drug company obtains a patent that meets these criteria after the NDA has been filed or approved, the company is required to file supplemental information, on the new patent within thirty days of the issuance of the new patent. *See* 21 U.S.C. s.s. 355(b)(1) & (c)(2). Upon approval of an NDA or receipt of supplemental patent information, the FDA publishes the submitted patent information in a book called the "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly referred to as the "Orange Book." *See id*. Since its approval in 1986, Bristol-Myers has sold buspirone tablets for the treatment of anxiety under the name Buspar(R). (*See* Brown Decl. Exs. 2, 8, 9, 14.)

As part of the ANDA process, an applicant must, in turn, make a certification as to each patent listed in the Orange Book that either "claims the listed drug [that the applicant claims is a bioequivalent] ... or ... claims a use for such listed drug...." 21 U.S.C. s. 355(j)(2)(A)(vii). Applicants with pending ANDAs must supplement their certifications to address any new Orange Book listings by the pioneer drug manufacturer, unless the new patents were listed more than thirty days after they were issued. *See* 21 C.F.R. s. 314.94(a)(12)(vi). The new applicant must certify either that (I) no patent information claiming coverage of

the drug or a use of the drug was ever submitted to the FDA, or, for each patent on which information has been submitted, that either (II) the patent has expired; (III) the patent is set to expire on a certain date; or (IV) the patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the ANDA has been submitted. *See* 21 U.S.C. s. 355(j)(2)(A)(vii)(I)-(IV). These are commonly referred to as Paragraph I, II, III and IV certifications, respectively. *See* Bayer AG, 212 F.3d at 1244.

Bristol-Myers's original '763 Patent covering buspirone was set to expire at the end of the day on November 21, 2000. In anticipation of this date, a number of Bristol-Myers's competitors began making preparations to manufacture and sell a generic form of buspirone tablets, including filing ANDAs for buspirone. By November 21, 2000, Mylan and Watson had received tentative approval of their ANDAs contingent only on the expiration of the '763 Patent. *See* Mylan Pharm., Inc. v. Thompson, 139 F.Supp.2d 1, 8 (D.D.C.), *rev'd on other grounds,* 268 F.3d 1323 (Fed.Cir.2001); *Watson Pharm., Inc. v. Henney,* Civ. No. S 00-3516, 2001 U.S. Dist. LEXIS 2477, at *3-4 (D.Md. Jan. 18, 2001). Mylan manufactured and was ready to ship its product at 12:00 a.m. on November 22, 2000. *See* Mylan Pharm., Inc. v. Thompson, 139 F.Supp.2d at 8.

B.

Before the '763 Patent expired, Bristol-Myers initiated a series of patent applications (the "Applications") that resulted in the '365 Patent. The prosecution history of these Applications is complex, but all of the Applications drew upon the same body of new scientific research. This new research indicated that the 6-hydroxy-metabolite has anxiolytic potential of its own and may even be the primary active agent in the causal mechanisms leading to the reduction of anxiety in successful uses of buspirone. *See* ' 365 Patent, at col. 3 ("We have discovered that [the 6-hydroxy-metabolite] ... is useful as an agent to treat anxiety ...."); *see generally* id. at cols. 3-10. The Applications suggest that the 6-hydroxy-metabolite is "the active metabolite of buspirone." Id. at col. 3.

On August 5, 1999, Bristol-Myers submitted the first of the series of patent applications (the "'842 Application") based on this new research. The '842 Application claimed:

1. A process for ameliorating an undesirable anxiety state in a mammal comprising systemic administration to the mammal of an effective but non-toxic anxiolytic dose of [the 6-hydroxy-metabolite] or a pharmaceutically acceptable acid addition salt, *prodrug,* or hydrate thereof.

U.S. Patent Application No. 09/368,842 (the "'842 Application"), at 12 (filed Aug. 5, 1999) (emphasis added), attached to Brown Decl. at A-7, A-20. FN3 A "prodrug" of a metabolite is a precursor drug that is converted into the metabolite during the ordinary processes of metabolization. Because buspirone is a prodrug of the 6-hydroxy-metabolite, the '842 Application indisputedly claimed use of buspirone to treat anxiety.

FN3. All references to the Brown Declaration with citations A 1 to F 154 are to pages that have been given those numbers by the parties and have been collected in Tabs A through F of Tab 21 to the Brown Declaration.

On August 8, 1999, Bristol-Myers also filed a petition to make the '842 Application "special," thus qualifying it for expedited processing under Title VIII, s. 708.02 of the Manual of Patent Examining Procedure ("MPEP"). *See* Petition to Make Special dated August 5, 1999, at 1-2 (filed August 8, 1999),

attached to Brown Decl. at A-29, A-29 to A-30. One condition for expedited processing is that an application be limited to a single invention, however, and the Patent Officer found that the '842 Application contained two patentably distinct inventions: one related to the "6-hydroxy-metabolite of Buspirone" and another related to "Buspirone *itself*." *See* Patent Office Action on '842 Application, at 2 (emphasis added), attached to Brown Decl. at A-35, A-36. The Patent Officer therefore refused to rule on the petition until Bristol-Myers elected one of the two inventions at issue. *See* Letter from Bristol-Myers to Patent Office dated November 24, 1999 ("Election Letter"), at 1, attached to Brown Decl. at A-32, A-32.

In response, Bristol-Myers elected to pursue a patent limited to uses of the prodrug buspirone. *See* Election Letter at 1-2. On December 13, 1999, the Patent Officer rejected the narrowed '842 Application under Sections 102(b) and 103(a) of Title 35 of the United States Code, explaining that (i) "[i]t [was] *admitted prior art* ... that the elected *PRODRUG Buspirone* is effective for treatment of anxiety disorders and depression"; (ii) the FDA-approved labeling instructions for Buspar(R), as revised in May 1998, were "clear evidence of *an on sale bar* to these claims," which were accordingly " *in the public domain* "; and (iii) use of buspirone to treat anxiety in the way claimed in the '842 Application was obvious from the admitted prior art. Patent Office Action on '842 Application, at 2-3. The Patent Officer explained further that "[t]o discover what happens when the patient swallows his prescribed Buspar pill, (Buspirone forms its 6-hydroxy-metabolite, *inherently*), is not a patentable discovery. It is *inherent*." Id. at 4. The Patent Officer also indicated, however, that "[a] divisional application [could still] be filed under 35 U.S.C. s. 121 on *the non-elected 6-hydroxy-metabolite*." Id. at 2 (emphasis added).

On January 18, 2000, Bristol-Myers filed a divisional application pursuant to 35 U.S.C. s. 121 (the "'161 Divisional Application"). *See* Data Sheet for U.S. Patent Application No. 09/484,161, at 1, attached to Brown Decl. at B-6, B-6. This Application was handled by the same Patent Officer. Bristol-Myers defined the claim at issue by formally requesting the Patent Officer to amend the language from claim one of the original '842 Application by deleting the word "prodrug." *See* Preliminary Amendment dated Jan. 18, 2000, at 1, attached to Brown Decl. at B-7, B-7. Bristol-Myers explained in this filing that "[a]mendment of the claim has been done in order to delete the claimed subject matter contained in the pending parent application [the '842 Application]," and that "[t]his claim amendment elects the non-elected claimed subject matter of the parent application." Id. at 2.

On June 6, 2000, Bristol-Myers filed four more applications, all of which were filed as continuations-in-part (or "CIP Applications") of the '161 Divisional Application and all of which were handled by the same Patent Officer as the prior two Applications. The first two (the "Non-Elected Subject Matter Applications") used the same language as the '161 Divisional Application, claiming, in relevant part, a processfor ameliorating anxiety comprising systemic administration of the 6-hydroxy-metabolite, but naming neither "buspirone" nor any "prodrug." *See* U.S. Patent Application No. 09/588,221, at 23, attached to Brown Decl. at C-11, C-36; U.S. Patent Application No. 05/588,222, at 23, attached to Brown Decl. at D-5, D-28. By contrast, the latter two (the "Improved Method Applications") claimed, among other things:

1. An improved process of ameliorating an undesirable anxiety state in a mammal by oral administration of *buspirone,* the improvement comprising the administration of buspirone, or a pharmaceutically acceptable acid addition salt thereof, in a manner favoring metabolic production of [the 6-hydroxy-metabolite] in the mammal.

. . . . .

7. The improved process of claim 1 wherein the pharmaceutically acceptable salt is buspirone hydrochloride.

See U.S. Patent Application No. 09/588,223, at 23 (emphasis added), attached to Brown Decl. at E-10, E-33; U.S. Patent Application No. 09/588,220, at 23 (emphasis added), attached to Brown Decl., at F-11, F-34. These Improved Method Applications also explicitly identified and claimed a number of purportedly non-obvious methods of administering buspirone so as to favor production of the 6-hydroxy-metabolite. *See* U.S. Patent Application No. 09/588,223, at 23 (claims 2 to 6); U.S. Patent Application No. 09/588,220, at 23 (claims 2 to 6). Although the claims in the four patent Applications differed, each used the same specification to describe the invention. On June 9, 2000, shortly after filing these four new Applications, Bristol-Myers abandoned its original '842 Application, *see* Request for Express Abandonment of '842 Application, attached to Brown Decl. at A 41, A 41, thus leaving five applications pending, including the '161 Divisional Application.

On July 18, 2000, Bristol-Myers filed a Preliminary Communication as part of the '161 Divisional Application, which presented a series of legal arguments concerning the obviousness of the allegedly novel uses of buspirone to favor production of the 6-hydroxy-metabolite that Bristol-Myers's new research recommended and discussed whether any uses had been anticipated by the prior art of buspirone use. *See* Preliminary Communication dated July 18, 2000, attached to Brown Decl. at B-40. The Preliminary Communication was directed at a defense of the '161 Divisional Application, which claimed the systemic administration of a dose of the 6-hydroxy-metabolite. With regard to obviousness, the Preliminary Communication stated that the "Applicant believes that the information regarding [the 6-hydroxy-metabolite] available to himself and others skilled in the art, not only did not suggest that [the 6-hydroxy-metabolite] be tested as an anxiolytic agent but, in fact, acted to teach away from such use for any hydroxy-buspirone metabolite." Id. at 7. With regard to anticipation, the Preliminary Communication argued that the prior art of buspirone use did not anticipate the effective method of using the drug allegedly identified in Bristol-Myers's new research because the prior art did not result in an effective anxiolytic amount of the 6-hydroxy-metabolite in the bloodstream on every occasion. *See* id. at 7-14.

The Preliminary Communication also stated that when Bristol-Myers used the term "systemic administration" in the application, Bristol-Myers intended to include the oral administration of the buspirone prodrug form of the 6-hydroxy-metabolite, and that the specification language made this definition clear. *See* id. at 3. Finally, the Preliminary Communicationargued that "the deletion of the term 'prodrug' from the claim presently before the Examiner did not change the scope of the Applicant's claimed invention, which is a method for treating anxiety by the systemic administration of an effective anxiolytic dose of [the 6-hydroxy-metabolite], *irrespective of how this systemically effective dose is accomplished*." Id. at 3 (emphasis added). Bristol-Myers did not file the Preliminary Communication in any of the other four pending Applications.

On September 8, 2000, the Patent Officer rejected the two Improved Method Applications on the same grounds that he had rejected the narrowed '842 Application. *See* Patent Office Action on '220 CIP Application, at 3-5, attached to Brown Decl. at E-51, E-53 to E-55; Patent Office Action on '223 CIP Application, at 3-5, attached to Brown Decl. at F-68, F-70 to F-72. The Patent Officer explained that the claims covered:

processes for ameliorating anxiety comprising the administration of the clinically useful anxiolytic drug, Buspirone, or its salts, known as " *Buspar* ", which has been on sale, and which inherently produces *in vivo* metabolites, including, *inter alia,* " *BMY 28674* ", its 6-hydroxy-metabolite. Even if there is no apparent

motivation to favor production of this metabolite, an on sale public use and sale bar is seen to exist, if the administration of BUSPIRONE or its salts by themselves inherently yields its " *BMY 28674* " 6-hydroxy-metabolite.

Patent Office Action on '220 CIP Application, at 2; Patent Office Action on '223 CIP Application, at 2.FN4

FN4. The Patent Officer also rejected the Improved Method Applications on provisional double patenting grounds, citing the fact that the two Applications overlapped with one another in scope. *See* Patent Office Action on '220 CIP Application, at 5-6; Patent Office Action on ' 223, at 5-6.

Between September 12, 2000 and September 13, 2000, the Patent Officer then rejected the two Non-Elected Subject Matter Applications and the '161 Divisional Application, all of which contained the same claim language. *See* Patent Office Action on '221 CIP Application, attached to Brown Decl. at C-110; Patent Office Action on '222 CIP Application, attached to Brown Decl. at D-39; Patent Office Action on '161 Divisional Application, attached to Brown Decl. at B-133. The Patent Officer did not reject these Applications on the merits but rather on provisional double patenting grounds. The Patent Officer explained that these Applications appeared to be either identical to one another or overlapping in scope because they all claimed a "process for ameliorating anxiety comprising administration of an effective anxiolytic dose of the 6-hydroxy-metabolite, ' *BMY 28674* ', of the clinically useful anxiolytic drug, Buspirone, marketed as ' *Buspar* '." Patent Office Action on '221 CIP Application, at 2; Patent Office Action on '222 CIP Application, at 2; Patent Office Action on '161 Divisional Application, at 2.

On September 22, 2000, Bristol-Myers expressly abandoned the '161 Divisional Application and one of the Non-Elected Subject Matter Applications. *See* Request for Express Abandonment of '161 Divisional Application, attached to Brown Decl. at B-137; Request for Express Abandonment of '222 CIP Application, attached to Brown Decl. at D-47. On that same day, Bristol-Myers requested that the Patent Officer reconsider the remaining Non-Elected Subject Matter Application on the ground that the problems of provisional double patenting had been removed. *See* Request for Reconsideration of '221 CIP Application, at 1-2, attached to Brown Decl. at C-114, C-114 to C-115. The Patent Officer agreed, and Bristol-Myers moved to make the Application special and to have it processed on an expedited basis before November 22, 2000, the date by which the '763 Patent was to expire. *See* Petition for Expedited Processing of ' 221 CIP Application, attached to Brown Decl. at C-160. The Patent Officer granted the motion to make the Application special, and, on November 21, 2000, less than one day before the '763 Patent expired, Bristol-Myers obtained the '365 Patent. *See* '365 Patent at 1. This Patent claims, in full:

1. A process for ameliorating an undesirable anxiety state in a mammal comprising systemic administration to the mammal of an effective but non-toxic anxiolytic dose of 6-hydroxy-8-[4-[4-(2-pyrimidinyl)-piperazinyl]butyl]-8-azaspiro[4.5]-7,9-dione or a pharmaceutically acceptable acid addition salt or hydrate thereof.

Id. at col. 16.

C.

Approximately eleven hours before the '763 patent expired, Bristol-Myers hand-delivered copies of the '365 Patent to the FDA and applied to have it listed in the Orange Book as covering buspirone. *See* Mylan

Pharm., Inc. v. Thompson, 139 F.Supp.2d at 8. At oral argument, Bristol-Myers indicated that this application did not include the prosecution history of the '365 Patent. Upon receiving the application, the FDA suspended approval of Mylan's and Watson's ANDAs for generic buspirone. Shortly thereafter, Mylan and Watson submitted papers to the FDA arguing that under Hoechst-Roussel Pharmaceuticals, Inc. v. Lehman, 109 F.3d 756 (Fed.Cir.1997), the '365 Patent should not have been listed because the Patent covered uses of the 6-hydroxy-metabolite, and patents for metabolites allegedly do not cover uses of a prodrug under *Hoechst*. Mylan and Watson also argued that the '365 Patent did not cover any of the uses of buspirone indicated in their ANDAs. *See* Mylan Pharm., Inc. v. Thompson, 139 F.Supp.2d at 8-9.

On November 30, 2000, Mylan Pharmaceuticals, Inc. filed a suit against Bristol-Myers and the FDA in the United States District Court for the District of Columbia, seeking, among other things, preliminary injunctive relief preventing the listing of the '365 Patent and ordering the FDA to approve its buspirone ANDAs immediately. *See* Mylan Compl. dated Nov. 30, 2000, attached as Ex. 16 to Brown Decl. Watson filed a similar suit in the United States District Court for the District of Maryland, naming FDA Commissioner Jane Henney as the sole defendant. *See* Watson Compl. dated Nov. 30, 2000, attached as Ex. 15 to Brown Decl. Bristol-Myers intervened as a defendant.

Mylan and Watson also filed supplemental Paragraph IV certifications with the FDA, claiming that their proposed buspirone products do not infringe the ' 365 Patent, and provided Bristol-Myers with notice of these certifications, as required by 21 U.S.C. s. 355(j)(2)(B). The FDA is required to approve an ANDA with a paragraph IV certification unless the pioneer patent holder files suit against the generic manufacturer within forty-five days from the receipt of such notice. *See* 21 U.S.C. s. 355(j)(5)(B)(iii). Under 35 U.S.C. s. 271(e)(2), the filing of an ANDA can itself constitute an act of infringement. If a patent-holder brings such an action within the forty-five day period, the FDA is prohibited from approving the pending ANDA for a period of thirty months unless the court hearing the patent infringement claims renders an earlier decision. *See* 21 U.S.C. s. 455(j)(5)(B)(iii). Bristol-Myers filed three patent infringement suits naming Mylan and/or Watson as defendants within the relevant time periods.

Thereafter, the two district courts that had been presented with motions for preliminary injunctive relief requiring that the '365 Patent be delisted from the Orange Book rendered decisions on the motions. The United States District Court for the District of Maryland rejected Watson's request for preliminary injunctive relief against the FDA Commissioner on the ground that the action was, in effect, an attempt to obtain judicial review of a purely ministerial administrative determination made by the FDA Commissioner. *See Watson Pharm., Inc. v. Henney,* Civ. No. S 00-3516, slip op. at 4 (D.Md. Jan. 17, 2001). The Court held that the Commissioner's decision was a purely ministerial act, which, as such, was neither arbitrary nor capricious, and was entitled to deference under Chevron U.S.A., Inc. v. Natural Resources Defense Council, 467 U.S. 837, 104 S.Ct. 2778, 81 L.Ed.2d 694 (1984).

In the case before the United States District Court for the District of Columbia, however, the court held that the action raised a primary challenge to Bristol-Myers's conduct in listing the '365 Patent. *See* Mylan Pharm., Inc. v. Thompson, 139 F.Supp.2d at 11. This conduct was not entitled to *Chevron* deference. The Court also held that Mylan had established a likelihood of success on the merits with regard to its proposed claim construction, such that the '365 Patent was not likely to cover the uses of buspirone that Bristol-Myers proposed in its Orange Book listing. *See* id. at 19-26. On the basis of these findings, as well as a finding that the public interest favored delisting, the Court issued a preliminary injunction requiring Bristol-Myers to take measures to delist the '365 Patent from the Orange Book. *See* id. at 29-30. The Court also directed the FDA to approve Mylan's ANDA for the manufacture and sale of generic buspirone. Id.

Bristol-Myers appealed, and, on October 12, 2001, the Court of Appeals for the Federal Circuit reversed the grant of the preliminary injunction on the ground that neither the patent laws nor the Hatch-Waxman Amendments provided for a private cause of action to delist a drug from the Orange Book. *See* Mylan Pharm., Inc. v. Thompson, 268 F.3d 1323, 1329-33 (Fed.Cir.2001). The Court of Appeals did not address the merits of the district court's claim construction analysis. *See* id. at 1323-33.

By this time, on August 15, 2001, the Judicial Panel on Multidistrict Litigation had consolidated and transferred to this Court the three patent infringement suits brought by Bristol-Myers and another patent action filed by Mylan Pharmaceuticals, Inc. against Bristol-Myers. The Panel had also transferred to this Court twenty-two antitrust suits brought by various plaintiffs against Bristol-Myers. In the patent infringement suits, Mylan and Watson now move for summary judgment on the ground that their manufacture and sale of generic buspirone for use in accordance with the FDA-approved labeling instructions for Buspar(R) does not infringe the '365 Patent, and that the ' 365 Patent would be invalid if the Patent did cover such uses.

III.

[1] Mylan and Watson argue that they are entitled to summary judgment on the patent infringement claims based on a finding that as a matter of straightforward claim construction, the '365 Patent does not cover the use of buspirone and is instead limited to a method of using the 6-hydroxy-metabolite. The initial question is whether the '365 Patent covers the use of buspirone, as Bristol-Myers contends, or does not cover such use, as Mylan and Watson contend.

[2] [3] Claim construction is a matter of law. *See* Markman v. Westview Instruments, Inc, 52 F.3d 967, 979 (Fed.Cir.1995) (en banc), *aff'd,* 517 U.S. 370, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). Courts determine the scope of a claim by applying well-known principles of claim construction and examining three relevant sources: the language of the claim, the specification and the prosecution history. *See* Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1583 (Fed.Cir.1996) ("The claims, specification, and file history ... constitute the public record of the patentee's claim, a record on which the public is entitled to rely."); Process Res. Corp. v. Delta Air Lines, Inc., No. 98 Civ. 5648, 2000 WL 145114, at (S.D.N.Y. Feb. 3, 2000).

A.

The language of a claim provides the starting point in a claim construction analysis. *See* Phonometrics, Inc. v. Northern Telecom Inc., 133 F.3d 1459, 1464 (Fed.Cir.1998); Digital Biometrics, Inc. v. Identix, Inc., 149 F.3d 1335, 1344 (Fed.Cir.1998); *see also* Thermalloy, Inc. v. Aavid Eng'g, Inc., 121 F.3d 691, 693 (Fed.Cir.1997) ("[T]hroughout the interpretation process, the focus remains on the meaning of claim language."). In this case, the '365 Patent claims:

[a] process for ameliorating an undesirable anxiety state in a mammal comprising systemic administration to the mammal of an effective but non-toxic anxiolytic dose of [the 6-hydroxy-metabolite or BMY 28674] FN5 or a pharmaceutically acceptable acid addition salt or hydrate thereof.

FN5. The claim uses the term "6 hydroxy 8 [4 [4 (2 pyrimidinyl) piperazinyl] butyl] 8 azaspiro[4.5] 7,9 dione," which is the complete formulation of the chemical compound.

'365 Patent, at col. 16.

The claim does not state that it covers the systemic administration of "buspirone" or of any "prodrug" of the 6-hydroxy-metabolite. The 6-hydroxy-metabolite is a distinct chemical compound from buspirone, and it would be incorrect to refer to a prodrug by the name of one of the metabolites it produces in the human body.FN6 Indeed, the ' 365 Patent carefully distinguishes between the two throughout the entire specification, sometimes producing graphs of levels of one in the bloodstream as a function of dosages of the other, and sometimes recommending ways of using one so as to favor production of the other. *See, e.g.,* ' 365 Patent, at cols. 1-2, 3-4, 5-7, 8-9, 13. Thus, on its face, the ' 365 Patent does not extend to the systemic administration of buspirone.

FN6. Buspirone has the structure of 8 [4 [4 (2 pyrimidinyl) 1 piperazinyl] butyl] 8 azaspiro[4.5]decane 7,9 dione, whereas the 6-hydroxy-metabolite has the structure of 6 hydroxy 8 [4 [4 (2 pyrimidinyl) piperazinyl] butyl] 8 azaspiro[4.5] 7,9 dione.

[4] The claim also refers to systemic administration of a "dose" of the metabolite. Although the term "dose" can sometimes be used simply to mean "quantity," its primary meaning, as both parties agree, is "the measured quantity of a medicine or other therapeutic agent *to be taken at one time or in a period of time*." Webster's Third New International Dictionary 676 (1993) (emphasis added); Stedman's Medical Dictionary (26th ed. 1995) ("The quantity of a drug or other remedy to be taken or applied all at one time or in fractional amounts within a given period."). The '365 Patent consistently uses the word "dose" to refer to an externally-measured amount of a chemical, which is to be ingested or administered into the body at one time, and "blood level" to refer to the changing amounts of a substance in the bloodstream. *See, e.g.,* '365 Patent, at cols. 2, 7, 8-9, 10 & figs. 3-5 (discussing, among other things, levels of the 6-hydroxy-metabolite in the bloodstream as a function of time, and after "multiple doses of oral buspirone"). This distinction in terminology makes sense, given the ordinary definition of "dose." The idea of a "dose" as a quantity that is "taken at one time" has a clear meaning in reference to an externally-measured amount of a substance that is to be ingested or administered into the body all at once, but would have no precise meaning if used to refer to *in vivo* levels in the bloodstream, which are constantly changing. *See, e.g.,* '365 Patent figs. 3-5 (presenting graph of "blood levels" of buspirone and its metabolites over time as a function of "doses" of buspirone taken at daily intervals).

Thus, as used in the '365 Patent, the phrase "systemic administration to the mammal of an effective but non-toxic anxiolytic dose of the 6-hydroxy-metabolite" refers to the administration of an externally-measured quantity of the metabolite into the body, and not to the administration of a dose of buspirone into the body, which, in turn, produces variable and changing levels (not doses) of the metabolite in the bloodstream. *See* '365 Patent, at col. 16. The language of the claim does not support Bristol-Myers's construction.

B.

[5] Bristol-Myers argues that this language must nevertheless be read in light of the patent specification, which states, at one point that:

Systemic administration may also be realized by a second method of achieving effective anxiolytic blood levels of [the 6-hydroxy-metabolite] which is to orally administer a precursor form of [the 6-hydroxy-metabolite]. Such prodrug forms would be administered in dosage amounts that would produce effective

anxiolytic effects without causing harmful or untoward side-effects. That is, systemic administration of [the 6-hydroxy-metabolite] may be accomplished by oral administration of a precursor or prodrug form of [the 6-hydroxy-metabolite], e.g., buspirone, to mammals.

'365 Patent, at cols. 11-12. Bristol-Myers adds, correctly, that "[a] patentee may choose to be his own lexicographer, and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history." *See* Vitronics, 90 F.3d at 1582 (citing Hoechst Celanese Corp. v. BP Chems. Ltd., 78 F.3d 1575, 1578 (Fed.Cir.1996)). In Bristol-Myers's view, the specification language provides a definition of the term "systemic administration" as including any administration of buspirone that produces an effective but non-toxic anxiolytic amount of the 6-hydroxy-metabolite in the bloodstream.

[6] [7] The specification does not support Bristol-Myers's interpretation. As Bristol-Myers agrees, the term "systemic administration" has a common and well-understood meaning in the medical community. (*See* Bristol-Myers's Br. at 17.) It refers to administration of a medicine throughout the patient's system, as through introduction into the bloodstream, and as opposed to administration only to a local area of the body. *See* Declaration of James Barbee, M.D. dated Nov. 19, 2001, at para. 8; *see also* Stedman's Medical Dictionary (26th ed.1995) (defining "systemic" as "relating to a system; specifically somatic, relating to the entire organism as distinguished from any of its individual parts"). The term "systemic administration" should maintain this meaning in the '365 Patent because patent law instructs that technical words appearing in patents should be presumed to be used, and to be intended to be understood, as they would be by persons experienced in the field of the invention. *See, e.g.,* Talbert Fuel Sys. Patents Co. v. Unocal Corp., 275 F.3d 1371, 1375 (Fed.Cir.2002); Hoechst Celanese Corp., 78 F.3d at 1578.

The language that Bristol-Myers cites does not provide a special definition of the term or use it in any different way. Rather, it assumes the ordinary meaning, and relies on it to assert that the systemic administration of the 6-hydroxy-metabolite can be *effected* or *achieved* by oral administration of a prodrug such as buspirone. This is a statement about cause and effect, not a definition. Put simply, the specification says that one way of getting the 6-hydroxy-metabolite into the entire body through the bloodstream is to administer oral doses of buspirone to a patient-a proposition that is undisputed among the parties. The specification does not say that the phrase "systemic administration" of a dose of the 6-hydroxy-metabolite *means* systemic administration of either a dose of the 6-hydroxy-metabolite or a dose of buspirone. Bristol-Myers attempts to claim that "systemic administration" is used in a specialized way in the '365 Patent, when the specification indicates no such specialized meaning.

[8] The language of the specification must also be read in context. To the degree that it identifies a use of buspirone, the language appears as the introduction to a series of paragraphs in which Bristol-Myers tries to distinguish this use from those that appear in the FDA-approved labeling instructions for Buspar(R). The very next sentence says: "However, *this* method of systemic introduction of [the 6-hydroxy-metabolite] *improves upon and differs from* the known standard method of oral administration of buspirone." Id. at col. 12 (emphases added). The specification then outlines the purported differences between the methods and states that the new method is " *in contradiction* to currently accepted methods of administration that are directed to maximizing blood levels of unchanged buspirone"; and is " *directly counter* to the past method of orally administering buspirone." Id. (emphases added). To the degree that the specification refers to any novel use of buspirone, the specification is thus clear that the use in question is not the one that appears in the FDA-labeling instructions for Buspar(R).

Finally, as described above, the same specification was used for four separate patent applications, including two that explicitly claim a method of using buspirone. The two Improved Method Applications were rejected by the Patent Office. It would be remarkable if the same specification was attempting to convey that the term "systemic administration ... of an effective ... dose of [the 6-hydroxy-metabolite]" was Bristol-Myers's specialized way of describing the administration of buspirone when that definition would only be needed in two of the patents Bristol-Myers was seeking and when the other two explicitly used the word "buspirone" to claim an improved method of using buspirone.

C.

[9] The third source of evidence for claim construction is the prosecution history of a patent. Facts from a prosecution history can be so critical to claim construction that they can trump otherwise clear language in a claim or specification. *See, e.g.,* Pall Corp. v. PTI Techs., Inc., 259 F.3d 1383, 1392 (Fed.Cir.2001) ("Even where the ordinary meaning of the claim is clear, it is well-established that '[t]he prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution.' ") (quoting Southwall Techs., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1576 (Fed.Cir.1995)); *see also* Rheox, Inc. v. Entact, Inc., 276 F.3d 1319, 1325 (Fed.Cir.2002).

[10] In this case, the prosecution history leaves no doubt that the '365 Patent does not cover the use of buspirone. Bristol-Myers argues that the prosecution history, when viewed as a whole, reveals a persistent series of attempts to obtain a patent that extends to uses of buspirone. The relevance of a prosecution history to claim construction is not, however, to determine what coverage the patent applicant would have wanted to obtain but rather whether, in order to prosecute the patent that it actually did obtain, the applicant made definitive statements or amendments that disclaimed or disavowed any subject matter. *See, e.g.,* Rheox, 276 F.3d at 1325-26; Digital Biometrics, 149 F.3d at 1347-48.

[11] [12] Use of this test serves an important public policy: the public and competitors have a right to rely on definitive statements made during prosecution history. *See* Digital Biometrics, 149 F.3d at 1347; Southwall Techs., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1575 (Fed.Cir.1995). There is also an equitable dimension to the test: it prevents applicants from construing claims more narrowly in order to obtain their allowance and then more broadly against accused infringers. *See* Spectrum Int'l, Inc. v. Sterilite Corp., 164 F.3d 1372, 1379 (Fed.Cir.1998). To that end, the prosecution history generally limits the interpretation of claim terms so as to exclude any interpretation that, based on the totality of the prosecution history, the patentee relinquished. *See, e.g.,* Rheox, 276 F.3d at 1325.

i.

In this case, Bristol-Myers argues that the prosecution history of the '365 Patent supports its claim that the Patent covers both (i) certain uses of the 6-hydroxy-metabolite to treat anxiety and (ii) any uses of buspirone that favor production of non-toxic but anxiolytically effective levels of the 6-hydroxy-metabolite in the bloodstream. The very first Application that Bristol-Myers filed based on its new research into the anxiolytic potential of the 6-hydroxy-metabolite indisputedly covered both of these methods-of-use claims. This was the '842 Application, which was filed on August 5, 1999 and claimed, in relevant part,

[a] process for ameliorating an undesirable anxiety state in a mammal comprising systemic administration to the mammal of an effective but non-toxic anxiolytic dose of *[the 6-hydroxy-metabolite] or a ... prodrug ... thereof*.

'842 Application, at 12. By claiming the systemic administration of specified doses of the 6-hydroxy-metabolite *or a prodrug thereof,* when buspirone is indisputedly a prodrug of the 6-hydroxy-metabolite, Bristol-Myers clearly applied for a patent covering the disputed uses of buspirone. However, any reasonable view of the subsequent history indicates that Bristol-Myers gave up a claim to the disputed uses of buspirone.

The '842 Application is the parent of the Application that finally resulted in the '365 Patent. When Bristol-Myers filed the '842 Application, Bristol-Myers applied to make it special and sought to expedite its processing. However, one condition on this kind of processing is that an application be limited to a single invention, *see* M.P.E.P. tit. VIII, s. 708.02, and the PatentOfficer found that the Application described two patentably distinct method-of-use inventions, one related to the "6-hydroxy-metabolite of Buspirone" and one related to "Buspirone *itself*." *See* Patent Office Action on '842 Application, at 2. Bristol-Myers was thus forced to elect between the two uses if it hoped to obtain expedited processing, and Bristol-Myers chose to pursue a patent limited to uses of buspirone in the '842 Application. *See* Election Letter 1.

On December 13, 1999, the Patent Officer rejected this narrowed Application pursuant to Sections 102(b) and 103(a) of 35 United States Code because such uses of buspirone were covered by the on sale bar in view of the prior years of Buspar(R) sales, and were obvious in light of the prior art of buspirone use. *See* Patent Office Action on '842 Application, at 2-4. This was the same Patent Officer who ultimately approved the final '365 Patent, and the Patent Officer never explicitly retracted these views. Thus, it is plain that the Patent Officer was unwilling to grant Bristol-Myers a patent extending to uses of buspirone.

ii.

Bristol-Myers's actions in response to the Patent Officer's rejection of the narrowed '842 Application on December 13, 1999 provide clear evidence for Mylan's and Watson's construction of the '365 Patent. In rejecting the narrowed '842 Application, the Patent Officer indicated that Bristol-Myers was still free to file "[a] divisional application ... under 35 U.S.C. s. 121 *on the non-elected 6-hydroxy-metabolite*." Patent Office Action on '842 Application, at 1 (emphasis added.) On January 18, 2000, Bristol-Myers filed such a divisional application (the '161 Divisional Application), and Bristol-Myers generated its claim language by amending the original language from claim one of the '842 Application to delete the term "prodrug," which had clearly referred to buspirone. The resulting claim language, which is precisely the same language found in the '365 Patent, was first presented to the Patent Officer in the '161 Divisional Application. The '365 Patent application was also a continuation-in-part of the '161 Divisional Application, and the prosecution history of this Application thus has bearing on the present claim construction analysis. *See, e.g.,* Medtronic, Inc. v. Advanced Cardiovascular Sys., Inc., 248 F.3d 1303, 1315 (Fed.Cir.2001) ("The prosecution history of a related patent can be relevant if, for example, it addresses a limitation in common with the patent in suit.") (collecting cases).

Bristol-Myers argues that its deletion of the word "prodrug" did not change the meaning of this claim language because the word "prodrug" is superfluous in light of Bristol-Myers's proposed definition of "systemic administration" from the specification. As discussed above, however, the specification does not contain a new definition of "systemic administration." Morever, Bristol-Myers's detailed and explicit actions in filing a divisional application and amending this language, just after the Patent Officer's rejection of the narrowed '842 Application, would make no sense if the amendment were superfluous.

Bristol-Myers's position is also inconsistent with the positions it took before the Patent Officer. In filing the

'161 Divisional Application, Bristol-Myers told the Patent Officer that "amendment of the claim has been done in order to delete the claimed subject matter contained in the pending" ['842 Application',] and that "[t]his claim amendment elects the non-elected claimed subject matter of the parent ['842 Application.]" Preliminary Amendment at 1. Bristol-Myers's proposed construction would, however, reclaimthat subject matter. The Patent Officer had also clearly indicated to Bristol-Myers that the original '842 Application contained two patentably distinct inventions.

Moreover, Bristol-Myers filed the '161 Divisional Application pursuant to 35 U.S.C. s. 121. Section 121 is entitled "divisional applications" and states, in relevant part, that "[i]f two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions." 35 U.S.C. s. 121. In construing this provision, the Court of Appeals for the Federal Circuit has held that:

Consonance requires that the line of demarcation between the "independent and distinct inventions" that prompted the restriction requirement be maintained. Though the claims may be amended, they must not be so amended as to bring them back over the line imposed in the restriction requirement.

Gerber Garment Tech., Inc. v. Lectra Sys., Inc., 916 F.2d 683, 688 (Fed.Cir.1990). The fact that Bristol-Myers obtained the '365 Patent in a continuation-in-part of the '161 Divisional Application, which contained the exact same claim language as the '365 Patent, strongly indicates that the ' 365 Patent claims a single invention directed to uses of doses of the 6-hydroxy-metabolite to treat anxiety.

Finally, any reasonable view of the prosecution history indicates that when Bristol-Myers filed its four patent applications on June 6, 2000, two of those applications-the Improved Method Applications-contained amended claim language explicitly using the word "buspirone" in order to claim certain limited uses of buspirone, while the other two-the Non-Elected Subject Matter Applications-omitted all explicit reference to the drug in order to distinguish the claim from the elected method of using buspirone that had been pursued in the '842 Application. It was one of the Non-Elected Subject Matter Applications-the '221 CIP Application-which used the same language as the ' 161 Divisional Application, and which did not refer at all to a use of the "prodrug," or "buspirone," that resulted in the '365 Patent.

In light of these facts, Bristol-Myers's declarations and amendments clearly narrowed the Application to uses of the 6-hydroxy-metabolite. *See, e.g.,* Rheox, 276 F.3d at 1325; Spectrum Int'l, 164 F.3d at 1378.

iii.

Bristol-Myers argues that there is another part of the prosecution history that supports its reading of the '365 Patent as covering uses of buspirone. In particular, as Bristol-Myers correctly points out, it submitted a document, which it entitled the "Preliminary Communication," as part of its '161 Divisional Application, which stated in no uncertain terms that omission of the word "prodrug" was not meant to exclude uses of buspirone that result in systemic administration of the 6-hydroxy-metabolite. The Preliminary Communication also presented a number of arguments to the effect that Bristol-Myers's amendments in the '161 Divisional Application did not change the scope of the claim.FN7

FN7. The significance that Bristol-Myers places on the Preliminary Communication in this litigation is somewhat undercut by the fact that it was not even disclosed in the papers on the preliminary injunction in the case before the District Court for the District of Columbia, and was only brought to that court's attention

at oral argument of that motion. *See* Mylan Pharm., Inc. v. Thompson, 139 F.Supp.2d at 26.

However, Bristol-Myers did not change the scope of the '161 Divisional Application by filing the Preliminary Communication. The Preliminary Communication was not and did not purport to be a formal amendment of the claim language. Bristol-Myers asked the Patent Officer not to act on the '161 Divisional Application until receiving the Preliminary Communication, but the document was not a required document. Rather, Bristol-Myers used the Preliminary Communication to present the Patent Officer with a series of legal arguments to the effect that its actions in filing the '161 Divisional Application and dropping the word "prodrug" from the original '842 Application did not change the meaning of the claim. Whether this is true is a matter of law, however, and, for the reasons discussed above, Bristol-Myers's amendments and conduct did limit the scope of the '161 Divisional Application.

The Preliminary Communication also presented statements concerning what Bristol-Myers meant to do when it dropped the word "prodrug" from the original '842 Application. The use of prosecution history in a claim construction analysis is not to uncover subjective intent on the part of an applicant, however, but rather to ensure that the public, including an applicant's competitors, may safely rely on the fact that an applicant will be bound by any definitive statements or amendments made to narrow a claim. *See, e.g., See, e.g.,* Rheox, 276 F.3d at 1325; Spectrum Int'l, 164 F.3d at 1378.

Under this test, it is highly relevant that Bristol-Myers explicitly disclaimed uses of buspirone in filing the '161 Divisional Application, that Bristol-Myers did so in order to distinguish a method of using buspirone that the Patent Officer had deemed unpatentable, and that Bristol-Myers obtained the '365 Patent as the continuation-in-part of a divisional application that would have been reasonably understood by all relevant parties and the public to be limited to a single invention comprised of a method of using the 6-hydroxy-metabolite. It is also highly relevant that Bristol-Myers never formally amended the claim in order to broaden its scope, and that Bristol-Myers obtained expedited processing of the '365 Patent, which is a process limited to applications directed to a single invention. It is not relevant, in light of these facts, that Bristol-Myers may have desired to maintain coverage of some uses of buspirone or may have argued that the claim language had this scope.

iv.

Further evidence in favor of Mylan's and Watson's claim construction derives from the way the Patent Officer handled Bristol-Myers's two Improved Methods Applications. These Applications were explicitly directed to the purportedly new and improved methods of using buspirone that its new research into the 6-hydroxy-metabolite recommended, and which purportedly differed from the uses indicated in the FDA-labeling instructions for Buspar(R). The Patent Officer nevertheless rejected these Applications, explaining that (i) the Applications claimed inventions that were identical or overlapping in scope with the prior art of buspirone use identified in the Buspar(R) labeling; (ii) these patents were in violation of an on sale bar, given the prior years of Buspar(R) sales; and (iii) these uses were obvious from, or anticipated by, the prior art, because use of buspirone inherently produces *in vivo* the 6-hydroxy-metabolite. *See* Patent Office Action on '220 CIP Application, at 3-5; Patent Office Action on '223 CIP Application, at 3-5.

The Patent Officer rejected these Applications on September 8, 2000, well after receiving the Preliminary Communication, which was filed on July 18, 2000. Therefore, even after receiving the Preliminary Communication, the Patent Officer was unwilling to grant Bristol-Myers a patent directed at even those

purportedly new methods of using buspirone that allegedly differed from the ones described in the FDA-labeling instructions for Buspar(R).

v.

In sum, every time Bristol-Myers explicitly claimed a use of "buspirone" or a "prodrug" of the 6-hydroxy-metabolite, the application was rejected. Bristol-Myers only obtained the '365 Patent after omitting all references in the claim to "buspirone" and any "prodrug," and after making express declarations that the amendments acted to exclude uses of buspirone. Viewed in its totality, this is a case where the prosecution history establishes beyond doubt that Bristol-Myers gave up a claim covering the use of buspirone in order to obtain a patent covering a method of using the 6-hydroxy-metabolite, and where, accordingly, Bristol-Myers cannot now reasonably assert a claim for the use of buspirone. *See, e.g.,* Rheox, 276 F.3d at 1325; Spectrum Int'l, 164 F.3d at 1378-79; Ahlstrom Machinery, Inc. v. Clement, 13 F.Supp.2d 45, 48 n. 2 (D.D.C.1998), *aff'd sub nom.* Kamyr, Inc. v. Clement, 217 F.3d 860 (Fed.Cir.1999) (per curiam). Hence, the '365 Patent does not cover any uses of buspirone.

IV.

[13] In any event, Mylan and Watson correctly argue that the '365 Patent would be invalid if construed to cover the use of buspirone, as Bristol-Myers contends. Mylan and Watson argue, more specifically, that the '365 Patent, so construed, would violate 35 U.S.C. s. 102(b), which renders unpatentable any invention that "was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States...." Id. If Bristol-Myers's proposed construction would render the '365 Patent invalid, this fact would provide an additional reason to reject that construction. *See, e.g.,* Wang Labs., Inc. v. America Online, Inc., 197 F.3d 1377, 1383 (Fed.Cir.1999) ("[C]laims are not properly construed to have a meaning or scope that would lead to their invalidity for failure to satisfy the requirements of patentability.").

i.

[14] Although there are a number of ways to establish a statutory bar under Section 102(b), Mylan and Watson argue, first, for an on sale bar. In order for an invention to generate an on sale bar, two conditions must be met: (1) the invention must have become the "subject of a commercial offer for sale" more than one year before the filing of the patent application; and (2) the invention must have been ready for patenting by that time, either by, for example, having been reduced to practice or having been disclosed in "drawings or other descriptions of the invention" that were sufficiently specific to enable a person skilled in the art to practice the invention. Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 67-68, 119 S.Ct. 304, 142 L.Ed.2d 261 (1998). In this case, it is undisputed that buspirone has been on the commercial market in this country as a drug for the treatment of anxiety since 1986, when Bristol-Myers first obtained and published its FDA-approved labeling instructions for Buspar(R). It is also undisputed that the invention was "ready for patenting" at that time because Bristol-Myers had in fact obtained the ' 763 Patent, which covered uses of buspirone to treat anxiety. Thus, both of the basic elements of an on sale bar are present in this case. *See* Special Devices, Inc. v. OEA, Inc., 270 F.3d 1353, 1355 (Fed.Cir.2001) (noting that these two inquiries "ordinarily end the two-part analysis under section 102(b)").

Moreover, the same undisputed facts establish that the art of using buspirone to treat anxiety, which Mylan and Watson now seek to practice, was (i) the subject of a patent (the '763 Patent); (ii) described in a printed publication (the FDA-approved labeling instructions for Buspar(R)); and (iii) in public use in this country

more than one year prior to the date on which Bristol-Myers applied for the '365 Patent. Mylan and Watson thus correctly argue that the prior art meets the basic criteria for establishing a statutory bar under Section 102(b).

Of course, in order for any of these statutory bars to apply to a particular patent, such as the '365 Patent, the prior invention that has been offered for sale, disclosed in a prior publication, patented or in public use for over a year must also lie within the scope of the new patent claim. *See, e.g.,* Scaltech v. Retec/Tetra, L.L.C., 178 F.3d 1378, 1383 (Fed.Cir.1999) (citing Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 339 U.S. 605, 607, 70 S.Ct. 854, 94 L.Ed. 1097 (1950)). The construction of the '365 Patent that Bristol-Myers proposes easily meets this criterion because Bristol-Myers vigorously asserts that the '365 Patent covers the effective use of buspirone to treat anxiety and concedes that buspirone is effective in treating anxiety in approximately 70% of the cases in which it is used. The use of buspirone to treat anxiety has plainly been on sale, covered by a prior patent and described in the FDA-approved labeling instructions for Buspar(R) since 1986. Viewing the record in a light most favorable to Bristol-Myers, these facts are alone sufficient to decide the issue of invalidity.

ii.

[15] [16] Bristol-Myers tries to avoid this straightforward conclusion by arguing that the question of the validity of the '365 Patent depends upon deciding material issues of fact that are in dispute between the parties, thus making summary judgment inappropriate. Bristol-Myers frames the dispute as if it reduces to the question whether the prior art of buspirone use inherently anticipates the invention described in the '365 Patent. *See, e.g.,* UMC Elecs. Co. v. United States, 816 F.2d 647, 656 (Fed.Cir.1987) (describing criteria for on sale bar as that (1) "there was a definite sale or offer to sell more than one year before the application for the subject patent" and (2) "the subject matter of the sale or offer to sell fully anticipated the claimed invention or would have rendered the claimed invention obvious by its addition to the prior art."). Bristol-Myers is correct that in order for a prior invention to embody some of the identical subject matter as that described in a new patent and raise a statutory bar on that basis, the prior invention must disclose each claim limitation of the new patent, either explicitly and in a manner that would be known to an ordinary person skilled in the art or inherently. *See* Scaltech, 178 F.3d at 1383-84; In re Schreiber, 128 F.3d 1473, 1477 (Fed.Cir.1997). Bristol-Myers is also correct that it is a question of fact whether an invention inherently anticipates a later claim. *See* In re Schreiber, 128 F.3d at 1477; In re Napier, 55 F.3d 610, 613 (Fed.Cir.1995). As the Court of Appeals for the Federal Circuit has explained:

The mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish inherency. However, if the natural result flowing from the operation of the process offered for sale would necessarily result in achievement of each of the claim limitations, then the claimed invention was offered for sale.

Scaltech, 178 F.3d at 1384 (citation omitted).

Bristol-Myers draws on these principles to argue that there is a material question of fact remaining as to whether the approved methods of using buspirone inherently or necessarily produce a non-toxic but anxiolytically-effective amount of the 6-hydroxy-metabolite in the bloodstream, and, hence, in Bristol-Myers's view, whether the prior buspirone sales were really sales of an identical invention to the one claimed in the '365 Patent. Bristol-Myers argues, further, that the prior art does not in fact have this effect with the kind of necessity that is required for anticipation by inherency because the prior art only has this

effect approximately 70% of the time.

[17] Bristol-Myers's arguments are misplaced. First, Mylan and Watson are only seeking to establish that the '365 Patent would be invalid if construed to cover the approved uses of buspirone, as Bristol-Myers claimed in its listing submissions to the FDA. There is no need to establish anticipation by inherency to answer whether this claim would be invalid by virtue of covering some of the identical subject matter as the prior art of buspirone because Bristol-Myers is arguing, in essence, that Mylan and Watson would violate the '365 Patent if they sold buspirone in accordance with the very same labeling and for the very same uses that the FDA approved for Bristol-Myers. It is axiomatic in patent law that that which would literally infringe if later in time anticipates if earlier. *See* Dow Chem. Co. v. Astro-Valcour, Inc., 267 F.3d 1334, 1339-40 (Fed.Cir.2001); Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1378 (Fed.Cir.2001); Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1324 (Fed.Cir.2001); Lewmar Marine, Inc. v. Barient, Inc., 827 F.2d 744, 747 (Fed.Cir.1987). By proposing a construction of the '365 Patent that literally would render this prior art infringing, Bristol-Myers has conceded the issue of invalidity as to this subsequently approved Patent.

[18] Second, Bristol-Myers fails to appreciate that its claimed construction of the '365 Patent would be invalid if merely some-and not only if all-of the prior uses of buspirone inherently anticipated the uses of buspirone that favor production of the 6-hydroxy-metabolite. Put differently, a patent that merely overlaps with a prior art can still be anticipated if each of its limitations is disclosed either explicitly or inherently by a prior art in the area of overlap. For example, in Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342 (Fed.Cir.1999), the Court of Appeals for the Federal Circuit examined a patent covering a blasting composition that contained an explicit limitation concerning "sufficient aeration ... entrapped to enhance sensitivity to a substantial degree." Id. at 1345 (quoting claim language). The Court of Appeals had to decide whether this patent was anticipated by two prior patents that covered blasting compositions that lacked this explicit limitation but that were otherwise identical. The Court noted that the prior art compositions produced ratios of up to 40% emulsion to 60% solid constituent, and this was sufficient aeration. *See* id. at 1348. However, the prior art was not limited to compositions with those ratios, and one prior art even taught away from compositions that would have this property. *See* id. at 1348-49. The Court of Appeals nevertheless found that the prior art anticipated the new patent because the prior art inherently produced sufficient aeration in a limited set of circumstances. *See* id. at 1349.

The Court of Appeals explained that "if granting patent protection on [a] disputed claim would allow the patentee to exclude the public from practicing the prior art, then that claim is anticipated, *regardless of whether it also covers subject matter not in the prior art*." Id. at 1346 (emphasis added). Bristol-Myers not only concedes but also vigorously asserts that in a limited range of circumstances, systemic administration of effective but non-toxic and anxiolytic amounts of the 6-hydroxy-metabolite can be achieved by using buspirone in accordance with the FDA-approved labeling instructions for Buspar(R). If the '365 Patent were to cover these uses, then it would be invalid under *Atlas Powder*.

Third, even in an area of overlap between a prior art and a patent that contains additional explicit limitations, the type of necessity needed for a prior art to anticipate a new invention is not, as Bristol-Myers appears to argue, absolute inevitability. All that is required is that Mylan and Watson can establish that some of the approved uses of buspirone actually cause, or regularly result in, the production of appropriate levels of the 6-hydroxy-metabolite in the bloodstream, as described in the '365 Patent. The natural process by which the human body metabolizes compounds into their metabolites, as described in the '365 Patent and in Bristol-Myers's papers, is sufficiently regular to meet this standard, even if the metabolic process breaks

down in certain cases or functions with some ordinary variability.

This case is thus similar to In re Omeprazole Patent Litigation, No. MDL 1291, 2001 WL 585534 (S.D.N.Y. May 31, 2001). In *In re Omeprazole,* the court examined a patent that claimed substances called sulphenamides and the administration of sulphenamides for use in inhibiting gastric acid secretion in the stomach lining. *See id*. at *3. There was, however, a prior art reference disclosing a method of using omeprazole for this same purpose, and omeprazole naturally produces sulphemanides *in vivo* after ingestion. *See id*. The parties disputed whether the new patent covered these particular kinds of sulphenamides, or only synthetically-produced sulphenamides. Because there was no genuine dispute that omeprazole is naturally converted into sulphenamides in the human body, the court found the prior art inherently anticipated the later disputed patent. *See id*. at *8-12.

The court found these facts sufficient to hold as a matter of law that if the new patent were construed to cover uses of omeprazole that produce sulphenamides *in vivo,* the new patent would have been invalid as inherently anticipated by the prior art reference concerning omeprazole. The court explained that the patent applicant had "merely attempted to patent the unpatentable-'a scientific explanation for the prior art's functioning.' " *Id*. at (quoting Atlas Powder, 190 F.3d at 1347). The court thus construed the claim more narrowly, so as to exclude coverage of the *in vivo* sulphenamides that would render the patent invalid. The same reasoning is applicable to the present case.

In sum, Bristol-Myers's proposed construction of the '365 Patent would render it invalid. This provides an additional reason to construe the ' 365 Patent more narrowly, as excluding uses of buspirone.

V.

Bristol-Myers moves for a *Markman* hearing to present evidence concerning the issue of claim construction. Bristol-Myers originally requested such a hearing by letter, but the Court denied the request for a formal hearing and instead indicated to the parties that they could bring any relevant factual matters to the Court's attention at oral argument on this summary judgment motion. The parties have done so.

[19] This procedure was appropriate and sufficient under the present circumstances.*Markman* does not require a district court to follow any particular procedure in conducting a claim construction analysis. *See* Ballard Med. Prods. v. Allegiance Healthcare Corp., 268 F.3d 1352, 1358 (Fed.Cir.2001). In this case, the Court has reviewed the entire claim language, specification and prosecution history of the '365 Patent, together with all of the other evidence presented by the parties on the motion for summary judgment, and this review is sufficient to decide this case as a matter of law. Bristol-Myers does not suggest any additional information it could produce. Moreover, for the reasons discussed above, the only factual issues that are even arguably relevant to the issue of whether the '365 Patent would be invalid if construed to cover uses of buspirone are facts that are undisputed. The parties have had ample opportunity to produce any other evidence or advance any arguments to the Court, and, in these circumstances, no further hearing is necessary.

CONCLUSION

For the foregoing reasons, the motion for summary judgment by Mylan and Watson finding that the '365 Patent does not cover uses of buspirone is granted. Mylan and Watson are directed to submit proposed judgments within five (5) days of the date of this Opinion and Order, together with any supporting memoranda addressing the appropriateness of the form of the proposed judgments. Bristol-Myers may

submit any proposed counter-judgments and/or supporting memoranda five (5) days thereafter.

SO ORDERED.

S.D.N.Y.,2002.
In re Buspirone Patent Litigation

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