

UNITED STATES DISTRICT COURT FOR
THE DISTRICT OF MASSACHUSETTS

ARIAD PHARMACEUTICALS, INC.,
MASSACHUSETTS INSTITUTE OF
TECHNOLOGY, THE WHITEHEAD
INSTITUTE FOR BIOMEDICAL RESEARCH,
and THE PRESIDENT AND FELLOWS OF
HARVARD COLLEGE

Plaintiffs,

v.

ELI LILLY AND CO.,

Defendant.

Civil Action No. 02 CV 11280 RWZ

U.S. District Judge
Rya W. Zobel

PLAINTIFFS' SUPPLEMENTAL TRIAL BRIEF

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Ariad Pharmaceuticals, Inc., Massachusetts Institute of Technology, The Whitehead Institute for Biomedical Research, and the Presidents and Fellows of Harvard College, (collectively “Ariad”), hereby submit this brief to supplement Plaintiffs’ Trial Brief filed April 4, 2004. (D.I. #270).

I. INTRODUCTION

Following three years of discovery, the Court in this civil action conducted a three-week jury trial from April 10 to April 28, 2006 on infringement of Ariad’s ‘516 patent, damages, and the affirmative defenses of non-enablement, lack of written description, and anticipation (novelty). On May 4, 2006, the jury returned a unanimous verdict finding Defendant Eli Lilly and Company (“Lilly”) liable as an infringer of the asserted claims of the ‘516 patent for the accused products, awarding Plaintiffs damages, determining the applicable priority date of the ‘516 patent, and finding that the asserted claims were valid against all of the grounds challenged by Lilly. (D.I. # 346).

There are a few discrete issues that remain for this Court to decide. The upcoming trial is not and should not be an opportunity for Lilly, through a different lead counsel, to reargue the issues that the jury has already decided. To the extent that the evidence was presented to the jury, the record is fixed and closed. Lilly should not be permitted to re-open the trial record and introduce different evidence from what was presented to the jury on overlapping issues. Not only would this serve to subvert the jury’s verdict, but it would potentially create a record where this Court and the Appellate Court would have evidence that the jury did not have, supposedly on new issues, but in reality based on a change in tactics and an attempt to change the record.

There remain four asserted defenses/counterclaims for the Court which Lilly must prove by clear and convincing evidence. These issues are that the ‘516 patent is: (1) unenforceable for inequitable conduct during prosecution; (2) unenforceable for prosecution laches; (3) invalid for

covering non-patentable subject matter (§ 101); and (4) invalid for indefiniteness. The potentially triable issues relating to these defenses are discussed below. The jury's verdict and the factual findings which underlay that verdict, and the evidence of record in this case, amply demonstrate that Lilly cannot meet its burden on any of these defenses to relieve it of the liability found by the jury.¹

II. INEQUITABLE CONDUCT

A. Legal Standard for Inequitable Conduct

A party seeking to have a patent declared unenforceable due to inequitable conduct “has a heavy burden to meet.” *Hoffmann-La Roche, Inc. v. Promega Corp.*, 323 F.3d 1354, 1359 (Fed. Cir. 2003). Inequitable conduct can arise only by clear and convincing evidence that applicants knowingly provided false material information or intentionally withheld material information, for the purpose of misleading or deceiving the patent examiner. *See Kao Corp. v. Unilever U.S., Inc.*, 441 F.3d 963, 971-72 (Fed. Cir. 2006); *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546 (Fed. Cir. 1998).

Materiality and intent are separate and distinct elements, both of which are essential to establish inequitable conduct. *See, e.g., M. Eagles Tool Warehouse, Inc. v. Fisher Tooling Co.*, 429 F.3d 1335, 1340 (Fed. Cir. 2006); *see also Amgen, Inc. v. Hoescht Marion Roussel, Inc.*, 314 F.3d 1313, 1357 (Fed. Cir. 2003) (a claim of inequitable conduct is “doomed” where there is no evidence of intent). Both materiality and intent are questions of fact, and the party asserting inequitable conduct must prove a threshold level of materiality and intent by clear and

¹ Plaintiffs contend that Lilly has failed to adequately state sufficient grounds to meet its burden on the issue of inequitable conduct -- or any other defense for that matter -- and Lilly should be limited at this time to those allegations on inequitable conduct as set forth in its interrogatory responses and expert reports. *S.C. Johnson & Son, Inc. v. Carter-Wallace, Inc.*, 781 F.2d 198, 200 (Fed. Cir. 1986).

convincing evidence. See *Digital Control Inc. v. Charles Machine Works*, 437 F.3d 1309, 1313 (Fed. Cir. 2006); *Baxter Int'l, Inc. v. McGaw, Inc.*, 149 F.3d 1321, 1327 (Fed. Cir. 1998).

Even if a defendant can establish the requisite level of materiality and intent, the Court must then carefully balance the equities to determine whether the patentee has committed inequitable conduct that warrants holding the patent unenforceable. See *Monsanto Co. v. Bayer Bioscience N.V.*, 363 F.3d 1235, 1239 (Fed. Cir. 2004). Materiality and intent are relational standards, the lesser the proof of one the more the proof of the other is required. See *Purdue Pharma L.P. v. Endo Pharm., Inc.*, 438 F.3d 1123, 1129; *Digital Control Inc. v. The Charles Machine Works*, 437 F.3d 1309, 1313 (Fed. Cir. 2006) (stating the less material any alleged omission or false statement, the greater the proof must be to demonstrate requisite intent).

Lilly's claim of inequitable conduct reduces to two ill-supported and unfounded theories: (1) that applicants intentionally withheld post-filing references indicating that events before the '516 invention could have under certain situations inhibited NF-kB; and (2) that applicants failed to correct an allegedly material "wrong disclosure" in the '516 patent regarding Figure 43. As shown below, Lilly cannot prove that either ground supports its defense of inequitable conduct.

B. The Allegedly Withheld References are Not Material

1. Standard for materiality

In evaluating materiality for the purpose of determining inequitable conduct, the Federal Circuit has consistently referred to the standard articulated in PTO Rule 56, describing the duty of candor and good faith before the PTO. See *Purdue Pharma L.P.*, 438 F.3d 1123, 1128; 37 C.F.R. § 1.56. Under the Rule² (emphasis added), information is material to patentability when

² To present a clearer and more objective definition of "material" information, the PTO revised Rule 56 in 1992 to apply to all pending or later filed applications. The Federal Circuit has applied the current standard to post-1992 prosecutions but noted the PTO did not intend to replace or supplant the pre-1992 rule, which defined material

(continued...)

“it is *not cumulative to information already of record* or being made of record in the application, *and*

- (1) It establishes, by itself or in combination with other information, a *prima facie* case of unpatentability of a claim; or
- (2) It refutes, or is inconsistent with, a position the applicant takes in:
 - (i) Opposing an argument of unpatentability relied on by the Office, or
 - (ii) Asserting an argument of patentability.”

Purdue Pharma L.P. 438 F.3d at 1129.

An essential prerequisite in showing materiality is that the information in issue is *not cumulative*. Cumulative information can never be material, and as such ends any inquiry to alleged inequitable conduct. Failure to disclose an otherwise material prior art reference will not support a finding of inequitable conduct if all the reference does is provide information that was already disclosed to or known to the Patent Office. *Regents of Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1574-75 (Fed. Cir. 1997); *Symbol Tech. Inc. v. Opticon, Inc.*, 935 F.2d 1569, 1582 (Fed. Cir. 1992). As shown below, the alleged withheld references relied on by Lilly were cumulative.

2. The allegedly material and undisclosed “after art” was cumulative to references that the applicants disclosed during prosecution

Lilly ignores the record in this case about what information was actually before the examiner in the ‘516 application. There can be no inequitable conduct in this case as cumulative information is never material and certainly, one cannot show deceptive intent because such non-

information as that which a reasonable examiner would have considered important in deciding whether to allow the application to issue. To the extent, however, that the pre-1992 rule more broadly defined materiality, that definition requires an accordingly higher requisite finding of intent. See *Digital Control Inc., v. The Charles Machine Works*, 437 F.3d 1309, 1316-17 (Fed. Cir. 2006); *Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1179 (Fed. Cir. 1995).

material information was not disclosed. *See e.g., Regents of Univ. of California*, 119 F.3d at 1574-75; *Symbol Tech. Inc.*, 935 F.2d at 1582.

Here, during the course of the prosecution, applicants provided the examiner with the same information that Lilly contends the applicants intentionally withheld from him: post-filing references disclosing that several “prior art” compounds under certain circumstances were said to be capable of inhibiting NF-κB activity. The file history indicates that numerous times, the examiner was aware of and reviewed these references, which disclose such information relating to the autoregulatory loop, aspirin and other salicylates, glucocorticoids and cyclosporin A. Lilly’s entire premise that applicants’ intention was to deceive the patent office by withholding this information is inaccurate and has no basis in logic. If applicants intended to deceive the examiner by keeping him in the dark about the potential effect of “old compounds” on NF-κB, they would not have provided him with numerous references and a declaration disclosing that exact information. Because of the training and experience of the examiner, who had a Ph.D., Lilly also cannot credibly argue that he did not understand and appreciate the references provided by the applicants. The record in the file wrapper is clear that he reviewed them. (See Ex. 1, September 12, 2001 Amendment and Response at ADL 0000882 and October 4, 2001 Notice of Allowability at ADL 0000952) (The cited excerpts from the ‘516 patent file wrapper, PTX 2, are attached hereto as Ex. 1).

For example, applicants submitted a 1994 reference, which disclosed that the use of glucocorticoids, under particular conditions, might affect NF-κB activity: “[t]he anti-inflammatory properties of steroids may be mediated in part by direct interaction with NF-κB.” (Ex. 1, January 14, 1999 Amendment and Response at ADL 0000601; Ex. 1, Siebenlist, et al. 1994 at ADL 0000664). Moreover, Siebenlist also disclosed that cyclosporin A could block

activation of NF- κ B. (Ex. 1 at ADL 0000661). The examiner indicated that he reviewed the documents that accompanied the Amendment and Response which included the Siebenlist reference. (Ex. 1, March 11, 1999 Office Action, ADL 0000611-621).

Later in the prosecution, applicants also submitted Fujihara, et al., 2000 in a September 12, 2001 Amendment and Response (Ex. 1 at ADL 0000904-912). The first paragraph therein expressly described aspirin and glucocorticoids as potential NF- κ B inhibitors: “A number of NF- κ B inhibitors have been described to date, including glucocorticoids, aspirin, gliotoxin, antioxidants such as pyrrolidine dithiocarbamate (PDTC) and acetylcysteine, and the cytokine IL-10.” (Ex. 1 at ADL 0000904).

Moreover, applicants submitted a declaration by inventor Dr. David Baltimore, which stated that under certain circumstances salicylates could reduce NF- κ B activity, and in support cited to Yan et al. 1999, which reported the effect of aspirin and other salicylates on NF- κ B in particular cell systems. (Ex. 1, Declaration of David Baltimore at ADL 0000895-896).

Lilly’s argument is not that any one of these references is any more probative than another. In other words, Lilly does not contend that the references on salicylates are more important than the references on glucocorticoids. As such, they are cumulative of each other, and the substantial amount submitted to the examiner by the applicants was sufficient to inform the examiner of this body of references. Clearly he considered these references and then still allowed the claims, in fact agreeing that the patent was properly described and enabled. (See, Ex. 1, October 4, 2001 Notice of Allowability at ADL 0000952). Lilly cannot create an issue of materiality on this record, and certainly not sustain a burden by clear and convincing evidence.

Since the post-filing references that Lilly argues were not disclosed to the patent office were all cumulative to the references noted above, which were submitted, they cannot be

material. Nonetheless, Lilly contends the examiner would not have considered the above references because they allegedly were not “properly” submitted in an Information Disclosure Statement (“IDS”). The simple fact that the examiner specifically noted that he reviewed these references puts this last dubious theory to rest. Cumulative references cannot be material, and as such cannot serve as the bases for inequitable conduct.

3. The jury’s verdict compels a finding that the references Lilly relies on do not have requisite materiality to prove inequitable conduct

In determining whether inequitable conduct has occurred after a jury verdict, the Court must defer to the jury’s findings underlying its verdict on patent validity insofar as common factual elements exist between the legal and equitable claims. *See Cabinet Vision v. Cabnetware*, 129 F.3d 595, 600 (Fed. Cir. 1997); *Therma-Tru Corp. v. Peachtree Doors, Inc.*, 44 F.3d 988, 994-95 (Fed. Cir. 1995).

In cases where a Judge and jury have overlapping issues a judge must abide by the jury’s findings. See Wright’s Fed. Prac. § 4418, Issue Preclusion--Within a Single Claim: Direct Estoppel (stating courts must attach issue preclusion or direct estoppel to a jury’s ruling on common legal or equitable issues); *Wang Laboratories, Inc. v. Mitsubishi Electronics America, Inc.*, 103 F.3d 1571 (Fed. Cir. 1997) (holding where a court’s findings directly contradict a jury finding, the jury’s findings trump and the court’s must be deemed erroneous); *Lopez v. Garriga* 917 F.2d 63, 67 (1st Cir 1990) (“When the court turned to the matter of equitable redress the jury’s fact finding was, of course, binding upon the trier as to common issues”).

The jury’s fact findings do not require express statements, but are gleaned from the verdict as “the law presumes the existence of findings necessary to support the verdict.” *Perkin-Elmer Corp. v. Computervision Corp.* 732 F.2d 888, 893 (Fed. Cir. 1984); *See Newell Companies, Inc. v. Kenney Mfg. Co.* 864 F.2d 757 (Fed. Cir ,1988) (“Judges must accept the

factual findings, presumed from a favorable jury verdict, which are supported under the substantial evidence/reasonable juror standard”). The court’s instructions to the jury provide further insight as to the issues the jury has resolved. *Id.*

In light of the numerous articles and references Lilly presented to the jury at trial, the jury unanimously found that the asserted claims are not expressly or inherently anticipated by any purported prior art publication or alleged prior public use. At trial, the Court afforded Lilly a full and fair opportunity to present its strongest evidence to argue that the asserted claims were inherently anticipated through prior public use of glucocorticoids, estrogen, vitamin D, cyclosporin A, antibiotics, salicylates, aspirin, and even red wine. This evidence included more than a dozen post-filing “after art” publications that Lilly put forth as purported evidence of inherency. The jury found none of these references to provide evidence that any method of use of any “old compound,” anticipated any of the asserted claims.³ Moreover, in view of the verdict, the testimony of Plaintiffs’ experts Dr. Ravetch and Dr. Prescott that these after art references do not establish that prior use of these compounds inherently reduced NF-kB activity and performed the claimed methods must be credited. The jury’s findings therefore compel the conclusion that none of these references render any of the asserted claims *prima facie* anticipated and at most should be accorded with minimal materiality if they were not cumulative. *See Therma-Tru*, 44 F.3d at 995; *see also Fresenius Medical Card Holdings, Inc. v. Baxter Int’l, Inc.*, 2006 WL 1646108, at *2-3 (N.D. Cal. June 12, 2006) (substantial overlap between evidence pertinent to validity and inequitable conduct).⁴ Since they are cumulative, no materiality can be

³ In *AGFA Corp. v. Creo Prods. Inc.*, (Fed. Cir. 2006), the court stated that although materiality and validity are not “common issues” in a strict sense, inequitable conduct and validity questions overlap “in consideration of some aspects of the same relevant evidence”.

⁴ The jury’s specific finding that the ‘516 invention is entitled to an April 1989 date precludes a finding that any intervening reference (published between April 21, 1989 and November 13, 1991) Lilly raised at trial is prior art.

found. Thus, Ariad respectfully proposes that the Court find that references that Lilly's experts relied on (or could have relied on) to prove anticipation can have no more than a low level of materiality because the jury found after considering the teaching of the references deemed most relevant by Lilly that the claims are not anticipated.

4. It is Unlikely during the '516 Prosecution That a Reasonable Examiner Would Have Considered Lilly's References Important To Patentability

a. During the time the '516 patent application was pending, the Patent Office understood the law of inherency to require recognition.

It would be improper for the Court to conduct its analysis of alleged inequitable conduct based on law which changed after the '516 patent issued. The analysis required necessarily must focus on the law and patent office procedure *in effect at the time of prosecution of the '516 patent* because that is what would have been available to guide the reasonable examiner's judgment.⁵

In the case of the '516 patent, prosecution was closed by December 2001 and the patent issued in June 2002. Thus, the Manual of Patent Examining Procedure ("MPEP") and prevailing case law promulgated before the patent issued should be used to judge whether a reference, provided that it is not cumulative, would have been important to the analysis of materiality.

During the time that the '516 patent application was pending, prevailing patent law emphasized that there was a "recognition" element involved with a claim of inherent anticipation. That law instructed that to establish that a particular element of a patent claim was inherently disclosed in a prior art reference, two things had to be proven: (1) that the missing descriptive matter was *necessarily present* in the prior art reference; and (2) that the missing

⁵ Even under the current law the jury rejected Lilly's prior art defenses. Mr. Lieberstein bases his allegations of inequitable conduct on 27 references related to glucocorticoids (13); cyclosporin (12); aspirin (1); and red wine (1). Dr. Manolagas testified on all of these topics (Ex. 2, Trial Tr., Day 10, 88:18 - 89:5), specifically referring to at least 12 of the references. The others are simply duplicative of the ones he did discuss.

descriptive matter would have been so recognized before the date of invention by one of ordinary skill. See *Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Educ. and Research*, 304 F.3d 1221, 1228 (Fed. Cir. 2002), *vacated and superseded*, *Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Educ. and Research*, 346 F.3d 1051, 68 U.S.P.Q.2d 1373 (Fed. Cir. 2003); *In re Robertson*, 169 F.3d 743, 745 (Fed.Cir.1999); *Electro Med. Sys., S.A. v. Cooper Life Sciences, Inc.*, 34 F.3d 1048, 1052 (Fed. Cir. 1994); *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268-69 (Fed. Cir. 1991) (requiring that the feature alleged to anticipate “be described in the reference, and that it would be so recognized by persons of ordinary skill” in order to anticipate).

During the course of the ‘516 prosecution, when the Patent Office first provided specific guidance on this issue, it instructed its examiners that the prevailing law on inherency required a “recognition” element. The Manual for Patenting Examining Procedure, an extensive manual promulgated by the PTO, provides patent examiners with the office’s interpretation of legal standards. The MPEP § 2112 expressly pointed out that extrinsic evidence “must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.”⁶ (Ex. 3, MPEP § 2112 (7th ed., rev. 1., Feb. 2000) (quoting *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999)). The MPEP retained a recognition requirement without change until after the ‘516 patent had issued. (Ex. 4, MPEP § 2112 (8th ed., Aug 2001) (8th ed. rev. 1, Feb. 2003)).⁷

⁶ While prior to this amendment, the MPEP did not specifically address recognition, the need for recognition was established by the prevailing case law at the time. See, e.g., *Electro Med. Sys., S.A. v. Cooper Life Sciences, Inc.*, 34 F.3d 1048, 1052 (Fed. Cir. 1994); *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268-69 (Fed. Cir. 1991)

⁷ It is undisputed that in 2004, two years after the ‘516 patent issued, there was a change in the MPEP relating to the law of inherent anticipation, which is argued to have expressly changed the “recognition” requirement in an inherent anticipation analysis. (Ex. 5, MPEP § 2112 (8th ed., Aug. 2001) (8th ed. rev. 2, May 2004)).

The Court should apply the law in effect during the prosecution of the '516 patent, which required a "recognition" element for an inherent anticipation analysis.⁸ During the '516 prosecution, the prevailing case law as reflected in the MPEP would have led an examiner to understand that post-filing art could not simply fill in the gaps where prior art (as read by those with skill who would recognize that which was inherent) was silent as to how the use of a compound might have affected NF-kB. The evidence would have to show that one of skill at the time of the '516 patent's claimed invention would have recognized in the prior art that NF-kB activity was being reduced. None of the post-filing references cited by Lilly could have provided such evidence. At trial, Lilly did not dispute that the inventors named and discovered NF-kB and the mechanism by which it works in cells and were the first to recognize any method that could be used for reducing NF-kB activity in cells. Before the inventors' work, the allegedly inherent effect of a compound on NF-kB that Lilly contends is proved in the "after art" could not have been recognized. The examiner would therefore have had little reason to consider any post-filing references as important in deciding the patentability of the claims, and such references should not be deemed material.

b. The grant of a reexamination order does not address materiality of the references

Finally, Lilly attempts to establish the materiality of the post-filing art by alluding to the order granting the pending re-examination of the '516 patent in the Patent Office. Earlier in this case, this Court addressed the potential relevance of these proceedings, and rightly ruled that they were not relevant. (D.I. # 231). In fact, the Court found that since they are not "final determinations" they had little probative value. (Pre Trial Hearing Transcript April 7, 2006,

⁸ This Court similarly did not charge the jury with a requirement of recognition. The requirement that inherency requires the feature to necessarily exist is still found in the MPEP. Plaintiff's position is that the Supreme Court precedent requiring recognition still applies unless and until that court changes its ruling.

53:13-15).⁹ Nothing further has occurred in the PTO in these proceedings to warrant changing the Court's prior ruling.¹⁰ The Patent Office has yet to issue any office action in the reexamination proceedings.

Evidence concerning the still pending reexaminations would have no probative value to a determination of the "materiality" of a reference. The Federal Circuit has repeatedly maintained that "the grant by the examiner of a request for reexamination is not probative of unpatentability" because it "does not establish a likelihood of patent invalidity". *Hoechst Celanese Corp. v. BP Chemicals Ltd.*, 78 F. 3d 1575, 1584 (Fed. Cir. 1996)¹¹ (citing *Acoustical Design v. Control Electronics Co.*, 932 F. 2d 939, 942 (Fed Cir. 1991)) ("Finally, it is clear that the initial rejection by the Patent and Trademark Office of original claims that were later confirmed on reexamination hardly justifies a good faith belief in the invalidity of the claims"); *see also*, *Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1428 (Fed. Cir. 1988).

The Patent Office applies an especially lenient standard in commencing re-examination proceedings. To initiate reexamination, the requestor need only show that there exists "a substantial new question of patentability" with regard to a single claim. 35 U.S.C. § 303. A "prima facie" case of unpatentability (required by the current standard for materiality) need not exist. (Ex. 6, Patent & Trademark Office, Manual of Patent Examining Procedure § 2242 (8th ed., last rev., Aug 2005) ("MPEP")). Under this standard, in 2005 the Patent Office granted 509

⁹ Plaintiffs have filed a motion in limine to preclude Defendant from offering evidence of the reexaminations or from relying on them to support its inequitable conduct allegations. (D.I. # 357).

¹⁰ Application Nos. 90/007,503, 90/007,828.

¹¹ Noting also that in 1994, that Patent Office granted 89% of the reexamination requests for that year, but that only 5.6% of the reexamined patents were completely rejected with no claims after reexamination. See *id.* at 1584.

requests and denied only 26 (less than 5% of the cases). (Ex. 7, PTO, Performance and Accountability Report Fiscal Year 2005).¹²

In addition, as explained above, the law on inherent anticipation as it is now being applied during the reexamination process is different from the law as it existed during the prosecution of the '516 patent. Cases relied on by Lilly in its original pretrial brief such as *Schering Corp. v. Geneva Pharmaceuticals Inc.*, 339 F.3d 1373 (Fed. Cir. 2003) and *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331 (Fed. Cir. 2005) did not even exist by June 2002. Whatever the law of inherency is today, as applied by the examiner in the re-examination, it could not have been known or expected in June 2002 when the '516 patent issued.

5. Applicants did not commit inequitable conduct by “failure to correct” figure 43 because the patent does not make any material “misstatements” about Figure 43

Figure 43 was added to the '516 patent application only in November 1991. The jury specifically found that the '516 patent is entitled to an April 1989 filing date, unequivocally establishing that the application fully taught and described the invention without the added disclosure of Figure 43. Even if Figure 43 had been erroneous (it was not), it is irrelevant to the Court's analysis based on the jury's verdict. Applicants could not have deceived the Patent Office by failing to cancel from the patent application correct information, which the jury verdict indicated was not even essential to teach and describe the claimed invention.

In any event, Lilly's argument that the '516 patent misrepresents the amino acid and DNA sequences depicted in Figure 43 as being those of I κ B α is also wrong. Lilly contends that the sequences instead correspond to a different protein, pp40 and that applicants' failure to correct this allegedly “misleading disclosure” was material and grounds for inequitable conduct.

¹² http://www.uspto.gov/web/offices/com/annual/2005/060413a_table13a.html (12/20/2005)

Even assuming the labeling of Figure 43 was a misstatement (it was not), misstatements alone without proof of materiality or proof that the misstatement was intentional do not demonstrate inequitable conduct. *See Hoffmann-La Roche, Inc. v. Promega Corp.*, 323 F.3d 1354, 1366-67 (Fed. Cir. 2003).

Lilly fails however to establish even the first step of its theory. Simply put, Figure 43 is correct. The '516 patent cannot misrepresent the information in Figure 43 because the sequences it depicts correspond to I κ B α . Substantial evidence confirmed at trial, including at least the following, supports that the information disclosed in Figure 43 is correct: (1) The 1994 Siebenlist reference discussed above, which applicants submitted and which the examiner considered during prosecution, expressly identifies the chicken "pp40" (as well as the human "MAD-3") as an I κ B- α . (Ex. 1, Siebenlist et al. 1994 at ADL 0000651); and (2) The '516 specification defines pp40 as an I κ B capable of use in the invention:

The I κ B gene and the encoded I κ B protein can be used to negatively regulate NF- κ B activity in cells. For example, the I κ B gene can be incorporated into an appropriate vector... The DNA used can have all or a portion of the DNA sequence of clone MAD-3, all or a portion of pp40 or all or a portion of another sequence which encodes a related or I κ B-like protein capable of inhibiting NF- κ B.

('516 Patent, col. 32, ll. 11-40).

Thus, under the working definition of I κ B given in the patent, Figure 43 is correct. This is further corroborated by the trial testimony of Plaintiffs' expert Dr. Kadesch, who explained that the 1991 filed application explicitly disclosed two I κ Bs (pp40 and MAD-3):

there were two references. One was as we've discussed Figure 43, which was the sequence of the I-kappaB pp40. That was the chicken gene that was discussed at some length earlier in the week. And there was also reference to a human gene for I-kappaB called MAD-3.

(Ex. 8, Trial Tr., Day 13, 53:20-24). Therefore, Lilly's argument with respect to Figure 43 is a red herring.

C. Lilly Has Failed to Allege Any Evidence Required to Meet its Burden of Proof for Intent

1. Standard for intent

To prove inequitable conduct defendant must prove by clear and convincing evidence that the applicant made a deliberate decision to deceive the Patent Office by withholding a known material reference. *See Kao Corp.*, 441 F.3d at 971-72; *Baxter*, 149 F.3d at 1329. “Deceptive intent is not inferred simply because information was in existence that was not presented to the examiner; and indeed, it is notable that in the usual course of patent prosecution many choices are made, recognizing the complexity of inventions, the virtually unlimited sources of information, and the burdens of patent examination.” *C.R. Bard, Inc. v. M3 Sys.*, 157 F.3d 1340, 1365 (Fed. Cir. 1998); *see also Upjohn Co. v. Mova Pharma. Corp.*, 225 F.3d 1306, 1312 (Fed. Cir. 2000). Discussing the intent element, the Federal Circuit has pronounced that “***To be guilty of inequitable conduct, one must have intended to act inequitably...***” *Cordis Corp. v. Boston Scientific Corp.*, 2006 WL 187683, *3 (Fed. Cir. June 29, 2006) (emphasis added) (citing *FMC Corp. v. Manitowoc Co.*, 835 F.2d 1411, 1415 (Fed. Cir. 1987)).

For inequitable conduct, a lack of disclosure when 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*, 429 F.3d at 1341; *Paragon Podiatry Lab. v. KLM Lab.*, 984 F.2d 1182, 1189 (Fed. Cir. 1993); *Kingsdown Med. Consultants Ltd. v. Hollister, Inc.*, 863 F.2d 867, 876 (Fed. Cir. 1998). Neither the materiality of the withheld reference nor even gross negligence of the applicant justifies an inference of intent to deceive. *See Halliburton Co. v. Schlumberger Technology Corp.*, 925 F.2d 1435, 1442 (Fed. Cir. 1991); *Baxter*, 149 F.3d at 1327; *see also Allen Eng’g Corp v. Bartell Indus., Inc.*, 299 F.3d 1336, 1352 (Fed. Cir. 2002) (materiality does not presume intent); *Braun Inc. v. Dynamics Corp. of Am.*, 975 F.2d 815, 822 (Fed. Cir. 1992).

Moreover, in order to establish an intent to deceive on the part of the person alleged to have withheld a reference there must be a showing that the person believed the reference to actually be credible and non-cumulative prior art. *See Flex-Rest, LLC v. Steelcase, Inc.*, --- F.3d ----, 2006 WL 1928697 at *9-*10 (Fed. Cir. July 13, 2006).

Lilly has not accused any particular person of inequitable conduct nor of having the specific intent to deceive the patent office. Lilly generally refers to the inventors and the prosecutors, but it cannot seriously intend that everyone who had anything to do with this patent application had deceptive intent. It is not sufficient for Lilly to make general allusions to intent; there must be specific evidence addressed to specific individuals. *Cordis*, 2006 WL 187683, at *3-*4 (Fed. Cir. June 29, 2006).

Before Plaintiffs are required to present any evidence on inequitable conduct, Lilly should specifically identify the individuals and their specific conduct that Lilly alleges constituted the inequitable conduct. General aspersions are not sufficient to meet Lilly's burden. As it is, "the habit of charging inequitable conduct in almost every major patent case has become an absolute plague" and disincentive to innovation. *Burlington Industries, Inc. v. Dayco Corp.* 849 F.2d 1418, 1422 (Fed. Cir. 1988).

2. There is no evidence that the applicants acted with deceptive intent

As demonstrated above, Lilly cannot prove by clear and convincing evidence that any of the so-called withheld references were material or not considered by the examiner, and the "false" information" in Figure 43 was actually wholly accurate, and clearly not relevant based on the jury's verdict. Even though the Court need not even reach this issue, Lilly has not advanced evidence, much less clear and convincing evidence, that any specific person involved in the '516 patent acted with the requisite deceptive intent.

One cannot even infer deceptive intent simply because an applicant took his obligation of disclosure seriously but decided that it was unnecessary to disclose work conducted years after his invention, which he considered cumulative or unreliable. *See Flex-Rest, LLC v. Steelcase, Inc.*, --- F.3d ----, 2006 WL 1928697 at *9-*10 (Fed. Cir. July 13, 2006) (the belief of the applicant that the cited references were “of uncertain import and reliability” and “in the main, cumulative” dictated a finding of no inequitable conduct).

That post-filing publications were not considered material “prior art” was entirely consistent with the guidance provided by the MPEP and the prevailing case law. Plaintiffs contend that there is no evidence from which one could infer that anyone associated with the prosecution of the ‘516 patent acted purposefully to deceive the Patent Office. Lilly cannot meet its heavy burden on intent to deceive, especially given the enhanced standard in the face of its weak evidence of materiality.

III. PROSECUTION LACHES DEFENSE IS ALSO DEFICIENT

Lilly cannot support its claims that the ‘516 patent is unenforceable under the doctrine of prosecution laches by clear and convincing evidence.

A. Legal Standard

The defense of prosecution laches will apply only if it can be demonstrated that a patent was obtained after an unreasonable and unexplained delay in prosecution. *In re Bogese II*, 303 F.3d 1372, 1367 (Fed. Cir. 2002); *Symbol Technologies, Inc. v. Lemelson Med.*, 277 F.3d 1361, 1363 (Fed. Cir. 2002). Lilly bears the burden of establishing unreasonable delay by clear and convincing evidence. *Novo Nordisk Pharm. Inc. v. Bio-Technology Gen. Corp.*, 2004 WL 1739720, at *33 (D. Del. Aug. 3, 2004), *vacated in part on other grounds*, 424 F.3d 1347 (Fed. Cir. 2005); *Gen-Probe, Inc. v. Vysis, Inc.*, 2002 U.S. Dist. LEXIS 25020 at *120 (S.D. Cal. 2002), *vacated on other grounds*, 359 F.3d 1376 (Fed. Cir. 2004). Furthermore, Lilly faces a

heavy burden in that the Federal Circuit and the District Courts have made clear that laches is an equitable tool to be used “sparingly in only the most egregious cases.” *Symbol Technologies v. Lemelson Med., (Symbol II)*, 422 F.3d 1378, 1385 (Fed. Cir. 2005); *Stambler v. RSA Security, Inc.*, 243 F. Supp. 2d 74, 76 (D. Del. 2003); *Intuitive Surgical, Inc. v. Computer Motion, Inc.*, 2002 WL 31833867, at *3 (D. Del. Dec. 10, 2002); see also *Digital Control, Inc. v. McLaughlin Mfg. Co., Inc.*, 248 F. Supp. 2d 1015, 1018 (W.D. Wash. 2003) (cases in which the Federal Circuit has recognized laches have been “truly ... extreme” cases involving “abusive” continuation applications extending beyond 20 years).

Demonstrating delay alone is insufficient as a matter of law to establish laches. Rather, a delay must be unreasonable and “there are no strict time limitations for determining whether continued refiling of patent applications is a legitimate utilization of statutory provisions or an abuse of those provisions.” *Symbol II*, 422 F.3d at 1385. Indeed, there is “sparse authority” for the relief Lilly seeks, which courts are reluctant to grant because of the difficulty in determining how much time is unreasonable. *Kothmann Enterprises, Inc. v. Trinity Indus., Inc.*, 2006 WL 89838, at *31 (S.D. Tex. Jan. 13, 2006). In this regard, courts have declined to find laches without evidence that the delay was both intentional and for an improper purpose. *Digital Control*, 248 F. Supp. 2d at 1018; see also *Verizon California, Inc. v. Katz Tech. Licensing, L.P.*, 2003 U.S. Dist. LEXIS 23553, at *69 (C.D. Cal., Dec. 2, 2003).

The Federal Circuit has recognized that there are many legitimate grounds for refiling a patent application, such that the doctrine of laches should be used rarely, “lest statutory provisions be unjustifiably vitiated.” *Symbol II*, 422 F.3d at 1385. Legitimate reasons for refiling include filing a divisional application in response to a requirement for restriction, or refiling an application containing rejected claims in order to present evidence of unexpected

advantages or to add subject matter in an attempt to support broader claims. *Id.*; *see also Kothmann*, 2006 WL 89838, at *31 (there was no unreasonable delay where much of the delay was due to overcoming the patent examiner's rejections). Moreover, an applicant need not prosecute all of its inventions at the same time in order to avoid a finding of unreasonable delay. *See Stambler*, 243 F. Supp. 2d at 76, n.3 (applicant acted reasonably in prosecuting various continuation and divisional applications during a seven year period in which applicant was prosecuting two other patent applications based on the original application). A small company like Ariad has no incentive to delay and had every motive to expedite the issuance of the patents licensed to it. This defense is entirely groundless.

B. Applicants did not unreasonably or inexplicably delay the prosecution of the '516 patent

Lilly has failed to present any coherent argument that there was any unreasonable or inexplicable delay in prosecution of the '516 patent. The '516 patent represents a breakthrough achievement that pioneered a new area of medical science. In view of the extensive disclosure of the application, which was supplemented through a number of continuation-in-part ("CIP") applications¹³, and intervening events, the length of prosecution is entirely reasonable.

1. Applicants did not delay prosecution through their initial election not to simultaneously prosecute all inventions

A patent can only claim a single invention. If more than one invention is claimed, the patent examiner can issue a restriction requirement mandating that applicants pursue claims to a single invention. The last CIP Application in the '516 history -- Serial No. 07/791,898 ("the

¹³ A "continuation-in-part" application (or "CIP" or "CIP application"), claiming filing date priority from a parent application, is one in which the applicant adds matter not disclosed in the parent, but repeats some substantial portion of the parent's specification, and has at least one common inventor as named in the parent application.

‘898 application”), was filed in 1991 and presented claims to several aspects of the invention.¹⁴ Applicants responded to a restriction requirement by electing to prosecute claims to methods of inducing gene expression. On July 1, 1994, the examiner issued a final office action, rejecting all of the pending claims. Applicants subsequently filed the ‘266 application on April 6, 1995 and a divisional of the ‘266 application, the ‘364 application, on June 5, 1995, which ultimately issued as the ‘516 patent.

Lilly’s patent expert Mr. Lieberstein contends that applicants could have filed divisional applications pursuing unelected claims at any time after receiving the December 16, 1992 restriction requirement.¹⁵ He argues that the slightly more than 2 years it took to do so constitutes unreasonable delay. Not surprisingly, Lilly’s expert does not provide any legal support for his contention. Applicants are not compelled to prosecute claims to all of the inventions disclosed in a single specification at the same time and as noted above, a decision to prosecute only a single invention does not constitute unreasonable delay. It is entirely reasonable that as a small, start-up company with limited resources, ARIAD might have wished to focus prosecution to limit prosecution costs.

2. Applicants did not delay prosecution of the ‘364 application

The ‘364 application, which ultimately issued as the ‘516 patent was subject to a restriction requirement. (Ex. 1, June 25, 1996 Office Action at ADL 0000439). Applicants elected to prosecute claims to “methods of activating or blocking the action of an NF- κ B precursor.” (*Id.*, 11/4/1996 Response to Restriction Requirement at ADL 0000444). Over the

¹⁴ The ‘364 application, from which the ‘516 patent issued, was a divisional application that resulted from a line of CIP applications first filed in 1986. From 1986 to 1991, applicants filed several applications that continued to add further material regarding the inventors’ ongoing work with NF- κ B, which had rapidly advanced the field.

¹⁵ Plaintiffs have moved to preclude attorney Lieberstein from offering his opinions on the equitable issues and supplanting the role and function of this Court. (D.I. # 357)

next five years, in the face of lengthy and detailed rejections from the examiner, applicants continued to diligently prosecute claims with subject matter similar to the originally filed claims. The Patent Office issued office actions on December 30, 1996; October 15, 1997; July 12, 1998; March 11, 1999; November 19, 1999; and August 11, 2000. On August 11, 2000, a single claim was indicated to be allowable but it was not until October 26, 2001 that applicants gained allowance of multiple claims.

All Lilly cites to as evidence of “unreasonable and inexplicable delay” during prosecution of the ‘364 application appears to be the length of time it took applicants to obtain allowable claims. This contention has no basis in law. Even a summary review of the prosecution makes obvious that the time it took to have these claims issue resulted entirely from the rigorous scrutiny to which the examiner subjected the application. Moreover, the prosecution history of the ‘364 application provides no evidence of any conduct by applicants to engage in any delay. Significantly, throughout the prosecution, the applicants repeatedly attempted to overcome rejections through successive amendments to the claims, detailed responses to each of the examiner’s arguments, and interviews with the examiner. It is clear that a small company such as Ariad wanted this patent to issue as soon as it was in condition to be allowed.

In fact, the applicants took advantage of certain procedural rules designed to shorten prosecution. In particular, after receiving two final rejections, the applicants properly availed themselves of the transitional procedures provided by 37 CFR § 1.129(a) to obviate the need for an appeal to the Board of Patent Appeals and Interferences, and instead continue prosecution. If such an appeal had been filed, a decision on that appeal would have been rendered in about two to four years after the filing of the applicants’ reply brief, thus creating delay in the issuance of the ‘516 patent.

IV. NON-PATENTABLE SUBJECT MATTER

Lilly has not disclosed precisely what it will argue to this Court as constituting the grounds for its defense under 35 U.S.C. § 101. Lilly's changing defense that the '516 patent claims are directed to non-patentable subject matter under 35 U.S.C. § 101 has fluctuated between two separate questions: (1) are the claims directed to one of the four statutorily defined categories of possibly patentable subject matter (process, machine, manufacture, or composition?); and (2) are the claims novel in view of processes that purportedly occur in nature? Only the former question is properly posed under 35 U.S.C. § 101. Questions of novelty are addressed under the provisions of 35 U.S.C. § 102, which in this case has been decided by the jury. Lilly's attempt to disguise a § 102 argument in terms of § 101, has been unsuccessfully attempted before by other litigants. Courts have routinely rejected anticipation arguments masked in an "*it-exists-in-nature*" theory under § 101.

For instance, the Court of Claims and Patent Appeals (predecessor to the Federal Circuit), in *Application of Bergstrom*, 427 F.2d 1394 (C.C.P.A. 1970), reversed a Patent Office rejection to an applicant's claims "as lacking in novelty under 35 U.S.C. § 101" because the compounds as claimed were "'naturally occurring' and therefore not new." The Court found that it was undisputed that the claimed compounds were not described in any prior art, and therefore did not lack novelty under section § 102. The Appeals Court rejected the Patent Office's position that the cited reference could be used to support a rejection under § 101, ruling that "that which possesses statutory novelty under the provisions of § 102 is also new within the intendment of § 101." *Id at 1249*. This interpretation of § 101 has been followed in subsequent decisions such as *In re Bergy*, 596 F.2d 952 (CCPA 1979) and *Titanium Metals Corp. v. Banner* (Fed. Cir. 1985) and cited with approval by the Supreme Court. *Diamond v. Diehr* 450 U.S. 175, 189 (1981) ("The question therefore of whether a particular invention is novel is wholly apart from

whether the invention falls into a category of statutory subject matter.”) (citing *In re Bergy*, 596 F.2d at 961 (CCPA 1979)).

The jury’s determination that the claims are not anticipated by natural compounds properly precludes Lilly from arguing that those same references or similar ones invalidate the asserted claims under the guise of an attack based on § 101. Plaintiffs have also filed a motion *in limine* with the Court on this issue. (D.I. # 356).

A. Statutory Subject Matter

Whether a claim is eligible for patent protection under § 101 is decided as a matter of law but “may require findings of underlying facts specific to the particular subject matter and its mode of claiming.” *Arrhythmias Research Tech. v. Corazonix Corp.* 958 F.2d 1053, 1055-56 (Fed. Cir. 1992).

As a matter of statutory interpretation, § 101 has been held to be extremely broad so as to reach nearly all new and useful processes. *Diamond v. Chakrabarty* 447 U.S. 303, 309 (1980). Section 35 U.S.C. § 101, recites:

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

However, the Supreme Court has recognized limits to § 101. Presently, “laws of nature, natural phenomena, and abstract ideas” are not embraced by the statutory terms of § 101. *Id.*; *Diehr*, 450 U.S. at 185. Yet, courts have worked to define these terms.

Judge Rader of the current Federal Circuit has explained that for years courts have floundered when attempting to enforce a legal standard embodied in obscure terms like “law of nature,” “natural phenomena,” “formulae,” or “algorithm.” *Arrhythmias*, 958 F.2d at 1062 (J. Rader, concurring). Justice Frankfurter also found that terms such as “the work of nature”

and the “laws of nature” only confuse the issue and noted the terms’ potential for causing vexatious litigation, stating “[a]rguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost every patent. *Funk Bros. Seed Co v. Kalo*, 333 U.S. 127, 134-35 (1948) (Frankfurter, J., concurring). Even today Justice Breyer concedes the category of non-patentable ‘phenomena of nature’ is not easy to define. “After all many a patentable invention rests upon its inventor’s knowledge of natural phenomena.” *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*, --- S.Ct. ----, 2006 WL 1699360 at *6 (June 22, 2006) (J. Breyer dissenting from decision to dismiss writ of certiorari).

Some of the most helpful guidance on the issue comes from Chief Judge Markey in *In re Sarkar*, 588 F.2d 1330, 1333 (CCPA 1979):

In making the application, each invention must be evaluated as claimed; yet semantogenic considerations preclude a determination based solely on words appearing in the claims. In the final analysis under s 101, the claimed invention, as a whole, must be evaluated for what it is.

Lilly’s assertion that the ‘516 claims encompass the cell’s own method for regulating its NF-κB activity (*i.e.* the “autoregulatory loop”), fails to properly consider the claimed invention as a whole and rests entirely upon an unsupported misreading of the claims. (D.I. #337 , pages 3 – 9). As construed by this Court, the ‘516 claims require “decreasing the function of NF-κB to act as an intracellular messenger that regulates transcription of particular genes, in response to certain stimuli.” (Ex. 9 at 2). Once it is understood that the claims are directed to a manipulation of the NF-κB pathway, it is clear that the claims as a whole are properly directed to statutory subject matter under § 101.

It is further clear from the ‘516 patent specification and the definition of the term “method,” agreed upon by the examiner and experts retained by both Plaintiffs and Lilly, that autoregulation is not encompassed by the ‘516 claims. While it is undisputed that the inventors

did make the groundbreaking discovery of NF- κ B and the mechanism by which it controls gene expression in the body (particularly that of genes involved in certain diseases), they did not claim this discovery. The inventors claimed methods by which NF- κ B could be artificially manipulated to alter the expression of certain genes controlled by NF- κ B. As stated in the '516 specification "[t]he subject invention further relates to methods of regulating (inducing or preventing) activation of NF- κ B, controlling expression of the immunoglobulin kappa light chain gene and of other genes whose expression is controlled by NF- κ B (e.g. HIV)¹⁶." ('516 patent col. 3, ll. 54-58).

Consistent with the invention stated in the '516 specification, in the final substantive office action issued by the Patent Office, the examiner stated that the claims "are drawn to various methods for modulating expression of NF- κ B-dependent gene expression in mammalian cells using an agent which has an effect on the structure or function of NF- κ B and/or I κ B." (Ex. 1 at ADL 0000825).¹⁷ The examiner made the statement knowing full well of the concept of the autoregulatory loop that Lilly asserts to be encompassed by the claims. (Ex. 1, Cong Sun, et al. 1993 at ADL 0000636-640; Ex. 1, Gilmore, et al. 1993 at ADL 0000641-647; Ex. 1, Siebenlist, et al. 1994 at ADL 0000648-673; and Ex. 1, Finco, et al. 1995 at ADL 0000675-684). With this information in hand, the examiner personally rewrote the claims of the '516 patent as issued. (See, Ex. 1 at ADL 0000923-953).

¹⁶ "HIV" refers to human immunodeficiency virus, the virus that causes AIDS.

¹⁷ While the claim language at the time of the office action was not identical to the claims that issued, the scope was similar:

57. A method for altering expression in a mammalian cell, of a gene whose expression is regulated by NF- κ B, comprising altering the level of NF- κ B-I κ B complex present in said cell with an agent that binds a NF- κ B protein or an I κ B protein and alters the association between the two proteins and alters expression of the gene.

Even Lilly's own expert, Dr. Peter Barnes, acknowledged that the claims require *manipulation* of the NF- κ B pathway.¹⁸ Dr. Barnes' understanding of the claims comports to the understanding of Plaintiffs' experts and the contemporaneous definition of the word "method." (Ex. 10, Taber's Cyclopedic Medical Dictionary, 16th ed. (1989) at 1120) ("the systematic manner, procedure, or technique in performing details of an operation, tests, treatment, or any act.")¹⁹; Ravetch Expert Report at ¶ 49; Prescott Expert Report at ¶ 115.

As this analysis suggests, the asserted claims are directed to processes which require reducing *induced* gene expression and other NF- κ B mediated effects, the claims are indeed directed to a "mode of treatment of certain materials to produce a given result." See *Diehr*, 450 U.S. at 183. With that the true § 101 analysis ends. See *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1342 (Fed. Cir. 2005) ("[e]ither the subject matter falls within Section 101 or it does not"). Lilly's attack on this basis fails as well.

B. Novelty

Wholly apart from whether the '516 patent claims are directed to subject matter that is eligible for patent protection under § 101 is the question of novelty. *In re Bergy*, 569 F.2d 952, 961 (CCPA 1979). Lilly's desire to prove that the claims of the '516 patent read on the activity

¹⁸ Q. And you don't understand the term method to imply that there's any human intervention or manipulative steps?

A. Well, I understand the method to be an intervention that would diminish the NF-kappaB pathway in some way.

Q. And when you say --

A. As a single event.

Q. And when you say an intervention, what do you mean?

A. I mean some sort of manipulation to a cell such as a drug administration that would have an inhibitory effect on the NF-kappaB pathway.

Q. And that's your understanding of method in the context of the 516 patent claims?

A. That's my understanding of it.

(Ex. 11, Barnes 12/13/05 Dep. at 48:23 - 49:14).

¹⁹ Lilly's attempt to define "method" as "process" is flawed. First, the patent statute defines "process" to encompass method, not *vice versa*. Second, the Act defines "process" as used in the Patent Act, not as used in an individual patent. Courts give a term the meaning that a person of ordinary skill in the art would understand to be its ordinary and customary meaning. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005).

of the body's natural production of "estrogens" prior to menopause (e.g. during pregnancy) amounts to nothing more than a veiled attempt to retry its novelty argument, already rejected by the jury. Lilly should be precluded from resurrecting its novelty argument under the auspices of § 101.

Having failed to prove prior public use of natural estrogen as a ground for invalidity at the jury trial, Lilly should not be allowed to reargue and present new evidence on the mechanism of natural estrogen. In his closing, Lilly counsel argued this exact point to the jury. For example Mr. Berghoff said "natural estrogen, as Dr. Manolagas explained to us, ... has a 100 percent effect on reducing NF-kappaB activity" (Ex. 12, Trial Tr., Day 14, 30:12-14). The jury did not believe Dr. Manolagas' theories on natural estrogen; the Court should reject a reexamination of Dr. Manolagas by Lilly's new counsel on the same claims rejected by the jury as a matter of elementary fairness. (Plaintiffs have filed a motion in limine to preclude Lilly from advancing this as a ground at the upcoming trial (D.I. # 356)). Moreover, the dictates of issue preclusion and direct estoppel counsel the preclusion of Lilly's § 101/§ 102 argument altogether.

Nevertheless, if the Court entertains Lilly's argument, to succeed on its § 101/§ 102 argument, Lilly must prove by clear and convincing evidence that the activity of a compound as it functions in the body naturally and necessarily meets each and every limitation of the asserted claims. In doing so, Lilly should not be allowed to rely on hearsay statements in scientific articles or other sources.

V. INDEFINITENESS

A claim meets the definiteness requirement so long as one of skill in the art could understand the bounds of the claim when read in light of the specification. *LNP Eng'g Plastics, Inc. v. Miller Waste Mills, Inc.*, 275 F.3d 1347, 1359-60 (Fed. Cir. 2001). Only if the claim is insolubly ambiguous should it be held invalid. *Metabolite Labs., Inc. v. Lab. Corp. of Am.*

Holdings, 370 F.3d 1354, 1366 (Fed. Cir. 2004). Lilly has indicated its belief that evidence adduced at the jury trial is sufficient for it to meet its burden and it seeks to admit no further evidence on this defense. In any case, the jury's verdict that the asserted claims are infringed and also satisfy the written description and enablement requirements creates a strong presumption that the patent claims also satisfy the definiteness requirement of § 112.

Moreover, the uncontroverted evidence at trial supports the conclusion that the asserted claims clearly and unambiguously defined the scope of the claimed subject matter to one of ordinary skill in the art. For example, Dr. Kadesch testified:

Q. And now, have you looked at Claim 80 and Claim 95, Claim 144, Claim 145?

A. Yes, I have.

Q. And as a scientist, are they clear to you?

A. Yes.

Q. And do you understand what's within them and outside of them?

A. Yes, I do.

(Ex. 13, Trial Tr., Day 13, 40:10-17).

Even though Lilly contends that it has no further evidence on this issue, Plaintiffs reserve the right to introduce any relevant evidence they deem necessary at the upcoming trial with the Court.

VI. CONCLUSION

The jury has already determined based on substantial evidence that the asserted claims are infringed, novel and supported by an enabling and sufficient written description. As demonstrated above, Lilly cannot meet its burden by clear and convincing evidence that any of the remaining grounds serve to render the asserted claims unenforceable or invalid and the Court should, for the foregoing reasons, dismiss those defenses and counterclaims based on those defenses.

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Respectfully Submitted

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CERTIFICATE OF SERVICE

I hereby certify that this document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non-registered participants on August 2, 2006.

/s/ Thomas F. Fleming