

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' REPLY TO LILLY'S PROPOSED FINDINGS OF FACT AND  
CONCLUSIONS OF LAW ON THE ISSUES OF (1) PATENTABILITY UNDER 35  
U.S.C. § 101, (2) INEQUITABLE CONDUCT, AND (3) PROSECUTION LACHES**

Leora Ben-Ami  
Patricia A. Carson  
Thomas F. Fleming  
KAYE SCHOLER LLP  
425 Park Avenue  
New York, NY 10022  
Tel: (212) 836-8000  
Fax: (212) 836-8689

Lee Carl Bromberg, BBO# 058480  
Kerry L. Timbers, BBO# 552293  
BROMBERG & SUNSTEIN LLP  
125 Summer Street  
Boston, MA 02110-1618  
Tel: (617) 443-9292

*Attorneys for Plaintiffs*

**TABLE OF CONTENTS**

	<b><u>Page</u></b>
I. INTRODUCTION .....	1
II. PATENTABLE SUBJECT MATTER .....	2
A. Conclusions of Law on Patentable Subject Matter Under § 101 .....	2
B. Conclusions of Law Regarding the Subject Matter of the Asserted Claims.....	4
C. Findings of Fact Regarding Lilly’s Failure to Prove That the Autoregulatory Loop Operates in Nature Within the Meaning of the Asserted Claims .....	14
D. Conclusions of Law: The Exclusion of the Autoregulatory Loop Model from the Scope of the Claims is Consistent with the Court’s Claim Construction.....	18
1. Ariad Is Not Judicially Estopped From Arguing that the Claims Do Not Cover the Autoregulatory Loop Model.....	22
E. Findings of Fact on the Absence of Evidence That the Autoregulatory Loop Operates Outside of the Laboratory, in Nature .....	23
F. Conclusions of Law: Dr. Ravetch’s Opinion on the Autoregulatory Loop Model Was Properly Disclosed .....	25
III. INEQUITABLE CONDUCT.....	26
A. Findings of Fact .....	26
1. Applicants Did Not Withhold or Misrepresent any Material Information Regarding Figure 43 With Intent to Deceive the Patent Office .....	26
a. One of Skill in the Art Would Not Consider Figure 43 Erroneous.....	26
b. Lilly’s Reliance on the Disclosure of Human Gene Therapy Does Not Support the Materiality of any Purported Error in Figure 43 .....	30
2. The Actions of Ariad’s Attorneys Does Not Establish Any Material Error in Figure 43 .....	32
3. None of the Applicants for the ’516 Patent or their Attorneys Intended to Deceive the Patent Office With Respect to Figure 43 .....	35
4. Findings of Fact: Lilly Has Shown No Evidence That the Inventors Knowingly Withheld Material Information Bearing on Inherent Anticipation With Intent to Deceive the PTO .....	39
5. Dr. Baldwin is the Only Inventor That Lilly Now Alleges Knowingly Withheld Material Information With Intent to Deceive the PTO.....	39
6. Dr. Baldwin Did Not Withhold Material References From the Patent Office .....	40
7. None of the Other Inventors Withheld Material References .....	44
8. Dr. Baldwin Did Not Intend to Deceive the Patent Office .....	42

B.	Conclusions of Law Regarding Inequitable Conduct .....	46
1.	Lilly Did Not Withhold or Misrepresent Any Material Information Regarding Figure 43 From the Patent Office.....	47
2.	No Material References Were Withheld From the Patent Office During Prosecution of the '516 Patent.....	52
3.	There is No Evidence That Anyone Involved With the Prosecution of the '516 Patent Had Any Intent to Deceive the Patent Office.....	55
IV.	PROSECUTION LACHES .....	57
A.	Findings of Fact .....	57
B.	Conclusions of Law .....	58
V.	RESERVED EVIDENTIARY CONCLUSIONS OF LAW.....	65
A.	The Reexamination Is Not Admitted Into Evidence.....	65
B.	Documents Relating to the Autoregulatory Loop Model Are Not Admitted Into Evidence .....	67
C.	Deposition Related Documents and Certain Deposition Testimony Are Not Admitted Into Evidence .....	68

**TABLE OF AUTHORITIES**

<b>CASES</b>	<b><u>Page(s)</u></b>
<i>AT&amp;T Corp. v. Excel Commc'ns, Inc.</i> , 172 F.3d 1352 (Fed. Cir. 1999).....	5
<i>Akzo N.V. v. United States Int'l Trade Comm'n</i> , 808 F.2d 1471 (Fed. Cir. 1986).....	52
<i>Alza Corp. v. Mylan Labs., Inc.</i> , No. 06-1019, ___ F.3d ___, 2006 U.S. App. LEXIS 22616 (Fed. Cir. Sept. 6, 2006).....	24, 25
<i>Amgen, Inc. v. Hoechst Marion Roussel, Inc.</i> , 314 F.3d 1313 (Fed. Cir. 2003).....	50
<i>Animal Legal Def. Fund v. Quigg</i> , 932 F.2d 920 (Fed. Cir. 1991).....	4, 7, 11
<i>Arrhythmia Research Technology, Inc. v. Corazonix Corp.</i> , 958 F.2d 1053 (Fed. Cir. 1992).....	4, 5
<i>Baxter Int'l, Inc. v. McGaw, Inc.</i> , 149 F.3d 1321 (Fed. Cir. 1998).....	52
<i>In re Bergstrom</i> , 427 F.2d 1394 (C.C.P.A. 1970) .....	6
<i>In re Bergy</i> , 596 F.2d 952 (C.C.P.A. 1979) .....	5, 6
<i>In re Bogese</i> , 303 F.3d 1362 (Fed. Cir. 2002).....	62
<i>In re Bolinger</i> , 356 F.2d 552 (C.C.P.A. 1966) .....	62
<i>Bruno Indep. Living Aids, Inc. v. Acorn Mobility Servs., Ltd.</i> , 394 F.3d 1348 (Fed. Cir. 2005).....	56
<i>Capon v. Eshhar</i> , 418 F.3d 1349 (Fed. Cir. 2005).....	50
<i>Cochrane v. Deener</i> , 94 U.S. 780 (1877).....	4

*Colonial Alloys Co. v. Kinkead Indus., Inc.*,  
399 F. Supp. 1062 (N.D. Ill. 1975) .....62

*ConnecTel, LLC v. Cisco Sys., Inc.*,  
2005 WL 366966 (E.D. Tex. Feb. 16, 2005) .....62

*Critikon, Inc. v. Becton Dickinson Vascular Access, Inc.*,  
120 F.3d 1253 (Fed. Cir. 1997).....56

*Crown Cork & Seal Co. v. Ferdinand Gutmann Co.*,  
304 U.S. 159 (1938).....66

*Cutting Room Appliances Corp. v. Weatherbee Coats, Inc.*,  
158 F. Supp. 231 (N.D. Ohio 1950).....62

*Diamond v. Chakrabarty*,  
447 U.S. 303 (1980).....9

*Diamond v. Diehr*,  
450 U.S. 175 (1981).....4, 5, 6, 10, 15

*Enzo Biochem, Inc. v. Gen-Probe Inc.*,  
323 F.3d 956 (Fed. Cir. 2002).....50

*Evans Med. v. Am. Cyanamid Co.*,  
11 F. Supp. 2d 338 (S.D.N.Y. 1998).....62

*Faigin v. Kelly*,  
184 F.3d 67 (1st Cir. 1999).....24

*Fiers v. Revel*,  
984 F.2d 1164 (Fed. Cir. 1993).....33, 35, 49

*Fox Indus., Inc. v. Structural Pres. Sys., Inc.*,  
922 F.2d 801 (Fed. Cir. 1990).....51

*Funk Bros. Seed Co. v. Kalo Inoculant Co.*,  
333 U.S. 127 (1948).....5, 11

*Gen. Elec. Co. v. De Forest Radio Co.*,  
44 F.2d 931 (3d Cir. 1930).....62

*Gen-Probe Inc. v. Vysis, Inc.*,  
No. 99-CV-2668H, 2002 U.S. Dist. LEXIS 25020 (S.D. Cal. Aug. 5, 2002) .....61

*Hebert v. Lisle Corp.*,  
99 F.3d 1109 (Fed. Cir. 1996).....57, 58

*Helene Curtis Indus., Inc. v. Sales Affiliates, Inc.*,  
105 F. Supp. 886 (S.D.N.Y. 1952).....62

*Hester Indus. v. Stein, Inc.*,  
963 F. Supp. 1403 (E.D. Va. 1997).....62

*In re Hyatt*,  
708 F.2d 712 (Fed. Cir. 1983).....13, 14, 15

*J.T. Eaton & Co. v. Atl. Paste & Glue Co.*,  
106 F.3d 1563 (Fed. Cir. 1997).....62

*K-2 Corp. v. Salomon S.A.*,  
191 F.3d 1356 (Fed. Cir. 1999).....19

*Kimberly-Clark Corp. v. Johnson & Johnson*,  
745 F.2d 1437 (Fed. Cir. 1984).....51

*Kingsdown Med. Consultants Ltd. v. Hollister, Inc.*,  
863 F.2d 867 (Fed. Cir. 1988).....58

*Kothmann Enters., Inc. v. Trinity Indus., Inc.*,  
2006 WL 89838 (S.D. Tex. Jan. 13, 2006) .....60, 62

*Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*,  
126 S. Ct. 2921 (June 22, 2006).....11, 12

*Laitram Corp. v. Morehouse Indus., Inc.*,  
1997 WL 33320572 (E.D. Cal. April 24, 1997) .....62

*Licciardi v. TIG Insurance Group*,  
140 F.3d 357 (1998).....27, 31, 33

*Lydon v. Boston Sand & Gravel Co.*,  
175 F.3d 6 (1st Cir. 1999).....24

*M. Eagles Tool Warehouse, Inc. v. Fisher Tooling Co.*,  
439 F.3d 1335 (Fed. Cir. 2006).....57

*Mackay Radio & Telegraph Co. v. Radio of America*,  
306 U.S. 86 (1939).....10

*McNeil-PPC, Inc. v. L. Perrigo Co.*,  
337 F.3d 1362 (Fed. Cir. 2003).....62

*Minn. Mining & Mfg. Co. v. Alphapharm Pty. Ltd.*,  
2002 WL 1352426 (D. Minn. Mar. 20, 2002).....62

*Moba, B.V. v. Diamond Automation, Inc.*,  
325 F.3d 1306 (Fed. Cir. 2003).....49, 50

*Molins PLC v. Textron, Inc.*,  
48 F.3d 1172 (Fed. Cir. 1995).....21, 66, 67

*Moraine Prods. v. ICI Am., Inc.*,  
538 F.2d 134 (7th Cir. 1976).....62

*O’Reilly v. Morse*,  
15 U.S. 62 (1854).....11

*Oakley, Inc. v. Sunglass Hut Int’l*,  
2001 WL 1683252 (C.D. Cal. Dec. 7, 2001) .....62

*Parker v. Flook*,  
437 U.S. 584 (1978).....4, 11

*Phillips v. AWH Corp.*,  
415 F.3d 1303 (Fed. Cir. 2005).....19, 20, 22

*Regents of the Univ. of Cal. v. Eli Lilly & Co.*,  
119 F.3d 1559 (Fed. Cir. 1997).....49, 53

*Rohm & Haas Co. v. Brotech Corp.*,  
127 F.3d 1089 (Fed. Cir. 1997).....62

*STX, Inc. v. Brine, Inc.*,  
37 F. Supp. 2d 740 (D. Md. 1999).....62

*Schering Corp. v. Amgen Inc.*,  
222 F.3d 1347 (Fed. Cir. 2000).....30

*Schering Corp. v. Geneva Pharmaceuticals, Inc.*,  
339 F.3d 1373 (Fed. Cir. 2003).....56, 69

*SmithKline Beecham Corp. v. Apotex Corp.*,  
403 F.3d 1331 (Fed. Cir. 2005).....7, 8, 10

*Stambler v. RSA Sec., Inc.*,  
243 F. Supp. 2d 74 (D. Del. 2003).....61

*State Street Bank & Trust Co. v. Signature Fin. Group, Inc.*,  
149 F.3d 1368 (Fed. Cir. 1998).....7, 13

*Symbol Techs. v. Lemelson Med., Educ. & Research Found., LP*,  
277 F.3d 1361 (Fed. Cir. 2002).....64, 65

*Symbol Techs. Inc. v. Opticon, Inc.*,  
935 F.2d 1569 (Fed. Cir. 1992).....53

*Symbol Techs. Inc. v. Lemelson Med., Educ. & Research Found., LP*,  
301 F. Supp. 2d 1147 (D. Nev. 2004), *aff'd*, 422 F.3d 1378 (Fed. Cir. 2005) .....62, 64

*Symbol Techs. v. Lemelson Med., Educ. & Research Found., LP*,  
422 F.3d 1378 (Fed. Cir. 2005).....60, 61, 63, 64, 67

*Syngenta Seeds, Inc. v. Monsanto Co.*,  
2004 WL 2106583 (D. Del. Sept. 8, 2004).....62

*Therma-Tru Corp. v. Peachtree Doors, Inc.*,  
44 F.3d 988 (Fed. Cir. 1995).....55

*United States v. Boylan*,  
898 F.2d 230 (1st Cir. 1990).....69

*United States v. Leon-Delfis*,  
203 F.3d 103 (1st Cir. 2000).....69

*Univ. of Rochester v. G.D. Searle & Co.*,  
358 F.3d 916 (Fed. Cir. 2004).....49

**STATUTES AND LEGISLATIVE MATERIALS**

35 U.S.C. § 100(b).....6

35 U.S.C. § 101.....2, 3, 16

35 U.S.C. § 112.....13

35 U.S.C. § 121.....67, 68

37 C.F.R. § 1.56.....51

S. REP. NO. 1979, 82d Cong., 2d Sess. (1952) .....4

H.R. REP. NO. 1923, 82d Cong., 2d Sess. (1952).....4

**MISCELLANEOUS**

*SmithKline Beecham Corp. v. Apotex Corp.*,  
2005 WL 2652620 (Oct. 13, 2005) (Petition for Writ of Certiorari).....8, 56

## I. INTRODUCTION

Plaintiffs Ariad Pharmaceuticals, Inc., Massachusetts Institute of Technology, The Whitehead Institute, and The President and Fellows of Harvard University (collectively “Ariad”) submit the following findings of fact and conclusions of law in reply to the Proposed Findings of Fact and Conclusions of Law submitted by Defendant Eli Lilly and Company (“Lilly”) on September 11, 2006. The following also supplements the Opening Findings of Fact and Conclusions of Law submitted by Ariad on September 11, 2006 which are incorporated herein by reference to the extent that Lilly raised new issues. Background information on the parties and this litigation is set forth in Ariad’s Opening Findings of Fact (“AFF”), and will not be repeated here. (AFF at 1-37). Ariad opposes and disputes Lilly’s Proposed Findings and Conclusions, and respectfully requests that the Court adopt Ariad’s submission. To spare the Court further extensive briefing, this submission highlights the errors in Lilly’s Proposed Findings and the points supporting Ariad’s positions. The issues addressed by the following submission are: (1) the alleged invalidity of the asserted claims for covering non-patentable subject matter under 35 U.S.C. § 101; (2) the alleged unenforceability of the asserted claims for inequitable conduct during prosecution; and (3) the alleged unenforceability of the asserted claims for prosecution laches.<sup>1</sup> This submission sets forth the Court’s rejections of Lilly’s proposed findings of fact and conclusions of law for each issue and then provides additional findings of fact and conclusions of law in support of those rejections.<sup>2</sup>

---

<sup>1</sup> To the extent that any of the following findings of fact or any of Ariad’s opening findings of fact is a conclusion of law, it is hereby adopted as a conclusion of law. To the extent that any of the following conclusions of law or any of Ariad’s opening conclusions of law is a finding of fact, it is hereby adopted as a finding of fact.

<sup>2</sup> Lilly has not offered any proposed findings of fact or conclusions of law on the issue of indefiniteness. Therefore, indefiniteness should no longer be an issue in this case. To the extent the Court considers indefiniteness, Ariad respectfully submits that the Court should adopt Ariad’s opening findings of fact and conclusions of law on the issue.

## II. PATENTABLE SUBJECT MATTER

### A. Conclusions of Law on Patentable Subject Matter Under § 101

1. The Court rejects Lilly's Proposed Conclusions of Law ("LCL") 2-32, 35-36, 73-74 regarding patentability under 35 U.S.C. § 101. The Court instead adopts Ariad's Opening Conclusions of Law ("ACL") 584-613.

2. Lilly's Proposed Conclusions of Law (LCL 29-32) make clear that §§ 101 and 102 of the Patent Act are distinct and separate inquiries. The cited cases and Lilly's Proposed Findings of Fact on the autoregulatory loop convince the Court that Lilly should have raised its arguments under § 102.

3. Therefore the Court rejects Lilly's "evidence" that the claims are invalid as non-patentable subject matter. The testimony of Dr. Latchman regarding the autoregulatory loop was nothing more than an attack on the novelty of the claims. Lilly's novelty defenses were tried to the jury and the jury found that the claims are novel.

4. Lilly also attempts to frame arguments regarding the "overbreadth" of the asserted claims and their purported lack of sufficient steps as relating to patentability under § 101. As seen below, these arguments are only properly made under § 112. Lilly has already tried its § 112 arguments to the jury and failed. Lilly may not attempt to revive them through § 101.

5. The eligibility of different types of subject matter for patent protection is governed in the Patent Act by § 101. One of the types of subject matter that may be patented includes a "process." (*See* ACL 574-77).

6. For purposes of § 101 a process is "a mode of treatment of certain materials to produce a given result. It is an act, or a series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing." *Diamond v. Diehr*, 450 U.S. 175, 183 (1981) (quoting *Cochrane v. Deener*, 94 U.S. 780, 787-88 (1877)).

7. Congress intended statutory subject matter under § 101 to “include anything under the sun that is made by man.” *Diehr*, 450 U.S. at 182 (quoting S. REP. NO. 1979, 82d Cong., 2d Sess., at 5 (1952); H.R. REP. NO. 1923, 82d Cong., 2d Sess., at 6 (1952)).

8. Courts have held that there are limitations to § 101 and not every discovery is eligible for protection. *Diehr*, 450 U.S. at 185. However, the Supreme Court’s decision in *Diehr* limited these classes of non-patentable subject matter to three categories – “laws of nature, natural phenomena, and abstract ideas.” *Arrhythmia Research Tech., Inc. v. Corazonix Corp.*, 958 F.2d 1053, 1065 (Fed. Cir. 1992) (Rader, J., concurring).

9. Courts and the Patent Office have also recognized that the Constitution prohibits a patent right in a human being. *Animal Legal Def. Fund v. Quigg*, 932 F.2d 920, 923 (Fed. Cir. 1991) (quoting 1077 Official Gazette 24 (April 21, 1987)). This unremarkable policy of Constitutional preemption does not exempt other organisms or biological processes from patent protection. *Id.* (noting that living organisms that are the product of “human ingenuity” are patentable).

10. These judicial exceptions to § 101 do not render a process “unpatentable simply because it contains a law of nature.” *Parker v. Flook*, 437 U.S. 584, 590 (1978). “It is now commonplace that an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.” *Diehr*, 450 U.S. at 187 (citing *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948)).

11. The only consideration regarding compliance with § 101, aside from utility (Lilly has not challenged that the claimed invention is useful), is what type of invention is claimed and whether it falls within a statutorily recognized category. *In re Bergy*, 596 F.2d 952, 960, 962 (C.C.P.A. 1979).

12. Rather than focusing on “non-statutory, vague classifications,” a process should be accorded protection if it fits within the “broad meaning of § 101.” *Arrhythmia Research*, 958 F.2d at 1065 (Rader, J., concurring). A process comes within the broad scope of § 101 if it involves transforming or reducing an article to a different state or thing. *AT&T Corp. v. Excel Commc’ns, Inc.*, 172 F.3d 1352, 1359 (Fed. Cir. 1999).

13. As seen below and in Ariad’s opening Conclusions of Law 584-613, the asserted claims satisfy the requirements of § 101.

**B. Conclusions of Law Regarding the Subject Matter of the Asserted Claims**

14. The asserted claims (set forth in independent form as agreed to by the parties at AFF 3-6) are directed to methods, or processes, for reducing the effects of extracellular influences on cells that induce activity of the nuclear transcription factor NF- $\kappa$ B. As Lilly’s expert, Dr. Latchman, testified, these claims cover “methods of manipulating NF- $\kappa$ B activity for therapeutic benefit.” (Bench Trial Tr. Day 2 at 20:18–21:5).

15. Contrary to Lilly’s allegations, the asserted claims do not merely recite the reduction of NF- $\kappa$ B activity but also require the modification of the effects of extracellular influences. In the case of claims 144 and 145, the claims specifically require the reduction of bacterial lipopolysaccharide [LPS]-induced expression of cytokines in respectively mammalian cells and human cells.

16. That the asserted claims encompass therapeutic methods is further supported by the jury verdict that claims 80 and 95 cover the use of Lilly’s pharmaceutical product EVISTA<sup>®</sup> for the prevention and treatment of post-menopausal osteoporosis, and that claims 144 and 145 cover the use of Lilly’s pharmaceutical product XIGRIS<sup>®</sup> for the treatment of severe sepsis. (AFF 23-26, 363).

17. The plain meaning of the term “method” in the asserted claims, and the meaning understood by one of ordinary skill in the art to which the ’516 patent pertains, requires purposeful human intervention to achieve a desired result. (Bench Trial Tr. Day 3 at 19:23–20:6).

18. As Lilly states in its Proposed Conclusions of Law, “the word ‘method’ in patent law is a term of art synonymous with the word ‘process’ used in § 101.” (LCL 50; 35 U.S.C. § 100(b)). As such, the terms “process” implies action that is undertaken or set in motion by human hands. A process is “is an act, or a series of acts performed upon the subject matter to be transformed and reduced to a different state or thing.” *Diehr*, 450 U.S. at 183. The asserted claims cover methods of manipulating induced NF- $\kappa$ B activity for therapeutic benefit and therefore cover processes within the meaning of § 101.

19. An inquiry into patentability under § 101 does not address questions of novelty of the claimed invention which are properly raised only under § 102. *Diehr*, 450 U.S. at 189-90; *In re Bergy*, 596 F.2d 952, 960 (C.C.P.A. 1979); *In re Bergstrom*, 427 F.2d 1394, 1401 (C.C.P.A. 1970).

20. Whether the claimed invention was new or instead was anticipated by prior use was an issue to be raised and decided at the jury trial. Lilly did not then proffer the autoregulatory loop model as a “prior use.” Lilly therefore waived any argument that the purported autoregulatory loop process provides evidence that the asserted claims lack novelty.

21. Lilly’s motion for summary judgment on § 101 set out to establish that the autoregulatory loop occurred for millions of years. Perhaps recognizing that this “prior use” argument was improper under § 101, Lilly’s new counsel now frames the issue as what the claims cover today. However, because the claims recite the *type* of subject matter considered

patentable under § 101, the *scope* of the claim today is immaterial. See *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1342 (Fed. Cir. 2005) (citing *Animal Legal Def. Fund*, 932 F.2d at 930).

22. Lilly asserts that the scope of the asserted claims is overly broad. (LCL 35-36). Lilly's proffered "overbreadth" defense is not recognized in patent law and is based on a distorted reading of § 101. See *State Street Bank & Trust Co. v. Signature Fin. Group, Inc.*, 149 F.3d 1368, 1377 (Fed. Cir. 1998).

23. Lilly's framing of the issue as whether or not the purported autoregulatory loop sometimes operates in nature to "infringe" the asserted claims (LCL 32) is not the proper inquiry under § 101. *SmithKline*, 403 F.3d at 1342 (Fed. Cir. 2005). Rather, the proper inquiry is whether "the claimed invention represents subject matter eligible for patent protection under § 101. With that conclusion, the inquiry under § 101 ends." *Id.*

24. A claim directed to patentable subject matter cannot be rendered unpatentable because it can be read to also encompass elements that could conceivably occur without human intervention. *Id.* ("the scope of the claims is not relevant to subject matter eligibility."); *State Street*, 149 F.3d at 1377 ("Whether the patent's claims are too broad to be patentable is not to be judged under § 101").

25. Contrary to Lilly's suggestion, (LFF 64) a claim is not required under § 101 to recite process steps or results that can only be achieved by human intervention. See *SmithKline*, 403 F.3d at 1336, 1342. If a claim includes certain elements that "read on" a natural process it should be addressed under §§ 102 or 103.

26. If the law were as Lilly argues, numerous inventions once considered patentable might be stripped of protection because of later discoveries of naturally occurring phenomena

that “read on” the claims or even because changes in nature itself have generated processes or substances that fall within the claims. As Lilly’s counsel noted in its certiorari petition to the Supreme Court on behalf of appellant in the *SmithKline* case, Judge Newman, in her dissent from the rehearing *en banc* in that case, warned against the dangers of invalidating patents based on the discovery of something previously unknown and undetected and unisolated:

The patentability of antibiotics, hormones, antibodies, and myriad other previously unknown or unisolated products [will] be called into question . . . , giving rise to uncertainty as to existing patents, as well as negation of searches for the beneficial components of existing materials.

*SmithKline Beecham Corp. v. Apotex Corp.*, 2005 WL 2652620, at \*4 (Oct. 13, 2005) (Petition For a Writ of Certiorari) (quoting Newman, J., dissenting from denial of rehearing *en banc* below).

27. “Subject matter does not take on a different eligibility status with adjustments in the scope of the proposed claim.” *SmithKline*, 403 F.3d at 1342. Thus, subject matter otherwise eligible for patenting, such as a method to inhibit chemical processes in a cell, does not lose this status simply because it is discovered that a phenomenon operating in nature comes within its scope.

28. A further example illustrates the untenability of Lilly’s interpretation of § 101. For instance an inventor could receive a patent claim to a novel mutated form of a bird flu virus that satisfied all the conditions for patentability exemplified in §§ 102, 103 and 112. Ten years later, the bird flu virus found in nature could mutate spontaneously and subsequently fit within the scope of the claim. Under Lilly’s conception of § 101, what was formerly a validly claimed invention would become unpatentable. Lilly’s interpretation that § 101 would render a properly

issued claim unpatentable because the claimed invention appeared in nature years after the patent issued must be rejected as a matter of law.

29. This also demonstrates the fallacy of Lilly's suggestion that claims may require language such as "non-naturally occurring" or other language denoting synthetic origins. (LCL 15-17). On the contrary, in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), the seminal case in which the Supreme Court confirmed the patentability of living organisms, Mr. Chakrabarty's claim to a "a bacterium from the genus *Pseudomonas* containing therein at least two stable energy-generating plasmids, each of said plasmids providing a separate hydrocarbon degradative pathway" was held patentable under § 101 without any limitation to the bacterium being "non-naturally occurring." The Chakrabarty claim would not become unpatentable under § 101 if natural bacteria were later discovered to possess the properties described in the claim, or if existing bacterial strains mutated such that they met the limitations of the claim. Lilly's argument that § 101 requires the asserted claims to recite "non-naturally occurring" or similar language has no basis in law.

30. Lilly has also misrepresented the holding in *SmithKline* relative to § 101 by suggesting that the claims at issue in that case were limited to synthetically produced PHC hemihydrate. Nothing in the claim language excluded naturally produced material. *See SmithKline*, 403 F.3d at 1334 ("The only claim at issue in this case is claim 1, which reads in its entirety: 'Crystalline paroxetine hydrochloride hemihydrate.'").

31. By reviewing the specification, the Court in *SmithKline* determined that the invention was directed to synthetically produced material. However, the evidence amply demonstrated that due to the "seeding" effect of the process of manufacturing the substance, it was subsequently produced naturally within the environment under the right conditions of

moisture and pressure without any willful human activity. *Id.* at 1336. Even though the patented substance was unintentionally produced “by nature,” the Federal Circuit did not find the subject matter of the claim unpatentable under § 101 merely because it was not limited to the synthetic substance.<sup>3</sup>

32. While certain categories of subject matter such as laws of nature, mathematical formulae and human beings have been held on their face to be non-patentable by the courts, a claim that properly covers synthetic substances, man-made articles or methods of human use of known materials or intervention in a natural process is valid under § 101. *See Diehr*, 450 U.S. at 187-88; *Mackay Radio & Telegraph Co. v. Radio of Am.*, 306 U.S. 86, 94 (1939).

33. Lilly’s vague allusions to general terms like “naturally occurring biological systems” (LCL 5) and “phenomena of nature” (LCL 18) are unavailing. “Everything that happens may be deemed ‘the work of nature,’ and any patentable composite exemplifies in its properties ‘the laws of nature.’ Arguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost every patent.” *Funk Bros.*, 333 U.S. at 134-35 (Frankfurter, J., concurring).

34. Specific types of subject matter held to be exempted from patent protection under § 101 include “a novel and useful mathematical formula”, *Flook*, 437 U.S. at 584, “the motive power of electromagnetism or steam,” *O’Reilly v. Morse*, 15 U.S. 62, 116 (1854), and “the heat of the sun, electricity, or the qualities of metals”, *Funk Bros.*, 333 U.S. at 130. *See Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 126 S. Ct. 2921, 2922-23 (June 22, 2006) (mem.)

---

<sup>3</sup> The Court held the subject matter invalid for inherent anticipation under § 102 because of the finding that trace elements of PHC hemihydrate were necessarily produced in the prior art. As noted above, Lilly has waived any argument that the autoregulatory loop is prior art under § 102.

(Breyer, J., dissenting from decision to dismiss writ of certiorari). Lilly has not established that the claimed subject matter is analogous to any of these types of laws of nature. (*See* LCL 37-74).

35. Lilly's arguments regarding unpatentability find no support in *Animal Legal Defense Fund*. (*See* LCL 14). That case simply notes that as a matter of policy and Constitutional law the Patent Office will not allow a patent claim claiming a human being, and does not in any way expand or alter existing precedent addressing § 101. *Animal Legal Def. Fund*, 932 F.2d at 923.

36. Lilly's reliance on Justice Breyer's opinion in dissent from the dismissal of certiorari in *Laboratory Corp.* is misplaced. (LCL 73). In that case, the claimed subject matter was a diagnostic correlation between deficiencies of two vitamins, folate or cobalamin, and elevated levels of the amino acid, homocysteine, in a patient. The claimed method simply instructed doctors to test the level of homocysteine using known assays and then analyze whether they were predictive of a vitamin deficiency. Justice Breyer opined that this "method" simply called for a user to 1) obtain test results and 2) think about them, and therefore added nothing to the scientific principle embodied in the correlation between elevated homocysteine and certain vitamin deficiencies. *Lab. Corp.*, 126 S. Ct. at 2927-28. Thus, Justice Breyer concluded that the claimed subject matter encompassed nothing more than an unpatentable "principle in natural philosophy or physical science." *Id.* at 2927.

37. The subject matter of the asserted claims is distinguishable from that in issue in *Laboratory Corp.* Justice Breyer pointed out that with advances in technology, the line between patentable and unpatentable is more difficult to discern applying traditional concepts, yet "many a patentable invention rests upon its inventor's knowledge of natural phenomena; many 'process' patents seek to make abstract intellectual concepts workably concrete; and all conscious human

action involves a mental process.” *Id.* at 2926. That an invention incorporates such concepts does not necessarily render such processes unpatentable.

38. Here, the asserted claims are directed to patentable methods for altering the natural cellular mechanisms that contribute to activation of NF-κB in response to extracellular influences. The claims apply the knowledge of a natural signaling pathway to perform manipulative and transformative acts on a cell with quantifiable results, and are therefore patentable.

39. Lilly’s assertion that the asserted claims “specify no disease to be treated, no active ingredient, no step of drug administration, no requirement for an effective dose, and no patient population” (LCL 35-36) is also irrelevant to the issue of patentability under § 101, which does not require that claims to therapeutic processes recite particular target diseases or pharmacological properties. Also, this assertion is undermined by Dr. Latchman’s ability to understand that the claims encompass therapeutic processes in spite of the alleged lack of specific elements that Lilly wrongly suggests are necessary.

40. The jury also found that the use of Lilly’s EVISTA<sup>®</sup> drug to treat the disease of post-menopausal osteoporosis infringes the asserted claims and the use of Lilly’s XIGRIS<sup>®</sup> drug to treat the disease of severe sepsis infringes the asserted claims. (AFF 23-26, 363). This finding further undermines Lilly’s suggestion that the claims must specifically recite a particular disease or drug administration regimen.

41. Further, the level of detail necessary to support the patentability of a claim should be determined under 35 U.S.C. § 112 and not § 101. *See State Street*, 149 F.3d at 1377; *In re Hyatt*, 708 F.2d 712, 714-15 (Fed. Cir. 1983). The jury already found that the subject matter of

the asserted claims is sufficiently described and enabled by the '516 patent. Further, Lilly has not provided any evidence to show that the asserted claims are indefinite.

42. The Court also rejects Lilly's contention that the asserted claims are only limited by their ultimate function or failure to recite any manipulative steps. (LCL 35, 74). Again this argument is properly raised only as a non-enablement defense under § 112 and not § 101. *Hyatt*, 708 F.2d at 714-15.

43. In its earlier motion for summary judgment (D.I. 176), Lilly argued that the claims of the '516 patent were not enabled because they failed to provide sufficient steps to allow one of skill in the art to practice their full breadth. Having lost on its arguments under § 112 in summary judgment and at trial, Lilly may not now resurrect them under the guise of § 101.

44. In any case, the ultimate function of the asserted claims to reduce the effects of certain extracellular influences was drafted by the patent examiner before allowance of the claims. (AFF 404-08). The steps for achieving this function are methods of reducing induced NF- $\kappa$ B activity and its intracellular effects.

45. The jury's findings of enablement and written description support the idea that such steps are actually provided in the patent. Moreover, the jury's finding of infringement identifies the administration of Lilly's accused drugs as a process practicing these steps.

46. Lilly's reliance on Guidelines from the U.S. Patent and Trademark Office ("PTO") also does not support its arguments for unpatentability under § 101. First, the PTO Guidelines "do not constitute substantive rulemaking and hence do not have the force and effect of law." (Guidelines at 2). Thus, any inconsistency between the Guidelines and the precedent of the Federal Circuit must be resolved in favor of the Court.

47. Further, even were this Court to follow the Guidelines, it is clear that the claims of the '516 patent would still constitute patentable subject matter.

48. As Lilly points out (LCL 28), the first step under the Guidelines is to determine “whether the claim falls within at least one of the four enumerated categories of patentable subject matter recited in section 101.” (Guidelines at 14-15). Here, the claims of the '516 patent are clearly directed to a process (or “method”), as both parties agree. (*See* AFF 364-65; LFF 17).

49. Under the next step, the examiner is to determine whether the claimed invention falls within a judicial exception to statutory subject matter, *i.e.*, is “directed to nothing more than abstract ideas . . . , natural phenomena, and laws of nature.” (Guidelines at 17).

50. Importantly (and which Lilly fails to point out), if the claims as a whole “perform a real-world function,” *i.e.*, are for a “practical application” of a judicial exception, the invention is eligible for protection. (*Id.* at 17-20). As the Guidelines explain, “[i]n determining whether the claim is for a ‘practical application,’ the focus is . . . on whether . . . the final result achieved by the claimed invention is ‘useful, tangible and concrete.’” (*Id.* at 20; emphasis removed). Claims are “useful, tangible and concrete” if they are for a use that is not abstract and that produces a “result that can be substantially repeatable.” (*Id.* at 20-22).

51. Claim 80 is directed to a method for modifying effects of external influences on a cell. Claim 95 is directed to a method for reducing the level of gene expression. Claims 144-145 are directed to methods for reducing bacterial LPS-induced expression of cytokines. (AFF 360-62). As even Lilly’s expert Dr. Latchman agreed, the '516 patent claims cover “methods of manipulating NF- $\kappa$ B activity for therapeutic benefit” and “of course they encompass therapeutic methods.” (Bench Trial Tr. Day 2 at 20:18–21:5). And, as the jury found, Ariad’s claims cover the use of Lilly’s pharmaceutical products. (Jury Trial Tr. Day 18 at 5:2–6:7).

52. Therefore, Lilly has failed to prove by clear and convincing evidence that the asserted claims are not patentable, for clearly they are.

53. Then, the Guidelines instruct that as long as the claims do not completely preempt a judicial exception – *i.e.*, “cover[] every substantial practical application thereof” – they meet the statutory requirement of § 101. (Guidelines at 20, 23). In *Diehr*, the Supreme Court held that “a claim drawn to subject matter otherwise statutory does not become nonstatutory simply because it uses” subject matter falling within an exception. 450 U.S. at 187. Holding the claims at issue to be eligible processes, the *Diehr* Court explained, “[t]heir process admittedly employs a well-known mathematical equation, but they do not seek to pre-empt the use of that equation. Rather, they seek only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process.” *Id.* (emphasis added).

54. Thus, were the Court to apply the Patent Office Guidelines, it would hold that all of Ariad’s asserted claims are to patentable subject matter.

55. The Court concludes that the asserted claims of the ’516 patent are directed to the type of subject matter historically recognized as patentable under § 101 and are not subject to any of the judicial exceptions to § 101.

C. **Findings of Fact Regarding Lilly’s Failure to Prove That the Autoregulatory Loop Operates in Nature Within the Meaning of the Asserted Claims**

56. The Court rejects Lilly’s Proposed Findings of Fact (“LFF”) 17-21, 25-67 regarding the impact of the autoregulatory loop model on patentability under 35 U.S.C. § 101. The Court instead adopts Ariad’s Opening Findings of Fact 359-428.

57. Even if Lilly's conception of § 101 were correct, Lilly has not proven by clear and convincing evidence that a purported cellular process referred to as the autoregulatory loop exists in nature and operates to reduce NF- $\kappa$ B activity within the meaning of the asserted claims.<sup>4</sup>

58. The Court finds that this model of "reduction" does not meet the requirements of the asserted claims as construed by the Court. (Bench Trial Tr. Day 1 at 48:21–52:1).

59. All of the claims require reducing NF- $\kappa$ B activity in cells in which the NF- $\kappa$ B activity has been "induced" or "activated" by extracellular influences. This Court has construed "reducing NF- $\kappa$ B activity" as "decreasing the function of NF- $\kappa$ B to act as an intracellular messenger that regulates transcription of particular genes, in response to certain stimuli." (Claim Construction Order, D.I. 75 at 2).

60. The '516 patent teaches that "induced" or "activated" NF- $\kappa$ B activity is a dynamic state resulting from the response to an inducing substance outside the cell.

61. As Dr. Ravetch explained, this dynamic response comprises all of the intracellular mechanisms that interact to produce a net effect that regulates the transcription of various genes. (Bench Trial Tr. Day 3 at 18:11–19:1, 21:14–22:3; Day 4 at 18:17–19:2). The autoregulatory loop, assuming it operates as Lilly asserts, is just one of these many mechanisms that contributes to the overall state of induction. The asserted claims require that this aggregate state and the associated levels of gene transcription are reduced after accounting for all the effects (natural or otherwise) including that of the autoregulatory loop.

62. As reflected in Example 8 of the '516 patent, an inducing substance produces a continuously varying state of NF- $\kappa$ B activity, due to the aggregate of all the mechanisms going

---

<sup>4</sup> Lilly cites no case where a court has applied each and every limitation of a claim to a natural phenomenon to prove it fails under § 101. As noted above, this type of analysis would only be appropriate in determining anticipation under § 102 or obviousness under § 103.

on within the cell. (*See* AFF 373-402; PTX 1, Example 8). The particular time course of the response depends on the inducing substance. (*See* AFF 373-402). For example, in response to PMA, the activation of NF- $\kappa$ B is transient (going up rapidly, peaking and then returning to baseline), while in contrast LPS produces a more sustained, level response (*See* AFF 373-402; PTX 1, Example 8).

63. Therefore, the extent to which NF- $\kappa$ B activity is induced by a particular stimulus is not defined by a single point in time. Rather, NF- $\kappa$ B activity is the sum total of the induced state over its entire duration (represented as the area under the curve). (*See* AFF 382-86).

64. Even if the autoregulatory loop functions as Lilly contends, Lilly's argument that the autoregulatory loop falls within the claims fails. It overlooks the fact that the overall extent to which NF- $\kappa$ B is activated over time in response to an inducing substance (that is, the overall induced state) takes into account the purported autoregulatory loop as well as all the other mechanisms inside the cell that contribute to the net induced state. The asserted claims require a decrease in this overall net state of activation, such that the whole area under the curve (which represents the state of activated NF- $\kappa$ B in the cell) is diminished. (AFF 371-98).

65. Dr. Latchman agreed that the autoregulatory loop theory is part of induction. (Bench Trial Tr. Day 1 at 145:22–146:20).

66. As '516 inventor Dr. Maniatis explained, the asserted claims are directed to methods for altering or "perturbing" the net effect of all the natural mechanisms that contribute to NF- $\kappa$ B activity. (*See* LFF 30). Such methods require actively manipulating or intervening in these natural processes to produce a desired effect. (Jury Trial Tr. Day 3 91:5–92:9). Dr. Ravetch also explained that the claimed methods were directed to purposeful acts of manipulation of these natural mechanisms in the cell. (Bench Trial Tr. Day 3 at 19:7–20:6).

67. Lilly misconstrues the testimony of Dr. Baltimore with respect to the autoregulatory loop. (*See* LFF 31). Dr. Baltimore was not asked about the loop model in relation to the claims of the '516 patent, and his testimony merely demonstrates his understanding that under certain conditions, he observed feedback mechanisms that appeared to contribute to the overall state of induction in the cell.

68. That both Dr. Maniatis and Dr. Baltimore noted that the autoregulatory loop may “naturally” function in cells in response to certain stimuli (such as DNA damage caused by sunlight) has no relevance to the validity of the claims. As noted above, the autoregulatory loop is just one of many potential cellular processes that contribute to the net effect of an inducing stimulus on activation of NF- $\kappa$ B. The cellular processes that play a role in this induction are not covered by the claims. Instead, the claims are directed to methods (requiring human intervention) for perturbing the net induced state that results from these cellular processes. (*See* LFF 29-31).<sup>5</sup>

69. The Court finds that because, within the meaning of the claims, the induced state of NF- $\kappa$ B factors in all the naturally occurring processes that contribute to the response to extracellular influences, the autoregulatory loop model itself does not practice the asserted claims. Even if the proper inquiry under § 101 were whether the claims “read on” a naturally occurring process (which as noted above is an issue properly raised only under § 102), there is no clear and convincing evidence here that the asserted claims would do so.

---

<sup>5</sup> Regardless of Lilly’s misinterpretation of the claims as covering the autoregulatory loop, exposure to sunlight on which Dr. Maniatis was questioned is not an “extracellular influence” or “external influence” as construed by the Court. According to the Court’s claim construction, both these terms refer to “inducing substances outside the cell.” (Claim Construction Order, D.I. 75 at 4). As Dr. Maniatis explained, exposure to sunlight causes DNA damage in the cell. It is the damaged DNA inside the cell (and not the sunlight) that functions as an inducer which activates NF- $\kappa$ B. Neither sunlight exposure (which does not act as the inducing substance) nor the damaged DNA (which is not outside the cell) is an “extracellular influence” or “external influence” according to the claims.

**D. Conclusions of Law: The Exclusion of the Autoregulatory Loop Model from the Scope of the Claims is Consistent with the Court's Claim Construction**

70. The Court rejects Lilly's Proposed Conclusions of Law 37-72 regarding the autoregulatory loop and patentability under § 101. Instead the Court adopts Ariad's Opening Conclusions of Law 584-96 and 614-23.

71. The Court rejects Lilly's argument that Ariad's position that the claims require a reduction in induced NF-κB activity is inconsistent with the Court's claim construction.

72. The Court adopted this construction in light of the teachings of the specification of the '516 patent. As discussed above, the '516 patent discloses the dynamic nature of induced NF-κB activity. (Claim Construction Order, D.I. 75 at 1, citing *K-2 Corp. v. Salomon S.A.*, 191 F.3d 1356, 1363 (Fed. Cir. 1999)); *see also Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (the patent specification is the primary guide for determining a claim's meaning).

73. The Court has construed "reducing NF-κB activity" as decreasing the function of NF-κB "in response to certain stimuli." (Claim Construction Order, D.I. 75 at 2).

74. As Dr. Ravetch explained, the response to a stimulus is a dynamic state. A stimulus that acts on a cell, through activation of NF-κB, triggers a cascade of events that produces an overall net effect. (Bench Trial Tr. Day 3 at 16:2-7). This net effect is the result of all the positive and negative loops occurring that are triggered by the stimulus. (*Id.* at 16:8-19). As Dr. Ravetch explained, to practice the asserted claims, "[y]ou decrease that activity, and that reduction of activity has to have a further effect, which is to reduce expression of said genes." (*Id.* at 16:19-21).

75. In forming his opinion that the autoregulatory loop is part of induction itself and therefore cannot alone practice the claims, Dr. Ravetch merely applied the Court's claim

construction requiring that “the function of NF- $\kappa$ B . . . in response to certain stimuli” be decreased. (*Id.* at 15:16–18:21). Ariad has not deviated from the Court’s claim construction.

76. The prosecution history of the ’516 patent also demonstrates that the applicants and the examiner understood that the natural operation of I $\kappa$ B on NF- $\kappa$ B was excluded from the scope of the claims. In particular, the examiner of the ’516 patent was aware of the autoregulatory loop model because during prosecution applicants disclosed references such as Shao-Cong *et al.* 1993, Gilmore and Morin 1993, Finco and Baldwin 1995, Siebenlist 1994 and Zabel and Baeuerle 1990 which teach the potential for resynthesized I $\kappa$ B to affect NF- $\kappa$ B and produce a transient response under certain conditions. (PTX 2A at ADL 0000637-40, 642-47, 675-84, 649-73).

77. Before allowing the claims of the ’516 patent, the examiner added limitations requiring that the methods of the claims achieve the specific result of reducing the effect of induction and therefore the process of resynthesized I $\kappa$ B affecting NF- $\kappa$ B activity during induction is not practicing the claims. (*See* PTX 2A at ADL 0000924).

78. This additional claim language, as construed by the Court requires that the net effect of all the mechanisms that constitute the state of induced NF- $\kappa$ B, including the regulation of transcription of particular genes, be reduced. Therefore, excluding the operation of the autoregulatory loop model presented by Lilly is not “reading limitations into the claims” as Lilly asserts. (*See* LCL 45-48).

79. There is no evidence, much less clear and convincing evidence, to support Lilly’s contention that the examiner of the ’516 patent would not have considered the disclosures in the references applicants submitted regarding the autoregulatory loop hypothesis and therefore could not have excluded it from the claim scope he suggested. The argument that an examiner’s

consideration of a reference is restricted to particular issues of patentability specifically pointed out by applicants has no basis in law or the realities of patent prosecution. (*See* AFF 56-57; ACL 522). Lilly's contention that the examiner would have only considered the references discussing the autoregulatory loop in the context of § 112 because that was the general topic of the Baltimore declaration with which they were submitted lacks merit.

80. In particular, the Baltimore declaration Lilly refers to points out that "it would be evident to one of skill in the art that the present application specifically contemplated NF- $\kappa$ B activation by a mechanism which included the phosphorylation of I $\kappa$ B and the subsequent proteolytic degradation of the modified I $\kappa$ B protein." (PTX 2A at ADL 0000626). The Baltimore declaration then points out, as further evidence for the nature of NF- $\kappa$ B activation described in the patent, the Shao-Cong, Gilmore, Finco and Siebenlist references which specifically disclose the possible feedback mechanism by which I $\kappa$ B resynthesized during induction recombines with NF- $\kappa$ B to inhibit it. (*Id.* at ADL 0000627). Thus, reading the Baltimore declaration as well as these references, a reasonable examiner could not fail to appreciate the potential import of the autoregulatory loop model.

81. That the examiner in fact considered this Baltimore declaration for its relevance to patentability is evidenced by examiner Robert Schwartzman's initials accompanying his handwritten note "considered 11/19/99" appearing on the face of the declaration. (*Id.* at ADL 0000625). An examiner, particularly a supervising examiner such as Dr. Schwartzman, is trained in patent law and understands the proper application of § 101. *See* MPEP §§ 2201, 2106; (Office Guidelines at 1-2).

82. As further evidence that the examiner of the '516 patent was aware of the autoregulatory loop hypothesis, before allowing the claims of the '516 patent, the examiner

considered the teaching of a reference, Zabel 1990, as indicated by his initials on Form PTO-1449 in the file history of the '516 patent. (PTX 2A at ADL 0000512). “The initials of the examiner placed adjacent to the citations on [Form] PTO-1449 . . . or its equivalent mean that the information has been considered by the examiner.” MPEP § 609 (emphasis added); *see also Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1184 (Fed. Cir. 1995).

83. Zabel postulated that resynthesis of I $\kappa$ B will affect the level of NF- $\kappa$ B activity in a way that may account for the transient NF- $\kappa$ B response observed when exposed to an extracellular influence like TPA. (*See* AFF 412-17).

84. Lilly’s reliance on the testimony of Ariad’s attorney, Dr. Matthew Vincent, regarding the disclosure of references with the Baltimore declaration does not support Lilly’s argument that the examiner did not have sufficient information to consider the relevance of an autoregulatory loop to patentability. On the contrary, Dr. Vincent clearly stated that “we cited the references with the understanding that they proved patentability.” (Bench Trial Tr. Day 3 at 108:25–109:1).

85. Lilly’s argument that the disclosure of the references cited to the examiner regarding the autoregulatory loop hypothesis would not have been considered because the then-pending claims required the use of an agent is unsupported by any evidence, and is further unavailing because the nature of NF- $\kappa$ B activity in its induced state was always considered relevant to the patentability of the claims as evidenced by the discussion in the Baltimore declaration.

86. Lilly cites no evidence as to how an examiner would have understood “agent” and why that would lead him to ignore references relating to the autoregulatory loop model. Moreover, whether or not the claims recited the use of an agent, the specification makes clear

that the invention did not include using IκB in a non-purified or natural form. (*See* AFF 423-28). One of skill in the art reading the '516 patent would understand the distinction between the role of natural IκB and a method of introducing extra IκB to practice the invention, and would appreciate that the operation of the former was excluded from the claims. (Bench Trial Tr. Day 1 at 150:17-21).

**1. Ariad Is Not Judicially Estopped From Arguing that the Claims Do Not Cover the Autoregulatory Loop Model**

87. The Court has already received extensive briefing at trial and then rejected Lilly's argument that Ariad is precluded from taking the position that the operation of the autoregulatory loop does not practice the claims because of Ariad's position during claim construction. The Court maintains that ruling.

88. In order to demonstrate judicial estoppel Lilly must demonstrate first that the allegedly estopping position and the estopped position are directly inconsistent, that is, *mutually exclusive*. *See Faigin v. Kelly*, 184 F.3d 67, 82 (1st Cir. 1999). However, as noted above, Lilly has failed to show that Ariad's position on the §101 issues deviates from the Court's claim construction.

89. The second condition that must be established for judicial estoppel to apply is that the responsible party must have succeeded in persuading a court to accept its prior position. *Lydon v. Boston Sand & Gravel Co.*, 175 F.3d 6, 13 (1st Cir. 1999). Even had Ariad's position during claim construction been inconsistent with its current position on the autoregulatory loop (which it was not), in construing "reducing NF-κB activity", the Court relied in part on Lilly's arguments. For instance, the Court favored Lilly's proposed "regulator of gene expression" instead of Plaintiffs' proposed "turns on" transcription. (D.I. 75 at 2; D.I. 69 at 4).

**E. Findings of Fact on the Absence of Evidence That the Autoregulatory Loop Operates Outside of the Laboratory, in Nature**

90. The Court rejects Lilly's Proposed Findings of Fact 18-21, 25-67 regarding the operation of the autoregulatory loop model. The Court instead adopts Ariad's Opening Findings of Fact 367-372, 429-493.

91. Lilly has not presented evidence to clearly and convincingly show that an autoregulatory loop functions within the meaning of the asserted claims outside the laboratory and under natural conditions.

92. Lilly's bald assertion that "the autoregulatory loop functions in human cells" (LFF 27, LCL 39) is unsupported by the record. The references Lilly relies upon as evidence as to how the autoregulatory loop functions in nature are limited to non-natural *in vitro* models and do not provide any link to observed natural phenomena *in vivo*. See *Alza Corp. v. Mylan Labs., Inc.*, No. 06-1019, \_\_\_ F.3d \_\_\_, 2006 U.S. App. LEXIS 22616, at \*\*24-28 (Fed. Cir. Sept. 6, 2006) ("The critical deficiency in the evidence presented by Alza was . . . that it failed to credibly link [*in vitro*] evidence with [*in vivo* activity] . . . evidence of *in vitro* dissolution rates is irrelevant absent evidence demonstrating that the *in vitro* system is a good model of actual *in vivo* behavior.").

93. Dr. Latchman agreed at trial that all the information he relies on in support of his conception of the autoregulatory model is taken from models. (AFF 447, 451, 455). One such model, discussed in the Ting and Endy paper, is merely based on a computer simulation, which in turn was purportedly based on data from another study that Dr. Latchman never disclosed as part of his opinion. The unsupported double hearsay Dr. Latchman relies upon does not provide clear and convincing evidence that the autoregulatory loop performs the process of the asserted claims.

94. Further, Dr. Latchman testified that he has not done any experimentation himself to verify the existence of the autoregulatory loop. (AFF 457). Dr. Latchman is also not a scientist with any particular expertise on I $\kappa$ B. (AFF 430).

95. Dr. Latchman admitted that he was aware of positive feedback loop models associated with induced NF- $\kappa$ B activity that are not accounted for in his model of the autoregulatory loop. (AFF 458).

96. Dr. Ravetch described how net induced NF- $\kappa$ B activity results from such positive feedback loops as well as other intracellular signaling mechanisms, all of which would overlap and interact with any potential negative autoregulatory loops. (*Id.*). Thus, the simplistic two-component model proposed by Dr. Latchman cannot fully or accurately represent the state of induction of NF- $\kappa$ B activity that is the subject of the asserted claims.

97. The testimony of Dr. Ravetch demonstrates that *in vitro* models, and in particular computer simulations, may be unreliable for modeling the complex intracellular signaling mechanisms such as NF- $\kappa$ B induction and are not always predictive of what will happen in cells in a natural environment. (Bench Trial Tr. Day 3 at 26:6–27:24). As Dr. Ravetch explained, Lilly's proffered evidence on the autoregulatory loop as postulated in laboratory experiments therefore does not show that this process will occur under natural conditions. (AFF 457-59).

98. Finally, none of the documents, DTX 469A, 119, 334, 490, 636, 2220, 3011, 3071 or 3072, can provide support for Lilly's arguments regarding the function of the autoregulatory loop model. As discussed in Section V.B. *infra*, these documents are inadmissible hearsay and have not been allowed into evidence.

**F. Conclusions of Law: Dr. Ravetch's Opinion on the Autoregulatory Loop Model Was Properly Disclosed**

99. Contrary to Lilly's assertions (LFF 67; LCL 43-44), Dr. Ravetch did not offer an opinion at trial that contradicts the disclosures already in his expert report.

100. With respect to the autoregulatory loop, Dr. Ravetch states explicitly in his report that he disagrees with the conclusions regarding the nature of the loop put forth by Lilly's expert, Dr. Barnes. In forming his opinions, Dr. Ravetch relied on the Court's Claim Construction Order, and this, together with the '516 specification and his knowledge of relevant art, informed his opinion that the purported autoregulatory loop would not meet all the limitations of the claims. (*See* Ariad's Opposition to Lilly's Motion *in Limine* to Preclude Dr. Ravetch From Testifying, D.I. 390, at 4).

101. Dr. Ravetch also submitted a declaration in support of Plaintiffs' opposition to Lilly's summary judgment motion based on the autoregulatory process, specifically opining that "negative feedback does not reduce NF- $\kappa$ B in the presence of an inducing substance" and therefore the autoregulatory process was not covered by the claims of the '516 patent. This declaration explicitly states that it supplements Dr. Ravetch's expert opinions. (*Id.* at 4-5).

102. Lilly's motion to strike the opinions regarding the autoregulatory loop in Dr. Ravetch's declaration was not granted. Instead, the Court has ruled in this case that an expert may rebut an opposing expert's opinion on a reference without specifically relying on that reference in their own report. (Jury Trial Tr. Day 13 at 95:1-10). Consistent with this ruling, Dr. Ravetch is permitted to rebut the testimony of Dr. Latchman with regard to the autoregulatory loop.

103. Lilly's reliance on *Licciardi v. TIG Insurance Group*, 140 F.3d 357 (1998), is misplaced as there the defendant's expert originally conceded that the plaintiff's original trauma

occurred but contested whether that led to a subsequent condition and later during trial disputed that the original trauma occurred at all. *See Licciardi*, 140 F.3d at 360, 363. Here, Dr. Ravetch has always disputed Lilly's characterization of the autoregulatory process and did not change that opinion at trial.

104. The Court permits into evidence Dr. Ravetch's opinions rebutting Lilly's description of the autoregulatory loop. His testimony illustrates the lack of any clear and convincing evidence for Lilly's contentions as to how the autoregulatory loop model functions in nature.

### **III. INEQUITABLE CONDUCT**

#### **A. Findings of Fact**

105. The Court rejects Lilly's Proposed Findings of Fact 68-192 regarding inequitable conduct. The Court instead adopts Ariad's Opening Findings of Fact 38-302.

##### **1. Applicants Did Not Withhold or Misrepresent any Material Information Regarding Figure 43 With Intent to Deceive the Patent Office**

106. Contrary to Lilly's Proposed Findings of Fact 22, 68-131, the Court finds no evidence of any material misrepresentation or omission by applicants or their attorneys with regard to Figure 43 during prosecution of the '516 patent.

##### **a. One of Skill in the Art Would Not Consider Figure 43 Erroneous**

107. Lilly's argument that there is a material error in Figure 43 of the specification of the '516 patent is not supported by clear and convincing evidence. Figure 43 provides a DNA and amino acid sequence that one of skill in the art would understand to be I $\kappa$ B- $\alpha$ , just as it is represented in the patent. (*See* AFF 213-15, 242-63, 271-87).

108. Lilly's assertion that "the skilled reader would assume that the 'I $\kappa$ B- $\alpha$ ' described in Figure 43 is mammalian" (LFF 72) lacks any factual or legal basis and in any event is irrelevant to the materiality of the sequence information presented in Figure 43.

109. Regarding Lilly's Proposed Findings of Fact 69-72, 78-83, the Court finds that Lilly has not provided clear and convincing evidence that the source (avian vs. mammalian) of the sequences in Figure 43 would be important to patentability.

110. Regarding Lilly's Proposed Findings of Fact 73-83, the Court finds that Lilly has not provided clear and convincing evidence that the alleged incompleteness of the amino acid sequence in Figure 43 would be important to patentability.

111. The '516 patent specification does not expressly or implicitly state that the sequences in Figure 43 are specifically mammalian I $\kappa$ B- $\alpha$ . (PTX 2A at col. 10, ll. 16-17).

112. In any case, the term I $\kappa$ B- $\alpha$  refers to a family of proteins that are grouped together by their function of inhibiting NF- $\kappa$ B. (Bench Trial Tr. Day 1 at 120:20-25). The asserted claims may be practiced by adding exogenous I $\kappa$ B- $\alpha$  to eukaryotic cells which would include cells of chickens; they do not require particular sequences. (Jury Trial Tr. Day 12 at 48:15-24).

113. One of skill in the art would understand that the type of activity associated with I $\kappa$ B- $\alpha$  could exist across different classes of organisms including mammals, such as mice, and chickens. (Bench Trial Tr. Day 1 at 120:20-25; 121:1-6).

114. Therefore, the mere fact that a particular experiment in the '516 patent discloses the isolation of I $\kappa$ B from 70Z/3 pre-B cells for use in one embodiment of the asserted claims would not make one of skill in the art believe that any I $\kappa$ B- $\alpha$  sequence disclosed in the patent must be a mouse or mammalian sequence.

115. Lilly's assertion that Figure 43 "includes sequences from a chicken protein called 'pp40'" (LFF 73), even accepted at face value, does not establish by clear and convincing evidence that there is any material error or misleading disclosure in the '516 patent that needed to be disclosed to the PTO.

116. The specification of the '516 patent identifies the pp40 protein found in avian cells, as well as the MAD-3 protein found in human cells, as I $\kappa$ B proteins capable of use in the claimed invention. (PTX 1 at col. 32, ll. 34-38; Jury Trial Tr. Day 13 at 83:11-19).

117. The evidence at trial further supports a finding of no material misrepresentation or omission since there was agreement in the art that pp40 is in fact an I $\kappa$ B capable of inhibiting NF- $\kappa$ B activity. (*See* AFF 256-61, 283).

118. Dr. Latchman previously testified to the jury that Figure 43 depicted the DNA and amino acid sequences for pp40. He later reversed himself at the bench trial and claimed that he had not realized there were discrepancies in the amino acid sequence of Figure 43 – after about 100 hours of work – until Lilly's new attorneys pointed it out to him. Dr. Latchman's untimely and unsupported opinion on this issue cannot be credited by the Court. (*See* AFF 271-82).

119. Even if Dr. Latchman's testimony were accepted by the Court, Lilly's arguments that the discrepancies found in the sequence of Figure 43 are in any way material to patentability of the claims of the '516 patent lack support in the record and are unfounded. Lilly has not proffered any evidence that the alleged differences between the amino acid sequence in Figure 43 and some other disclosure of the pp40 sequence (which Lilly does not clearly identify) would have any effect on its function as I $\kappa$ B- $\alpha$ . Thus, Lilly has not shown that the classification of the Figure as such is in error.

120. Lilly's allegation that "deletion of the carboxy-terminal amino acids blocks the ability of I $\kappa$ B- $\alpha$  to inhibit DNA binding of NF- $\kappa$ B" (LFF 76) is irrelevant. The evidence supports that, regardless of whether deletion of the carboxy-terminal amino acids of I $\kappa$ B- $\alpha$  blunts its ability to inhibit binding of NF- $\kappa$ B to DNA, truncated I $\kappa$ B is still able to interact with NF- $\kappa$ B in order to form an inactive complex. (DTX 24 at 653).

121. The Court rejects Lilly's argument (*see* LFF 75) that the alleged presence of 82 "extra" amino acids on the "amino" end of the molecule in Figure 43 supports that it is not an accurate representation of an I $\kappa$ B- $\alpha$  protein. Dr. Latchman testified that he was aware of the presence of these additional amino acids when he told the jury that Figure 43 depicted pp40. (Bench Trial Tr. Day 1 at 108:12-17). Thus, Lilly cannot be credited when it argues that these amino acids support some material mistake in the Figure.

122. Ariad's purported admission that Figure 43 does not fully correspond to the amino acid sequence for I $\kappa$ B- $\alpha$  (LFF 74) also does not further Lilly's argument in light of Dr. Latchman's admission that "extra" amino acids on the "amino" end of the molecule don't matter.

123. According to Dr. Latchman, as of November 1991 no one had yet published a clone which was named I $\kappa$ B- $\alpha$ . (Bench Trial Tr. Day 1 at 98:23-99:11). However, applicants disclosed relevant information to the examiner that documented the progress of classifying different types of I $\kappa$ B proteins and the source of pp40 and MAD-3. (*See* AFF 244-51).

124. For instance, the applicants had submitted to the examiner the Davis *et al.* 1991 paper which identifies the pp40 rel-associated protein as functionally related to I $\kappa$ B and the Haskill *et al.* 1991 article which first identified the MAD-3 clone as encoding a protein with I $\kappa$ B-like activity. *Id.* Both of these references are cited on the face page of the '516 patent and

were published before Ariad filed its November 1991 application. (PTX 1 at pp. 1-2); PTX 2A at ADL 0001410.17-1410.25, 1086-1089).

125. Dr. Latchman believed it was appropriate to characterize an amino acid sequence he considered to be “pp40-like” as pp40 to the jury. (Bench Trial Tr. Day 1 at 113:9-18, 118:9–119:3).

126. As reported in the Siebenlist *et al.* 1994 review paper – which was submitted to and considered by the examiner during prosecution of the ’516 patent – scientists established a consensus that both the pp40 and MAD-3 proteins are properly classified as I $\kappa$ B- $\alpha$ . (See AFF 258-60).<sup>6</sup>

127. In keeping with the practice of classifying I $\kappa$ B proteins according to their function and in light of the fact that no I $\kappa$ B- $\alpha$  sequence had yet been disclosed at the time of filing, applicants for the ’516 patent were well within their rights in calling the sequences in Figure 43 I $\kappa$ B- $\alpha$ . Later research in the field confirms the validity of this classification. (See AFF 256-63). Applicants’ choice of nomenclature for Figure 43 is not objectively incorrect.

128. Applicants also kept the examiner informed on relevant information concerning the classifications of I $\kappa$ B proteins so that the examiner could have made an informed determination about the nature of the sequences in Figure 43. (See AFF 244-51, 253-55, 258).

**b. Lilly’s Reliance on the Disclosure of Human Gene Therapy Does Not Support the Materiality of any Purported Error in Figure 43**

129. Lilly’s arguments (LFF 79-83) that the disclosure in the ’516 patent that the claimed invention had utility in the context of human gene therapy renders the representation of

---

<sup>6</sup> Lilly misleadingly cites to *Schering Corp. v. Amgen Inc.*, 222 F.3d 1347, 1354 (Fed. Cir. 2000) for the proposition that the conformation that pp40 belongs to the family of I $\kappa$ B- $\alpha$  in later art is not probative of materiality. *Schering* provides no support for Lilly’s position as it addressed proper claim scope, not materiality of information in the specification of a patent. *Id.*

Figure 43 as I $\kappa$ B- $\alpha$  a material error has no basis in law or fact. Lilly's generalities concerning the difficulties of human gene therapy are not relevant to materiality and are not supported by the record.

130. There is no evidence that a mammalian gene of I $\kappa$ B would be preferred over pp40 for human gene therapy.

131. Dr. Kadesch explained that those of skill in the art could apply published information and well known techniques of cloning and gene synthesis to obtain DNA sequences in order to practice the asserted claims. (Jury Trial Tr. Day 13 at 55:17–61:20).

132. Dr. Latchman also testified that one of skill in the art reading the disclosure of the '516 patent with Figure 43 would proceed to screen a library of human genes to find the clone. (Jury Trial Tr. Day 11 at 139:12–140:9). Thus, Dr. Latchman tacitly acknowledged that one of skill in the art would possess the knowledge to search for human DNA sequences to practice human gene therapy. Ariad did not need to disclose teachings already known in the art in order to support its claims.

133. Further, the jury heard Dr. Latchman's opinions regarding human gene therapy and nevertheless returned a verdict finding enablement and sufficient written description for the full scope of the asserted claims of the '516 patent. (D.I. 346 at 4). This also undermines Lilly's argument regarding alleged difficulties associated with using the sequences in Figure 43 for human gene therapy.

134. The jury also found that the asserted claims are entitled to priority from Ariad's '436 application filed in April of 1989 which did not include Figure 43. (*Id.*). Based on this determination, it is presumed that one of skill in the art could practice the full scope of the asserted claims without reliance on the disclosure in Figure 43 at all.

135. In addition to finding that the claims were supported without Figure 43, the jury's verdict necessarily also presumes that the November 1991 application which included Figure 43 enabled and described the full scope of the claims. Thus, the disclosure of Figure 43 as I $\kappa$ B- $\alpha$  did not render human gene therapy non-enabled.

136. Lilly's argument regarding human gene therapy is also premised on the misconception that the claims require a specific DNA sequence that may be used in human gene therapy. However, the claims are not so limited and therefore not subject to the requirements for identifying DNA according to its structure rather than by its function. *See Fiers v. Revel*, 984 F.2d 1164, 1169, 1171 (Fed. Cir. 1993) (claims to a DNA "having a particular biological activity or function . . . require[] a precise definition, such as by structure, formula, chemical name, or physical properties"). This principle, mistakenly cited by Lilly would only be relevant if the asserted claims recited particular DNA sequences in terms of their functional utility in human gene therapy applications.

137. The asserted claims describe methods for modifying the effects of extracellular influences by reducing NF- $\kappa$ B activity without limitation to particular DNA sequences. That human gene therapy is but one potential embodiment of these claims but does not place any heightened burdens on Ariad regarding the disclosures of DNA sequences in the patent beyond what is necessary to enable and describe the claimed invention.

**2. The Actions of Ariad's Attorneys Does Not Establish Any Material Error in Figure 43**

138. The Court rejects Lilly's arguments (LFF 89-109) that deletion of Figure 43 from the two divisional applications to the '516 patent by Ariad's attorneys supports a finding of a material error in Figure 43. Amendments to the figures in the divisional applications which

claimed certain assays has no bearing on the materiality of any alleged issue with Figure 43 to the '516 patent which contains wholly different claims. (*See* AFF 216-41, 264-70).

139. The attorneys that submitted the amendments in the divisionals deleting Figure 43, first Lisa Warren and then Isabelle Clauss, were no longer involved with the prosecution of the '516 patent when the claims that issued were allowed and had no knowledge of what the issued claims required. (*See* AFF 225, 228, 234-35).

140. At the time Ms. Warren submitted the amendment in the '266 divisional application, none of the present claims of the '516 patent were pending. (*See* DTX 967 at 21; PTX 2A at ADL 0000923-953, 10/4/01 Examiner's Amendment (proposing allowed claim language)).

141. After Ms. Warren originally submitted the amendment deleting Figure 43 in the '266 application and the prosecution of that application closed in 1997, the prosecution of its sister applications including the '516 patent was transferred from her firm, Hamilton Brooks Smith & Reynolds, to the Foley Hoag firm where Ms. Clauss worked. (Bench Trial Day 3 at 46:5-12, 49:8-10).

142. At neither the time Ms. Clauss submitted in the '397 application substantially the same amendment deleting Figure 43 as submitted in the '266 application nor the time she signed an amendment in the '266 application resubmitting the one originally filed (after it was misplaced the first time), were the present claims of the '516 patent pending. (*See* DTX 966 at 22; Clauss Dep. at 47:15-48:16, 49:8-50:17; PTX 2A at ADL 0000923-53, 10/4/01 Examiner's Amendment (proposing allowed claim language)).

143. As Lilly points out, the amendments in the divisionals cancelled numerous other figures in addition to Figure 43. (LFF 92). This fact merely underscores that Lilly has proffered

no clear and convincing evidence of intent to mislead the PTO, and that applicants did not attach any particular significance to the cancellation of Figure 43.

144. Ms. Clauss did not draft the amendments submitted in the '266 or '397 applications. (Clauss Dep. at 44:10–45:2, 63:22–64:3).

145. Ms. Clauss testified that she may have become aware of a purported issue with Figure 43 only by reading the amendment originally submitted by Ms. Warren in the '266 application. (*Id.* at 57:8-17). There is no evidence that Ms. Clauss ever performed any independent evaluation of the sequences in Figure 43 herself to determine whether there was any error in the figure.

146. Matthew Vincent worked with Ms. Clauss at Foley Hoag and had responsibility for the prosecution of the '516 patent application and related applications. (AFF 229). In early 2001 when Dr. Vincent moved to Ropes & Gray the prosecution of the '516 patent and related applications was transferred with him. (Bench Trial Tr. Day 3 at 44:1-6, 46:16-24). Ms. Clauss stayed at Foley Hoag and did not work on the '516 patent application thereafter. (Clauss Dep. at 32:1-13). Nor did Ms. Clauss have any further communications with Dr. Vincent or anyone else at Ropes & Gray concerning the subject matter of the '516 patent or its prosecution. *Id.*

147. As Lilly points out, Ms. Clauss only submitted the amendments in the divisional applications after the claims in those applications had been allowed. (*See* LFF 92, 100). Ms. Clauss testified that it was her practice to address possible problems with figures after allowance because to do otherwise would be impractical. (*Id.* at 64:4-18). Ms. Clauss also explained that such a determination regarding a figure would depend on a case by case analysis. (*Id.* at 64:19–65:7). Since, Ms. Clauss was no longer involved with the prosecution of the '516

patent at the time the claims were allowed she was not in a position to perform this assessment with respect to Figure 43 in the '516 patent.

148. Ms. Clauss also explained that, consistent with their understanding of the duty of candor, it was the policy in her practice with Dr. Vincent to not leave a figure in an application if they determined it was in error *and* they determined it was crucial to the claimed invention. (*Id.* at 65:8-17).

149. Ms. Clauss could not have had any particular belief as to the materiality of Figure 43 (whether it was right or wrong) to the issued claims of the '516 patent because she had ceased working on the prosecution of the '516 patent by the time the claims were drafted and allowed.

150. Dr. Matthew Vincent remained responsible for the prosecution of the patent when he moved to Ropes & Gray. Dr. Vincent was never made aware of any purported issue regarding Figure 43. (Bench Trial Tr. Day 3 at 64:18–65:3).

151. Lilly has not proffered any evidence as to how or why Sharon Hausdorff at Ariad may have reviewed Figure 43 in connection with the amendments submitted in the divisional applications. In any case, any statement or action Lilly offers by Sharon Hausdorff at Ariad regarding a purported error in Figure 43 is hearsay and not admissible to support the assertion that any of the applicants believed Figure 43 was erroneous.

**3. None of the Applicants for the '516 Patent or their Attorneys Intended to Deceive the Patent Office With Respect to Figure 43**

152. The Court rejects Lilly's Proposed Findings of Fact 110-31, because Lilly has not shown sufficient evidence that anyone with a duty of candor to the Patent Office involved with the prosecution of the '516 patent knowingly intended to conceal or misrepresent any

information concerning Figure 43. Instead, the Court adopts Ariad's Opening Findings of Fact 288-302.

153. Lilly has limited its allegations of inequitable conduct concerning Figure 43 to Isabelle Clauss and Matthew Vincent. (LFF 118). Although, Lilly mentions Sharon Hausdorff in its proposed findings of fact, it is precluded by its prior representation from accusing Ms. Hausdorff or anyone else within Ariad of inequitable conduct based on its prior representations. (See Letter of Charles Lipsey, Ex. A to Ariad's Opening Findings of Fact and Conclusions of Law).

154. In any case, Lilly has not adduced any evidence that any employee of Ariad committed inequitable conduct.

155. Ms. Clauss did not form any belief that a purported error in Figure 43 was material to the claims that issued in the '516 patent because she was no longer involved in the prosecution at the time the claims issued. (See ¶¶ 139-46, *supra*).

156. Any evidence that Ms. Clauss viewed the withdrawal of Figure 43 from the divisional applications as having any importance to the '516 patent application is equivocal at best. Contrary to Lilly's assertions, (LFF 119), Ms. Clauss testified only that she thought the information was "probably" material to claims in the '516 patent application that she cancelled less than a month after resubmitting the petition deleting the figures in the '266 application. (Clauss Dep. at 71:8-72:21; 73:5-12; PTX 2A at ADL 0000517-19). Moreover, Ms. Clauss did not prepare the amendments deleting Figure 43 from the divisional applications and did not perform any independent evaluation of what type of DNA or amino acid sequences the Figure actually depicted. (See ¶¶ 144-45, *supra*).

157. The Court rejects Lilly's suggestion that Ms. Clauss's submission of amendments in the divisional applications after allowance of the claims in those applications somehow supports a finding of inequitable conduct. (*See* LCL 99). The Court finds that it was Ms. Clauss's practice to wait until allowance of the claims in an application before addressing issues with the figures or entering other kinds of typographical and ministerial alterations. (Claus Dep. at 44:1-9, 64:4-18).

158. Since it was her practice to determine whether to correct figures in an application only after the claims were finally allowed, Ms. Clauss had no reason to make any corrections to the '516 patent application while the claims were still pending at the time she stopped working on it.

159. Ms. Clauss could not have intended to deceive the Patent Office with respect to any information concerning Figure 43 because she assumed that Dr. Vincent would make the appropriate determination as to whether or not the figures were germane to the claims at the time of allowance. (LFF 121).

160. There is no convincing evidence that Ms. Clauss actually told Dr. Vincent that there was any need to submit a petition for correction regarding Figure 43 in the '516 patent application. (Bench Trial Tr. Day 3 at 64:18-65:3). There is no convincing evidence that Dr. Vincent ever believed there was a material error in Figure 43. (AFF 292-95). Moreover, Lilly has not offered any evidence of culpable neglect to explain its assertion (LFF 126) that Dr. Vincent should have known of a purported error.

161. Contrary to Lilly's assertions regarding the general practice of Ms. Clauss and Dr. Vincent (LFF 124) there is no evidence that he reviewed the amendments Ms. Clauss submitted removing Figure 43 from the divisional applications. (Bench Trial Tr. Day 3 at

110:22–111:20; AFF 292-95). Even if he had seen the amendments, that alone is insufficient to support a finding that he believed cancellation of the figures to be material to the '516 patent and intended to conceal that information from the PTO.

162. In any case, Dr. Vincent explained that he would not have necessarily considered the cancellation of a large number of figures to be an extraordinary event. (Bench Trial Tr. Day 3 at 113:12-21). Lilly has not offered evidence that supports its assertion (LFF 104) that the deletion of several figures from an application is necessarily an unusual event in patent prosecution. Lilly has not adduced evidence to suggest that the cancellation of the figures from the divisional applications was anything more than a ministerial act.

163. During prosecution Dr. Vincent had hand delivered to the Patent Office the Davis and Haskill references disclosing the known I $\kappa$ B proteins. (PTX 2A at ADL 0000511-14). Davis in particular identifies the pp40 protein and describes it as having I $\kappa$ B-like functionality. (PTX 2 at ADL 0001086-89). Dr. Vincent's disclosure of this information to the examiner undermines any claim that Dr. Vincent intended to conceal information relating to the I $\kappa$ B protein identified in Figure 43.

164. Finally, the Court rejects Lilly's argument (LFF 110-17, 130, LCL 99-100) that the applicants' attorneys for the '516 patent were motivated to conceal a purported error in Figure 43 after they learned of it by a desire to avoid refiling the application and losing eligibility for a longer patent term as a pre-June 8, 1995 filer under the Uruguay Round Agreement Act ("URAA"). Lilly claims that Ms. Clauss was aware of the purported error in Figure 43 as of May 18, 1998. (See LFF 95). On June 10, 1998 she submitted her first amendment and response in the '516 patent application canceling the claims to which she said Figure 43 was "probably" material. (See ¶¶ 156, *supra*). If Ms. Clauss believed at that time that Figure 43 has raised an

issue with respect to any of the remaining pending claims she could have addressed it without any prejudice to Ariad's patent term.

165. At this time, the applicants for the '516 patent were not "out of time and out of options" as Lilly asserts. (LCL 99). The amendment and response Ms. Clauss filed was only the first of two after-final amendments applicants could file under the transitional rules.

166. Similarly, Dr. Vincent could not have had any motivation to conceal an error with Figure 43 in order to extend the patent term. If Ms. Clauss had indeed discussed it, Dr. Vincent would have been aware of the petition removing the Figure from the '266 application when Ms. Clauss refiled it – a time when Ariad still had the right to two transitional after-final responses in the '516 patent prosecution.

**4. Lilly Has Shown No Evidence That the Inventors Knowingly Withheld Material Information Bearing on Inherent Anticipation With Intent to Deceive the PTO**

167. The Court rejects Lilly's Proposed Findings of Fact 132-191 regarding the non-disclosure of information allegedly bearing on inherent anticipation. Instead the Court adopts Ariad's Opening Findings of Fact 42-136.

168. The Court finds that the cited references DTX 24, 25, 28 and 473 are cumulative and are not material. Lilly has failed to come forward with clear and convincing evidence that any one of these references would be considered important by a reasonable examiner.

**5. Dr. Baldwin is the Only Inventor That Lilly Now Alleges Knowingly Withheld Material Information With Intent to Deceive the PTO**

169. In connection with its inequitable conduct allegations, Lilly refers to six '516 patent inventors, Drs. Baltimore, Sharp, Maniatis, Baeuerle, Sen and Baldwin. (LCL 118). Only in the case of Dr. Baldwin does Lilly even attempt to explain the basis for its allegations. The Court finds none of the evidence that Lilly has specifically identified regarding these inventors,

including Dr. Baldwin, constitutes clear and convincing evidence supporting its allegations that they knowingly withheld material information with intent to deceive the PTO.

**6. Dr. Baldwin Did Not Withhold Material References From the Patent Office**

170. Lilly argues that Dr. Baldwin knew that four “prior art” compounds (glucocorticoids, salicylates, cyclosporin A and resveratrol) had been reported to inhibit NF-κB activity and was also aware that these compounds had been administered to people in the prior art. (See LFF 139-46). Lilly bases its argument on purportedly undisclosed information contained in two post-filing reviews, Baldwin 1996 (DTX 24S) and Baldwin 2001 (DTX 25), and two additional post-filing publications Dr. Baldwin co-authored, Scheinman *et al.* 1995 (DTX 28) and Holmes-McNary 2001 (DTX 473).<sup>7</sup> Lilly implies that Dr. Baldwin understood that this information was material, and therefore intentionally withheld material references from the PTO.

171. As to these four references, to the extent that Lilly relies on these references as purportedly disclosing use of glucocorticoids, salicylates, cyclosporin A or resveratrol to reduce NF-κB activity within the meaning of the claims, the Court finds these references all cumulative, and therefore not material, in view of references that applicants provided to the PTO during prosecution. (See AFF 47-732, 73, 75-76, 78-81, 84-85, 89, 92-94, 96, 99-100, 105-08, 111-15).

172. The Court rejects Lilly’s argument that the examiner would not have considered the disclosures in the submitted references regarding the potential for “old compounds” to inhibit NF-κB activity in terms of novelty. (LFF 151). Lilly has not overcome the evidence that the examiner indicated during prosecution that he considered these references in determining the applicants’ arguments for patentability and that this consideration was not limited to any one

---

<sup>7</sup> At trial, the Court did not allow DTX 28 or DTX 473 into evidence. Based on the rulings at the bench trial, Lilly may not rely on statements in references not accepted into evidence to support its allegations.

ground. (AFF 46-71). In particular, Lilly's assertion that, even applying a "cursory review" standard, the examiner would not have noticed the sentence in the first paragraph of the Fujihara reference regarding possible inhibitors of NF-kB activity is not convincing. (*See* LFF 172, 174).

173. Further, Lilly's reliance on the testimony of Dr. Vincent as to why applicants submitted certain references to the examiner with the Baltimore declaration is unavailing. (LFF 163-65). Taken in context, Dr. Vincent only stated that "we cited the references with the understanding that they proved patentability" and he did not indicate that there was any limitation as to what issues they expected the examiner to review them for. (Bench Trial Tr. Day 3 at 108:25-109:1).

174. Even if the references Lilly cites were not cumulative, these references could only have a minimal degree of materiality in view of the jury finding that none of the references Lilly relied on at trial provided evidence that prior use of any compound used any of the claimed methods. (*See* AFF 80-82, 94-95, 97-98, 107, 109-10, 113-15).

175. The Court finds there is no clear and convincing evidence in the trial record that even if Holmes-McNary 2001 (DTX 473) were not cumulative, that any of the information in Holmes-McNary 2001 would be material. No expert testified on the disclosure of DTX 473 and the article was never identified as a deposition exhibit by any witness.

176. Lilly has not identified any evidence in the record demonstrating that in red wine, resveratrol functions as an active ingredient. There is no clear and convincing evidence in the record that red wine affects NF-kB.

177. Lilly has not identified any evidence in the record that red wine contains resveratrol in the same chemical form as used in the experiments reported in Holmes-McNary 2001 (DTX 473). The purity of resveratrol is always an issue as to the potential effects that

resveratrol might have in a particular system. (Baldwin Depo. Tr. at 170:21–171:4). Lilly has not identified any evidence that resveratrol in the same form as used in Holmes-McNary 2001 was ever used in human or mammalian cells in the prior art.<sup>8</sup>

**7. Dr. Baldwin Did Not Intend to Deceive the Patent Office**

178. The Court rejects Lilly’s Proposed Findings of Fact 192 and Conclusions of Law 101-02 regarding an alleged intent to deceive. Instead the Court adopts Ariad’s Opening Findings of Fact 137-57.

179. The Court finds that Dr. Baldwin did not withhold DTX 24, 25, 28, 473 or any other reference with an intention of deceiving the PTO.

180. Lilly implies that since there is no evidence that Dr. Baldwin retracted DTX 24, 25, 28 or 473, he must have understood the information in these publications as reliable and therefore material. (*See* LCL 101). The Court finds no basis for this inference.

181. Regarding studies his laboratory conducted with glucocorticoids and with resveratrol, Dr. Baldwin explained that while he stood by the results he obtained in the particular experimental systems he used, other investigators had not been able to reproduce his results in different experimental systems. (Baldwin Depo. Tr. at 170:9–171:14, 202:23–203:6, 205:5–18, 222:19–223:24).

182. In view of the contradictory findings and lack of reproducibility between different investigators, Dr. Baldwin did not believe that the results of his studies could be generalized. (Baldwin Depo. Tr. at 157:2–13, 202:23–203:6, 205:5-18, 207:14-19, 169:10–171:4). For example, Dr. Baldwin did not consider his studies to provide data linking his findings with what

---

<sup>8</sup> Lilly listed its expert on red wine and resveratrol as Dr. Jesus Egido on the pretrial order and indicated it would call him as a live witness. (D.I. 236). Lilly never presented him as a witness at either trial.

happens necessarily during administration of glucocorticoids to humans. (Baldwin Depo. Tr. at 207:14–208:7, 208:11-12).

183. Lilly argues that Dr. Baldwin’s two review articles indicate that Dr. Baldwin also knew that other post-filing references had reported that salicylates and cyclosporin A had been observed to inhibit NF-kB activity. The Court disagrees that such evidence warrants an inference that Dr. Baldwin understood or believed such information was material to patentability of the claimed invention of the ’516 patent.

184. For example, Dr. Baldwin indicated that where he had not done the experiments, he had no way of knowing whether work done by others that he cited in his review articles was accurate or not. (Baldwin Depo. Tr. at 232:13–233:17). In fact, Dr. Baldwin indicated that much of the reported work on the ability of compounds to reduce NF-kB in defined laboratory experiments “has not been reproducible,” and had “not withstood scientific evidence.” (Baldwin Depo. Tr. at 143:23–144:17, 146:11-20).

185. In view of the contradictory findings and lack of reproducibility between different investigators, Dr. Baldwin did not believe that the results of post-filing studies on the effects of cyclosporin A or salicylates on NF-kB could be generalized. (Baldwin Depo. Tr. at 172:6–173:17, 231:20–234, 232:13–233:17, 154:15–19, 165:3–17, 167:25–168:13). Given the ambiguity of these findings, he did not believe it was necessary to disclose such information to the PTO. (*Id.* at 144:12-17, 167:25–168:13).

186. In this regard, the Court is unconvinced that the single comment by Dr. Baldwin that he would not want to inundate the PTO with “every report – of things that affect NF-kappa.B one way or the other” provides any evidence of intent to deceive the PTO. (*See* LFF 149 (emphasis added)).

**8. None of the Other Inventors Intended to Withhold Material References**

187. Lilly identifies no evidence from the trial record indicating that Dr. Baltimore, Dr. Sharp or Dr. Maniatis was aware of any specific reference that Lilly contends was allegedly withheld from the PTO, or that they intentionally withheld any such reference from the PTO. Lilly's vague contention that these inventors were aware of "developments" and a "body of literature after the filing date of the '516 patent" has not been proven by clear and convincing evidence and cannot form a basis for inequitable conduct. (LCL 118). Further, both before and during the bench trial, Lilly did not base any of its allegations on the failure of Dr. Sharp or Dr. Maniatis to disclose references to the PTO. (*See* AFF 42-45). Lilly therefore waived any right to do so now.

188. Apart from Dr. Baldwin, Dr. Baeuerle and Dr. Sen are the only other inventors Lilly mentions in connection with its allegations of inequitable conduct. (*See* LCL 118). Lilly's only basis for alleging these inventors intended to deceive the PTO is its argument that three post-filing articles were not disclosed to the PTO: one post-filing review article co-authored by Dr. Baeuerle (Baeuerle and Henkel 1994 DTX 303 at 149) and two post-filing publications co-authored by Dr. Sen (Wang *et al.* 1999 DTX 87; McCaffrey *et al.* 1994 DTX 88). (*See* LCL 118).

189. There is no evidence in the trial record of the materiality of any of these references. Lilly did not raise any of these references either at the jury trial or at the bench trial. As such, the Court finds Lilly has waived any right to rely on these references in support of its allegations on inequitable conduct. Based on the rulings at the bench trial, Lilly may not rely on or cite references not accepted into evidence in support of its allegations. The Court rejects Lilly's attempts to now designate these references as evidence and holds these references inadmissible based on its prior rulings. (*See* AFF 45).

190. The Court finds, further, that had it been allowed in evidence, the Baeuerle and Henkel 1994 review (DTX 303 at 149), to the extent it purportedly proposes an autoregulatory loop model, is cumulative and therefore not material to information already before the examiner, including Shao-Cong Sun *et al.* (1993) (PTX 2A at ADL 0000637-40), Gilmore and Morin (1993) (PTX 2 at ADL 0000642-47), Finco and Baldwin (1995) (PTX 2 at ADL 0000675-84) and Siebenlist *et al.* (1994) (PTX 2A at ADL 0000649-73).

191. There is no evidence in the record that at any time during prosecution Dr. Baeuerle believed that any statements made in the Baeuerle and Henkel 1994 review (DTX 303) were material to the claimed invention of the '516 patent. At best, Lilly implies only that the review contained material information that Dr. Baeuerle should have disclosed. In the absence of any evidence of intent on the part of Dr. Baeuerle, the Court finds that the trial record provides no basis from which to infer that Dr. Baeuerle withheld any information with intent to deceive the PTO.

192. The Court finds, further, that had it been allowed in evidence, Wang *et al.* (DTX 87), to the extent it purportedly discloses use of glucocorticoids to reduce NF-kB activity within the meaning of the asserted claims, is cumulative and therefore not material, in view of Siebenlist and Fujihara (PTX 2 at ADL 00000649, 904).

193. There is no evidence in the record that Wang *et al.* (DTX 87) provides additional information about the potential effect of glucocorticoids beyond Scheinman (DTX 28), which the Court holds is cumulative and therefore not material, in view of Siebenlist and Fujihara. (*See* AFF 76, 78, 80). Thus, there is no evidence in the record that Wang *et al.* (DTX 87) provides any additional information that would render it reliable and non-cumulative, in view of Siebenlist and Fujihara (PTX 2 at ADL 00000649, 904).

194. The Court finds, further, that had it been allowed in evidence, McCaffrey *et al.* 1994 (DTX 88), to the extent it purportedly discloses use of cyclosporin A to reduce NF-kB activity within the meaning of the asserted claims, is cumulative and therefore not material, in view of Siebenlist (PTX 2 at ADL 0000661).

195. There is no evidence in the record that McCaffrey *et al.* 1994 (DTX 88) provides additional information about a potential effect of cyclosporin A on NF-kB beyond Baldwin 1996 (DTX 24A), which the Court holds is cumulative and therefore not material, in view of Siebenlist. (*See* AFF 85, 89, 94). Thus, there is no evidence in the record that McCaffrey *et al.* 1994 (DTX 88) provides any additional information that would render it reliable and non-cumulative, in view of Siebenlist (PTX 2 at ADL 0000661).

196. There is no evidence in the record that at any time during prosecution, Dr. Sen believed that any information about cyclosporin A in Wang *et al.* (DTX 87) or in McCaffrey *et al.* 1994 (DTX 88) was material to the claimed invention of the '516 patent. At best, Lilly implies only that these publications constituted material information that Dr. Sen should have disclosed. In the absence of any evidence of intent on the part of Dr. Sen, the Court finds that the trial record provides no basis from which to infer that Dr. Sen withheld any information with intent to deceive the PTO.

**B. Conclusions of Law Regarding Inequitable Conduct**

197. The Court rejects Lilly's Proposed Conclusions of Law 75-120 regarding inequitable conduct. Instead, the Court adopts Ariad's Opening Conclusions of Law 509-60.

198. Balancing all the proffered evidence of materiality and intent, the Court concludes that none of the applicants or their attorneys or anyone else involved with the prosecution of the '516 patent owing a duty of candor to the Patent Office committed inequitable conduct.

**1. Lilly Did Not Withhold or Misrepresent Any Material Information Regarding Figure 43 From the Patent Office**

199. Lilly has not established by clear and convincing evidence that any material error exists in Figure 43. Instead, the evidence supports that the applicants were correct in identifying Figure 43 as the DNA and amino acid sequences for an I $\kappa$ B- $\alpha$  protein.

200. Lilly has not offered clear and convincing evidence that Figure 43 does not accurately depict a pp40 amino acid sequence.

201. The Court concludes that the information contained in Figure 43 is in no way misleading and does not inhibit the practice of any of the embodiments of the invention provided in the '516 patent.

202. The jury verdict finding that the asserted claims are fully described and enabled by the specification and that this support existed even without Figure 43 as of the filing of Ariad's April, 1989 application also strengthens the conclusion that there is no issue with Figure 43 material to the claimed invention.

203. Lilly's arguments regarding experiments involving mammalian cells and applications of the claimed invention in human gene therapy misconstrue the standard of what is considered important to issues of patentability under § 112. The asserted claims are directed to methods of manipulating induced NF- $\kappa$ B activity in cells without limitation to particular applications in gene therapy.

204. In *Fiers*, the Federal Circuit reiterated that claims to DNA having a particular biological activity or function must be defined other than by that biological activity or function alone. 984 F.2d at 1169-71; *see also Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997) ("An adequate written description of a DNA . . . 'requires a precise definition, such as by structure, formula, chemical name, or physical properties.'"). However,

this rule is limited to claims reciting particular DNA sequences or chemicals defined in terms of their functional utility. *See, e.g., Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1320-21 (Fed. Cir. 2003); *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927 (Fed. Cir. 2004). The asserted claims are directed to methods of manipulating induced NF- $\kappa$ B activity in cells without limitation to particular DNA or amino acid sequences.

205. Moreover, the Federal Circuit later clarified that “Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.” *Moba*, 325 F.3d at 1320 (quoting *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003)) (emphasis added); *accord Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002) (“It is not correct . . . that all functional descriptions of genetic material fail to meet the written description requirement.”); *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005) (“The descriptive text needed to meet [the written description requirement] varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence.”). Since one of skill in the art would understand the DNA and amino acid sequence in Figure 43 to be I $\kappa$ B- $\alpha$  (*see* AFF 218), the claims would be adequately described even were the *Lilly* rule to apply.

206. Additionally, the recent *Falko-Gunter Falkner v. Inglis* case in the Federal Circuit makes clear that applicants need not specifically describe DNA nucleotide sequences that are already published in the art in order to provide adequate written description. “Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here ‘essential genes’), satisfaction of the written

description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences.” *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1368 (Fed. Cir. 2006).

207. Here, the claims are not even limited to particular or “essential” genes. Nonetheless applicants for the ’516 patent still disclosed to the examiner the Davis reference known in the art in September, 1991 (prior to the filing of the November, 1991 application in which Figure 43 was added) that provides the DNA sequence and predicted amino acid sequence for pp40 and identified it as IκB-α.

208. The withdrawal of Figure 43 from the divisional applications after their claims were allowed does not support the existence of any issue with the figure material to the claims that issued in the ’516 patent. The claims pending in the ’516 patent at the time Figure 43 was withdrawn from its divisional applications were all subsequently cancelled.

209. PTO Rule 1.56 specifically states that “information material to the patentability of a claim that is cancelled or withdrawn from consideration need not be submitted if the information is not material to the patentability of any claim remaining under consideration in the application.” 37 C.F.R. § 1.56; *see also Kimberly-Clark Corp. v. Johnson & Johnson*, 745 F.2d 1437, 1457 (Fed. Cir. 1984) (“the key issues of materiality and intent should be decided with reference to the claims of the patent. What we see here, however, is an attempt by defendants to build a case of ‘fraud’ by reason of non-disclosure of prior art material only to abandoned claims long since cancelled during prosecution after being rejected by the examiner as unpatentable for reasons not involving the uncited prior art. To base a conclusion of ‘fraud’ on such grounds is to deal with a hypothetical situation, not with reality.”).

210. However, Lilly cites *Fox Industries* for the proposition that “the Court must look to the patent’s entire prosecution history,” and that a “court may look beyond the final claims to their antecedents” when deciding issues of inequitable conduct. (Lilly CL80 (citing *Fox Indus., Inc. v. Structural Pres. Sys., Inc.*, 922 F.2d 801, 803-04 (Fed. Cir. 1990))). Lilly’s use of *Fox* is misplaced. *Fox* involved a series of three continuation applications and the nondisclosure of an anticipatory brochure that described the entirety of the structure set forth in most of the issued claims. As the Federal Circuit explains, “*Fox* simply applies the principle long held in this court that omission of a reference material to certain claims cannot be cured simply by canceling or amending those claims during prosecution so that they do not issue in the same form in which they were drafted.” *Baxter Int’l, Inc. v. McGaw, Inc.*, 149 F.3d 1321, 1331 (Fed. Cir. 1998).

211. The “fruit of the poisonous tree” doctrine that *Fox Industries* applies which holds that inequitable conduct in one application may infect related applications has no bearing on the situation in issue in which post-allowance corrections in divisional applications are offered as evidence of materiality. Lilly has not offered clear and convincing evidence that the withdrawal of Figure 43 and numerous other figures from the divisional applications was anything more than a ministerial act or that it had any materiality to the claims that ultimately issued in the ’516 patent.

212. The Court also rejects Lilly’s contention that arguments made by Ms. Clauss and Dr. Vincent relying on the disclosure of I $\kappa$ B during prosecution of the ’516 patent support the existence of a material misrepresentation regarding Figure 43’s depiction of I $\kappa$ B. (LFF 97-98). When Dr. Vincent submitted the response containing the argument to which Lilly refers, he had hand delivered together with the response an Information Disclosure Statement containing the Davis 1991 reference describing the pp40 sequence as an I $\kappa$ B- $\alpha$  protein. (PTX 2A at 0000511-

40). These were both received by the Patent Office on June 11, 1998. Thus, the examiner was also in possession of the information contained in Davis when Ms. Clauss submitted the response in 1999 which Lilly cites as referring to DNA encoding I $\kappa$ B.

213. As a matter of law, such attorney arguments cannot constitute misrepresentations where, as here, the Patent Office can judge the argument for itself based on available information. *See, e.g., Akzo N.V. v. United States Int'l Trade Comm'n*, 808 F.2d 1471, 1482 (Fed. Cir. 1986) (holding that an argument for distinguishing prior art, even though favorable to the applicant's position, was not a material misrepresentation because the examiner could reach his/her own conclusions regarding the prior art).

214. Furthermore, at the time Dr. Vincent and Ms. Clauss submitted arguments to the Patent Office relying on the disclosure in the patent to support the expression of I $\kappa$ B, there was pending a claim specifically reciting "a gene construct for expressing an I $\kappa$ B polypeptide..." (PTX 2A at ADL0000525, 598). Applicants later cancelled this claim. Thus, even assuming *arguendo* that Dr. Vincent's and Ms. Clauss's arguments for patentability in the responses Lilly cites were entirely dependent upon an I $\kappa$ B protein sequence, these arguments were directed to a claim that was cancelled. Therefore, these attorney arguments cannot support materiality with reference to any claim for which applicants sought allowance.

215. Finally, the Court concludes that applicants' attorneys' submission of both the Davis 1991 reference and the Haskill 1991 reference disclosing the MAD-3 clone for human I $\kappa$ B renders cumulative any information concerning the petitions of correction in the divisional applications regarding Figure 43.

**2. No Material References Were Withheld From the Patent Office During Prosecution of the '516 Patent**

216. Lilly has not offered clear and convincing evidence that any of the four after art references concerning “old compounds” it asserts were inequitably withheld during prosecution of the '516 patent are material.

217. Cumulative references cannot be material; 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 the Univ. of California*, 119 F.3d at 1574-75; *Symbol Techs. Inc. v. Opticon, Inc.*, 935 F.2d 1569, 1582 (Fed. Cir. 1992). The references Lilly cites do not provide any information concerning the possible effects of “old compounds” on NF- $\kappa$ B activity that was not already before the examiner of the '516 patent in the Siebenlist, Fujihara and Yan references or the February 2001 Baltimore declaration disclosed by applicants during prosecution. (*See* AFF 54-71). Therefore, the Court concludes that the references Lilly cites are cumulative.

218. Lilly has not established that the examiner would not have considered the disclosed references for all issues of patentability, including § 102. This contention is undermined by the fact of the examiner's indication in the file history that he considered the references and specifically reviewed the references Ariad cited in its September 12, 2001 response, including Fujihara, the Baltimore declaration and Yan, in making the determination that the claims were allowable. (*See* AFF 65-66). Moreover, Lilly's contention that novelty would not have been a consideration in reviewing these references is undermined by its own arguments elsewhere that “the issue of inherent anticipation was at the forefront of examination for several years.” (LCL 116).

219. The conclusion that the cited references lack materiality is also buttressed by the lack of evidence showing that the results described therein could be reliably extrapolated back to the conditions under which “old compounds” were administered in the prior art. (*See* Jury Trial Tr. Day 13 at 28:9–29:15; Day 12 at 111:8–111:25, 142:18–144:16, 146:9–147:3).

220. The jury verdict holding that the asserted claims were not anticipated by the prior administration of glucocorticoids, aspirin or other salicylates, cyclosporin A, red wine or any other prior art compound also suggests that the cited references which pertain to the purported effects of such compounds on NF- $\kappa$ B activity should be accorded only minimal materiality, if any.

221. According to Lilly, Ariad contends that the decision in *Therma-Tru Corp. v. Peachtree Doors, Inc.*, 44 F.3d 988 (Fed. Cir. 1995), “precludes consideration of the materiality of the Baldwin publications in view of the jury verdict on anticipation.” (LCL 110). Lilly has misconstrued Ariad’s position. Ariad simply stated that the jury verdict “constrains the findings in this case,” and that, based on the verdict, the Court should accord the references minimal materiality. (ACL 534-35).

222. Regardless of Lilly’s attempts to confuse the issue, the holding of *Therma-Tru* is clear. As even Lilly recognizes, *Therma-Tru* held that a finding of materiality must not contravene a jury’s findings with respect to validity. (LCL 111). As the Federal Circuit explained, “[t]he avoidance of conflict with the implied findings underlying the jury verdicts of infringement and validity weighs against the district court’s finding that material information was withheld.” *Therma-Tru*, 44 F.3d at 995. The cases Lilly cites are not to the contrary – for they merely state that the test for materiality is what a reasonable patent examiner would consider (LCL 113), a point with which Ariad agrees. (*See* ACL 534 (the jury verdict “informs

the Court's determination of whether a reasonable examiner would have considered such evidence [to be material]”). Therefore, as properly informed by the jury verdict, the Court concludes that these references would be accorded minimal materiality if they were not cumulative.

223. Also, there is no evidence that a reasonable examiner would have considered the cited post-filing references material in light of the guidelines in effect in the MPEP at the time which required allegedly inherent features to be contemporaneously recognized in the prior art to support an anticipation rejection and several cases at the time that also held there was a contemporaneous recognition requirement for inherent anticipation. (*See* AFF 120-21). The MPEP and the caselaw concerning contemporaneous recognition did not change until after issuance of the '516 patent. (*See* AFF 122).

224. The Court does not credit Lilly's argument that there was no shift in the law of inherency toward eliminating contemporaneous recognition after issuance of the '516 patent. As Lilly's counsel has argued to the Supreme Court,

Following [the Supreme Court's] teaching, the federal courts, including until recently the Federal Circuit, routinely opined that there could be no inherent anticipation based on the unintended, unappreciated results of prior art. . . . The Federal Circuit abandoned [the Supreme Court's] limited inherent anticipation doctrine in *Schering Corp. v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373 (Fed. Cir. 2003).

*SmithKline Beecham Corp. v. Apotex Corp.*, 2005 WL 2652620, \*13, \*15 (Oct. 13, 2005)

(Petition For a Writ of Certiorari).

225. The Court therefore concludes that Lilly has failed to establish that a reasonable examiner would have applied post-filing art to an analysis of inherent anticipation while the

Federal Circuit and the Patent Office were indicating that a contemporaneous recognition requirement applied.

**3. There is No Evidence That Anyone Involved With the Prosecution of the '516 Patent Had Any Intent to Deceive the Patent Office**

226. Lilly argues that applicants “who ‘make no effort to offer a good faith explanation’” for why a reference was not cited, beyond mere conclusory statements, “cannot avoid an inference of wrongful intent.” (LCL 87 (citing *Bruno Indep. Living Aids, Inc. v. Acorn Mobility Servs., Ltd.*, 394 F.3d 1348, 1354 (Fed. Cir. 2005); and quoting *Critikon, Inc. v. Becton Dickinson Vascular Access, Inc.*, 120 F.3d 1253, 1267 (Fed. Cir. 1997))). Lilly is simply wrong. This is neither a correct statement of those cases, nor a correct statement of the law of intent.

227. As a later Federal Circuit case points out, “in *Bruno Living* . . . there were circumstances beyond the lack of a good faith explanation from which one could infer intent.” *M. Eagles Tool Warehouse, Inc. v. Fisher Tooling Co.*, 439 F.3d 1335, 1342 (Fed. Cir. 2006).

228. In *M. Eagles*, the Federal Circuit specifically addressed whether lack of a good faith explanation is sufficient to find intent – and held that it is not. The Court stated that, “[w]hen the absence of a good faith explanation is the only evidence of intent, . . . that evidence alone does not constitute clear and convincing evidence warranting an inference of intent.” *Id.* at 41. In *M. Eagles*, “there [was] no evidence from which to infer intent beyond the lack of a good faith explanation for the nondisclosure,” and thus the Court held that, “[w]ithout any other evidence of intent, we cannot find that a lack of a good faith explanation for the nondisclosure is sufficient to constitute clear and convincing evidence that [the patentee] acted with a culpable intent to deceive the PTO.” *Id.* at 1342-43.

229. Therefore, the Court holds that Lilly has failed to prove by clear and convincing evidence that anyone involved with the prosecution of the '516 patent acted with an intent to

deceive the Patent Office. Even were Lilly correct that there is no “credible explanation for the nondisclosure of material information” (LFF 131), without some other factual basis, the mere lack of a good faith explanation is insufficient to support a finding of culpable intent as a matter of law. *See also id.* at 42 (citing *Hebert v. Lisle Corp.*, 99 F.3d 1109, 1116 (Fed. Cir. 1996)).

230. “To establish inequitable conduct, the information that is known to the applicant and not provided to the PTO must be both material to patentability and withheld in order to deceive or mislead the examiner. An applicant cannot be held to have acted inequitably for not providing the examiner with information that was not material and that was not culpably withheld.” *Hebert*, 99 F.3d at 1115 (emphasis added); *see also id.* (inequitable conduct “requires proof, by clear and convincing evidence, that material information was withheld from the patent examiner, with the intent thereby to deceive or mislead the examiner into granting the patent”).

231. “[A] finding of deceptive intent can not be based on mere inference or even on gross negligence; there must be ‘conduct, viewed in light of all the evidence, including evidence indicative of good faith, [that] must indicate sufficient culpability to require a finding of intent to deceive.’” Intent to deceive cannot be inferred solely from the fact that information was not disclosed; there must be a factual basis for a finding of deceptive intent. *Hebert*, 99 F.3d at 1116 (quoting *Kingsdown Med. Consultants Ltd. v. Hollister, Inc.*, 863 F.2d 867, 876 (Fed. Cir. 1988)).

232. Lilly has not offered any evidence to support a conclusion that Ms. Claus acted with an intent to deceive the Patent Office. That Ms. Claus did not disclose the deletion of Figure 43 from the ’397 and ’266 applications in the ’516 patent cannot constitute inequitable conduct, because the claims pending in the ’516 patent at the time were cancelled. Moreover, Ms. Claus was no longer involved in the prosecution of the ’516 patent at the time the claims

were amended to the form in which they ultimately issued. The evidence supports Ms. Clauss's good faith belief that Figure 43 was not crucial to the claimed invention of the '516 patent and that if necessary any issue with the figures would be addressed by Matthew Vincent at the time of allowance.

233. The evidence also supports Dr. Vincent's good faith belief that there was no error in Figure 43. Lilly has not offered any evidence to suggest that Dr. Vincent viewed any deletions of figures by Ms. Warren or Ms. Clauss in the divisional applications which issued as the assay patents to have any bearing on the claims he prosecuted to issuance in the '516 patent. The Court concludes that Dr. Vincent had no intent to conceal or misrepresent anything about Figure 43 during prosecution and therefore did not commit inequitable conduct.

234. Based on the trial record, the Court also finds no clear and convincing evidence that at any time during prosecution, Dr. Baldwin understood or believed any of the four references Lilly alleges he failed to disclose were material to the patentability of the claimed invention of the '516 patent. The Court finds that Dr. Baldwin's testimony indicates a good faith basis for believing that there was no reason these references had to be provided to the PTO. The Court therefore concludes that Dr. Baldwin did not culpably withhold any material information with the intent to mislead or deceive the PTO and therefore did not commit inequitable conduct.

#### **IV. PROSECUTION LACHES**

##### **A. Findings of Fact**

235. The Court rejects Lilly's Proposed Findings of Fact 193-234 regarding prosecution laches. Instead the Court adopts Ariad's Opening Findings of Fact 303-58.

236. The Court finds that neither the applicants for the '516 patent nor their attorneys engaged in any unreasonable or inexplicable delays during prosecution. Lilly has provided no

evidence that any of the applicants or their attorneys engaged in deliberate and egregious delays to prolong prosecution.

237. The Court rejects Lilly's inference that either the applicants or their attorneys took advantage of any procedural rules to delay prosecution. In view of the complex nature of the invention, that applicants availed themselves of the full statutory six month period for responding to office actions does not constitute unreasonable delay.

238. Similarly, that applicants availed themselves of transitional practice rules to continue prosecution after final rejections does not constitute unreasonable delay. Such procedures were established after the harmonization of patent terms under the URAA agreement to prevent prejudice to applicants with then pending applications. These transitional procedures were allowed as of right to all similarly situated applicants.

239. Unlike the applicant in *Symbol*, there is no evidence that after having claims allowed or issued, applicants here engaged in a strategy of redrafting claims to cover commercially marketed applications of their invention.

**B. Conclusions of Law**

240. The Court rejects Lilly's Proposed Conclusions of Law 121-32 regarding prosecution laches. Instead the Court adopts Ariad's Opening Conclusions of Law 561-69.

241. The defense of prosecution laches will apply only if Lilly can demonstrate by clear and convincing evidence that the '516 patent was obtained after an unreasonable and unexplained delay in prosecution. (*See* ACL 561-62). This Lilly has failed to do.

242. As recently noted, "only one district court . . . has found prosecution laches, and in that case the delays were as long as 39 years." *Kothmann Enters., Inc. v. Trinity Indus., Inc.*, 2006 WL 89838, at \*31 (S.D. Tex. Jan. 13, 2006). That is because laches is a remedy to be used

“sparingly in only the most egregious cases.” *Symbol Techs. v. Lemelson Med., Educ. & Research Found., LP*, 422 F.3d 1378, 1385 (Fed. Cir. 2005).

243. Here, Lilly has failed to prove that the prosecution of the '516 patent was unreasonable, much less that it was “most egregious.” For instance, there is no evidence in the record of how the prosecution of the '516 patent compares to other patent prosecutions in the field of biotechnology, and there is no evidence that the practices Ariad engaged in during prosecution were different from those for other biotechnology patents.

244. Nor is there evidence in the record that the pendency of the '516 patent was significantly longer than that of similar pioneering biotechnology inventions. Ariad's applications covered an extensive body of pioneering work by 13 inventors; for instance, the '898 CIP was recognized by the PTO as constituting 21 separate inventions. (*See* AFF 313). Although Lilly infers that three years is typical for patents generally (LFF 206), the face of Lilly's own patent on methods of NF- $\kappa$ B modulation shows that it took them eight years to prosecute it. (PTX 3).

245. Lilly argues that the prosecution history of the '516 patent “spanned over 16 years from January 9, 1986, to its issue date of June 25, 2002.” (LCL 121). To begin with, the proper measurement of the pendency of the prosecution cannot extend beyond the priority date.

246. Since the jury decided that the effective filing date of the '516 patent is April 21, 1989 (D.I. 346), the Court finds that the pendency of the '516 patent is, at the longest, thirteen years. Moreover, since Ariad was under no duty to prosecute divisional applications in parallel (*see* AFF 334, ACL 565), it is reasonable to measure the prosecution of the '516 patent as extending back only to June 5, 1995, the date when the '364 application was filed. (*See* AFF 335; PTX 1 at ADL 000001; DTX 2).

247. In *Symbol* – the only district court case finding laches – the delays were so “extraordinary” that the patents at issue “occupied the ‘top thirteen positions’ for the longest prosecutions from 1914 to 2001.” 422 F.3d at 1386. Nevertheless, laches is not found by merely measuring the length of prosecution, but rather by proving that the prosecution contained delays that were unreasonable or unexplainable. *See, e.g., Stambler v. RSA Sec., Inc.*, 243 F. Supp. 2d 74, 76 (D. Del. 2003) (“Considering the prosecution history as a whole, seven years does not represent an unreasonable delay.”); *Gen-Probe Inc. v. Vysis, Inc.*, No. 99-CV-2668H, 2002 U.S. Dist. LEXIS 25020, at \*122 (S.D. Cal. Aug. 5, 2002) (“[T]he Court finds that the eleven years between filing and issuance of the . . . patent is not unreasonable.”); *Kothmann*, 2006 WL 89838, at \*31 (citing six cases where laches was not found, with delays of between seven and fifteen years).<sup>9</sup>

248. Moreover, Lilly must prove that the delays occurred by reason of culpable neglect. *See In re Bogese*, 303 F.3d 1362, 1366 (Fed. Cir. 2002); *Symbol Techs. Inc. v. Lemelson*

<sup>9</sup> Moreover, even a cursory look through the case law reveals numerous other examples of patent prosecutions that extended far beyond a three year period, covering a century of patent practice and a wide range of art. *See, e.g., Rohm & Haas Co. v. Brotech Corp.*, 127 F.3d 1089, 1090 (Fed. Cir. 1997) (23 and 25 years for two patents on copolymer beads and processes for their preparation); *Oakley, Inc. v. Sunglass Hut Int’l*, 2001 WL 1683252, at \*2 (C.D. Cal. Dec. 7, 2001) (16 years for colored films for sunglasses); *In re Bolinger*, 356 F.2d 552 (C.C.P.A. 1966) (14 years for a method and apparatus for crimping yarn); *Evans Med. v. Am. Cyanamid Co.*, 11 F. Supp. 2d 338, 346 (S.D.N.Y. 1998) (8, 10 and 12 years for three patents on antigens and vaccines for whooping cough); *Gen. Elec. Co. v. De Forest Radio Co.*, 44 F.2d 931, 938 (3d Cir. 1930) (12 years for a vacuum tube); *ConnectTel, LLC v. Cisco Sys., Inc.*, 2005 WL 366966, at \*3 (E.D. Tex. Feb. 16, 2005) (eleven years for telephone routing technology); *STX, Inc. v. Brine, Inc.*, 37 F. Supp. 2d 740, 746 (D. Md. 1999) (eleven years for improvements to lacrosse sticks); *Syngenta Seeds, Inc. v. Monsanto Co.*, 2004 WL 2106583, at \*1 (D. Del. Sept. 8, 2004) (ten years for patents relating to insect resistant seeds); *Laitram Corp. v. Morehouse Indus., Inc.*, 1997 WL 33320572, at \*1 (E.D. Cal. April 24, 1997) (ten years for two patents on conveyor belts); *Moraine Prods. v. ICI Am., Inc.*, 538 F.2d 134, 138 (7th Cir. 1976) (ten years for a pharmaceutical composition); *Helene Curtis Indus., Inc. v. Sales Affiliates, Inc.*, 105 F. Supp. 886, 889 (S.D.N.Y. 1952) (ten years for a permanent waving solution); *Cutting Room Appliances Corp. v. Weatherbee Coats, Inc.*, 158 F. Supp. 231, 232 (N.D. Ohio 1950) (ten years for a material spreading machine); *Colonial Alloys Co. v. Kinkead Indus., Inc.*, 399 F. Supp. 1062, 1063 (N.D. Ill. 1975) (nine years for a method of treating aluminum); *Minn. Mining & Mfg. Co. v. Alphapharm Pty. Ltd.*, 2002 WL 1352426, at \*1 (D. Minn. Mar. 20, 2002) (eight years for patents to pharmaceutical compounds and methods for their manufacture); *J.T. Eaton & Co. v. Atl. Paste & Glue Co.*, 106 F.3d 1563, 1572 (Fed. Cir. 1997) (eight years for an adhesive mousetrap); *McNeil-PPC, Inc. v. L. Perrigo Co.*, 337 F.3d 1362, 1371 (Fed. Cir. 2003) (seven years for two pharmaceutical composition patents); *Hester Indus. v. Stein, Inc.*, 963 F. Supp. 1403, 1408 (E.D. Va. 1997) (seven years for a steam oven).

*Med., Educ. & Research Found., LP*, 301 F. Supp. 2d 1147, 1156 (D. Nev. 2004), *aff'd*, 422 F.3d 1378 (Fed. Cir. 2005).

249. Lilly has failed to present clear and convincing evidence of Ariad's culpable neglect. As was detailed in Ariad's Opening Findings of Fact (*see* AFF 306-58), and summarized above, Ariad prosecuted the '516 patent diligently. For example, Ariad consistently responded in a timely manner to office actions, and did not delay prosecution through its filing of continuation, CIP and divisional applications. Most of this time was spent responding to the examiner's rejections. Likewise, much of the time required for prosecution can be explained by the time it took for the PTO to act – which in some instances was more than one year. Significant changes to the law occurred multiple times during prosecution, requiring action by both Ariad and the examiner.

250. The Court holds that these explanations, as well as the others put forth by Ariad in their Opening Findings of Fact, are reasonable and cannot constitute culpable neglect. As the Federal Circuit explained in *Symbol IV*, “[t]here are legitimate grounds for refiling a patent application which should not normally be grounds for a holding of laches, and the doctrine should be used sparingly lest statutory provisions be unjustifiably vitiated.” 422 F.3d at 1385.

251. For example, the Court noted that “it cannot, without more, be an abuse of the system to file divisional applications” following a restriction requirement, that “one might legitimately refile an application containing rejected claims,” that “[c]ommonly, and justifiably, one might refile an application to add subject matter in order to attempt to support broader claims,” and that “[o]ne may also refile an application even in the absence of any of these reasons, provided that such refiling is not unduly successive or repetitive.” *Symbol IV*, 422 F.3d at 1385.

252. By contrast, “refiling an application solely containing previously-allowed claims for the business purpose of delaying their issuance can be considered an abuse of the patent system.” *Id.* This Ariad has not done.

253. Nor has Ariad engaged in the other acts condemned by the court in *Symbol*. There, the patentee redrafted his claims repeatedly to take advantage of advances in the art, and “added new claims to cover commercial inventions in the market place years after his original patents had expired . . . precisely the type of prejudice to the public which the equitable doctrine of prosecution laches is designed to guard against.” *Symbol III*, 301 F. Supp. 2d at 1156; *see also Symbol IV*, 422 F.3d at 1386.

254. In *Symbol*, in the late 1990’s applicant continued to redraft claims (which applicant contended were supported by its original 1960’s applications) directed to entirely different inventions in order to capture later commercial developments. That applicants waited more than ten years after their original patents had expired to do this showed their culpability in delaying prosecution. *See Symbol III*, 301 F. Supp. 2d at 1156.

255. The Court concludes that here the applicants’ conduct does not constitute the type of culpable and egregious delay at issue in *Symbol*. The claims of the ’516 patent were allowed only about three years after the first related patent issued. During this time applicants diligently sought issuance of claims directed to a single aspect of the subject matter disclosed in their application. During this time applicants never engaged in any strategy to redraft these claims to cover different inventions.

256. Lilly argues in particular that the prosecution of the ’516 patent was unreasonable because Ariad “requested and paid for three-month extensions of time in order to extend the grace period for response to the 6-month maximum time permitted by the patent statute.” (LFF

210-11). As Ariad pointed out in its Opening Findings of Fact, a six-month period is in fact established by the Rules. (AFF 314). However, “[c]ommonly, an examiner may first set a shortened statutory period for filing a response,” which an applicant may petition to extend to the statutory limit by paying a fee. (*Id.* (citations omitted; emphasis added)). The Court concludes that taking six months to respond to office actions does not constitute unreasonable delay.

257. Lilly also argues that “Ariad has provided no legitimate reasons for failing to appeal the final rejections issued in the ’901 and ’436 applications,” as well as the ’397 and ’364 applications. (Lilly FF221-28). Instead, Ariad chose to cancel the pending claims in those applications and pursue different claims. The Court finds this course of action reasonable and entirely consistent with Ariad’s intent to prosecute their invention diligently and expeditiously.

258. Had Ariad decided to appeal the rejections rather than work with the PTO to redraft the claims, the applications would have been on hold pending resolution of the appeal. Thus, there is no assurance that the patents would have issued any sooner, and quite possibly the appeals process could have taken longer. Regardless, Ariad had the right to choose between different statutorily permitted courses of action, and they should not be penalized for doing so.

259. The Court further holds that such action was not unreasonable simply because it preserved the longest patent term available to Ariad.

260. The Supreme Court cases Lilly cites, *Woodbridge* and *Webster Electric* (*see* Lilly CL122), are inapposite, and neither of them reflects the doctrine of prosecution laches as it exists today.

261. In *Woodbridge*, the PTO examined the inventor’s patent on projectiles, and having found it allowable, ordered it to issue. 263 U.S. at 52. In response, the inventor asked that it be held in secret within the PTO, then “sat down and waited [9½ years] until after the

Civil War came on in 1861 before seeking to avail himself of the patent,” even though it “might have been had at any time in that period for the asking.” *Id.* at 56. Moreover, following the 9½ year delay, the inventor “applied for a change of specifications and claims, so that he might cover the patents of these subsequent inventors.” *Id.* at 57. After the application was rejected on grounds of abandonment, the inventor waited until 1879 before appealing. *Id.* at 54. Thus, *Woodbridge* does not shed light upon either modern prosecution laches law or this case, as it deals with delay that was clearly intentional, and that occurred after the patent was allowed to issue. See *Symbol Techs. v. Lemelson Med., Educ. & Research Found., LP*, 277 F.3d 1361, 1369 (Fed. Cir. 2002) (Newman, J., dissenting) (“surely this is not ‘laches,’ for Woodbridge had already lost his statutory right to a patent”).

262. Here, for instance, there is no evidence that there were allowed claims that Ariad did not permit to issue. A notice of allowance for the ’516 patent claims was not mailed until October 4, 2001. (PTX 2 at ADL 0000923-953, 956). Ariad paid the issue fee on December 4, 2001 (PTX 2 at ADL 0001015), and the Patent Office issued the ’516 patent on June 25, 2002. (PTX 1).

263. Further, the inventor’s “plan of nonaction” in *Woodbridge* was contrary to a letter he addressed to the PTO, agreeing to allow the patent to issue within one year. 263 U.S. at 52. More importantly, such nonaction “was not in accord with the rules of procedure in the Patent Office, but was in plain violation of the statutory law.” *Id.* at 63. This is in clear distinction with the actions of the patentee here, as none have been shown to be in violation of statutory law or accepted patent practice.

264. In *Webster Electric*, the Supreme Court held that “in cases involving laches . . . [a] two-year time limit prima facie applies to divisional applications and can only be avoided by

proof of special circumstances justifying a longer delay.” 264 U.S. at 471. There, the applicant waited over eight years to file a divisional, and could show “no just excuse for the failure to assert the broader claims” earlier; indeed, he delayed with the intent of covering recent developments. *Id.* at 466 (“We are not dealing . . . with the simple case of a division of a single application for several independent inventions”).

265. The rule in *Webster* was repudiated shortly thereafter by the Supreme Court. *See Crown Cork & Seal Co. v. Ferdinand Gutmann Co.*, 304 U.S. 159, 166-68 (1938); *Symbol II*, 277 F.3d at 1369 (Newman, J., dissenting). Furthermore, *Webster* is contrary to current law placing the burden on the party raising the defense of laches, and permitting the filing of divisionals at any time before issuance of the parent application. *See Symbol IV*, 422 F.3d at 1385; 35 U.S.C. § 121.

266. Therefore, the Court concludes that no prosecution laches occurred with respect to the '516 patent. The record does not show by clear and convincing evidence that the applicants engaged in any unreasonable and unexplained delays in prosecuting the '516 patent.

## **V. RESERVED EVIDENTIARY CONCLUSIONS OF LAW**

### **A. The Reexamination Is Not Admitted Into Evidence**

267. As described in Ariad's opening Findings of Fact 638-47, the reexamination of the '516 patent was commenced on the basis of unsubstantiated and unverified arguments submitted by Lilly and its expert Dr. Manolagas which were not known by applicants and not before the examiner during prosecution of the '516 patent and therefore is not relevant to any issue before the Court.

268. To the extent Lilly claims that the reexamination is not premised on its own representations to the Patent Office because Mr. Bawa also submitted a petition for reexamination, this only provides further evidence that the Patent Office is considering

information and arguments that were not known by applicants and not available to it during prosecution of the '516 patent.

269. Further, the Patent Office is conducting the reexamination of the '516 patent based on different standards of law regarding inherent anticipation than were applied during prosecution of the '516 patent. (*See* ACL 645). The Patent Office is not applying any contemporaneous recognition requirement in the reexamination, as it was instructed by the MPEP and substantial caselaw during prosecution.

270. The reexamination is not probative to the issue of inequitable conduct. The Court is not persuaded by the authority Lilly cites in support of admitting the reexamination. For instance, Lilly misleadingly cites to *Molins*, a case where the patentee sought to rely on evidence of the reexamination proceeding because the claims had not been held invalid in that proceeding based on the references alleged to be material by the defendant in the district court. (LCL 134). The district court still found materiality based on other grounds, such as the reference's disclosure of other elements not in the prior art and its identification as the closest prior art in a foreign prosecution. *Molins*, 48 F.3d at 1179-80. Thus, the mere fact of the reexamination was not considered probative to the ultimate determination of materiality. The Federal Circuit rejected the patentee's attempt to reverse the judgment of the Court by relying on the examiner's decision in the reexamination. *Id.* at 1179.

271. The holding in *Molins* therefore supports the proposition that the judgment of the PTO is no substitute for the discretion of the district court with respect to a determination such as materiality.

272. The Court rules that documents and other evidence pertaining to the reexamination are inadmissible.<sup>10</sup>

**B. Documents Relating to the Autoregulatory Loop Model Are Not Admitted Into Evidence**

273. Lilly seeks to introduce into evidence certain documents, particularly DTX 469A, 119, 334, 490, 636, 2220, 3011, 3071 and 3072 purportedly relating to the “state of the art” concerning the autoregulatory loop model. (LCL 135-138). These documents are inadmissible hearsay and the Court rejects Lilly’s attempt to supplement the record with them.

274. The Court does not credit Lilly’s argument that *Schering* supports that the proffered references are admissible evidence on the state of the art. (LCL 137, citing *Schering Corp.*, 339 F.3d at 1377-78 (Fed. Cir. 2003)). With respect to DTX 3011, 3071 and 3072, these documents are merely slides that Lilly prepared to support its conception of the autoregulatory loop model and therefore would never have been available to one of skill in the art anyway.

275. The Court also concludes that the completeness doctrine of Fed. Rules Evid. 106 does not support the admissibility of Hoffmann et al. The completeness doctrine is generally applied only when portions of a single document or a single document from a unitary compilation or set of documents commonly maintained in the same file is offered. *United States v. Boylan*, 898 F.2d 230, 256-58 (1st Cir. 1990) (“the usual problem concerns an excerpt from a single document which neglects some revealing context of the whole”). Clearly, the fact that Hoffmann is the subject of commentary in the Ting and Endy article does not meet this standard. Moreover, the completeness doctrine has not been held to be an independent ground for

---

<sup>10</sup> Were the Court to admit the reexam into evidence, it would provide more evidence that the determination of whether a “natural process” meets all the limitations of a claims is performed under § 102 and not § 101. In the first non-final office action in the reexam, the examiner issued a § 102 rejection based on the human body’s purported natural production of glucocorticoids. (*See* Reexamination, 8/2/06 Office Action at p. 55).

admissibility in the First Circuit, and Lilly has not established that there is any other reason to admit Hoffmann. *See id.* at n.16; *United States v. Leon-Delfis*, 203 F.3d 103, 115 (1st Cir. 2000).

276. Accordingly, the Court rules that DTX 469A, 119, 334, 490, 636, 2220, 3011, 3071 and 3072 are not accepted into evidence.

**C. Deposition Related Documents and Certain Deposition Testimony Are Not Admitted Into Evidence**

277. Lilly also seeks to introduce into evidence portions of the depositions of Drs. Baltimore, Baldwin, Baeuerle and Sen into evidence as well as references Lilly alleges are associated exhibits. For all the reasons set forth above, as well as the reasons set out in Ariad's Opposition to Lilly's Motion to Overrule its Objections to Lilly's Deposition Designations and Corresponding Exhibits (D.I. 381), the Court rules that the documents proffered with the depositions are inadmissible. In the case of some of these documents such as DTX 469A and 473, the documents were never even introduced at the depositions anyway. With respect to the designated deposition testimony to which Ariad has lodged objections the Court sustains those objections and rules those portions will not be introduced into evidence.

278. Even had Ariad's position during claim construction been inconsistent with its current position on the autoregulatory loop (which it was not), in construing "reducing NF- $\kappa$ B activity," the Court relied in part on Lilly's arguments. (*See* ¶ 89, *supra*; D.I. 75).

Dated September 29, 2006

Respectfully Submitted

By:

**Attorneys for Plaintiffs**

ARIAD Pharmaceuticals, Inc.,  
Massachusetts Institute of Technology, the  
Whitehead Institute for Biomedical  
Research, and the President and Fellows of  
Harvard College

/s/ Thomas F. Fleming

Leora Ben-Ami  
Patricia A. Carson  
Vladimir Drozdoff  
Thomas F. Fleming  
KAYE SCHOLER LLP  
425 Park Avenue  
New York, NY 10022  
Tel: (212) 836-8000  
Fax: (212) 836-8689  
tfleming@kayescholer.com

Lee Carl Bromberg, BBO# 058480  
Kerry L. Timbers, BBO# 552293  
BROMBERG & SUNSTEIN LLP  
125 Summer Street  
Boston, MA 02110-1618  
Tel.: (617) 443-9292  
Fax: (617) 443-0004  
ktimbers@bromsun.com

**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 September 29, 2006.

/s/ Thomas F. Fleming