United States Court of Appeals for the Federal Circuit

2008-1248

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

Plaintiffs-Appellees,

v.

ELI LILLY AND COMPANY,

Defendant-Appellant.

Stephen S. Rabinowitz, Fried Frank Harris Shriver & Jacobson LLP, of New York, New York, argued for plaintiffs-appellees. With him on the brief were James W. Dabney, John F. Duffy, Mitchell Epner, and Randy C. Eisensmith. Of counsel on the brief were Leora Ben-Ami, Matthew McFarlane, Christopher T. Jagoe, Sr., Howard S. Suh, and Patricia A. Carson, Kay Scholer LLP, of New York, New York.

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Appealed from: United States District Court for the District of Massachusetts

Judge Rya W. Zobel

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MASSACHUSETTS INSTITUTE OF TECHNOLOGY,
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Plaintiffs-Appellees,

v.

ELI LILLY AND COMPANY,

Defendant-Appellant.

Appeal from the United States District Court for the District of Massachusetts in case No. 02-CV-11280, Judge Rya W. Zobel.

DECIDED: April 3, 2009

Before LINN, PROST, and MOORE, Circuit Judges.

Opinion for the court filed by Circuit Judge MOORE. Concurring opinion filed by Circuit Judge LINN.

MOORE, Circuit Judge.

Plaintiffs-Appellees Ariad Pharmaceuticals, Inc., Massachusetts Institute of Technology, the Whitehead Institute for Biomedical Research, and the Presidents and Fellows of Harvard College (collectively, Ariad) sued Defendant-Appellant Eli Lilly and Company (Lilly) in the United States District Court for the District of Massachusetts for infringement of claims 80, 95, 144, and 145 (the asserted claims) of U.S. Patent No. 6,410,516 (the '516 patent). A jury found infringement of claims 80 and 95 with respect

to Lilly's drug Evista, and claims 144 and 145 with respect to Lilly's drug Xigris. The jury also concluded that the asserted claims were not invalid for anticipation, lack of enablement, or lack of written description.

Both at the close of Ariad's case-in-chief and again after the jury verdict, Lilly moved for judgment as a matter of law (JMOL) that the asserted claims were not infringed and were invalid for anticipation, lack of enablement, or lack of written description. Following a separate bench trial, the district court ruled that the asserted claims were directed to patentable subject matter and that the '516 patent was not unenforceable due to inequitable conduct or prosecution laches. Ariad Pharms., Inc. v. Eli Lilly & Co., 529 F. Supp. 2d 106 (D. Mass. 2007). Lilly appeals several rulings, including the court's denial of its JMOL motion and the court's ruling on inequitable conduct. For the reasons set forth below, we reverse-in-part and affirm-in-part.

BACKGROUND

The technology in this case involves gene regulation. Transcription factors are molecules found in cells that regulate the extent to which genes are expressed. There are hundreds of different transcription factors that perform in concert with other molecules in the cell to control cellular behavior. Unsurprisingly, this network of cellular signals is fertile ground for the development of therapeutic compounds. In the mid-1980s, the inventors of the '516 patent discovered an important transcription factor that they named NF-κB. NF-κB is akin to an all-purpose cellular paramedic. When the cell receives a harmful extracellular influence, such as lipopolysaccharides produced by bacteria, NF-κB is activated. Once activated, NF-κB travels to the nucleus of the cell and fulfills its role as a transcription factor, inducing the expression of numerous genes

and causing the cell to produce the corresponding proteins. These proteins, for example certain cytokines, help the cell survive the extracellular influence, but they can be harmful in excess—not unlike how a fever is thought to combat infection but can cause harm if left unchecked. Once the offending extracellular influence diminishes, for example, following the administration of antibiotics for a bacterial infection, NF-κB activity decreases and the cell returns to its original state.

The inventors of the '516 patent further realized that if NF-κB activity could be reduced artificially, it could ameliorate the harmful symptoms of diseases that trigger NF-κB activation—not unlike how aspirin can reduce a fever without actually treating the underlying infection. The asserted claims, rewritten to include the claims from which they depend, are as follows:

> 80. [A method for modifying effects of external influences on a eukaryotic cell, which external influences induce NF-κB-mediated intracellular signaling, the method comprising altering NF-κB activity in the cells such that NF-κB-mediated effects of external influences are modified, wherein NF-κB activity in the cell is reduced] wherein reducing NF-κB activity comprises reducing binding of NF-κB to NF-κB recognition sites on genes which are transcriptionally regulated by NF-κB.
>
> 95. [A method for reducing, in eukaryotic cells, the level of expression of genes which are activated by extracellular influences which induce NF-κB-mediated intracellular signaling, the method comprising reducing NF-κB activity in the cells such that expression of said genes is reduced], carried out on human cells.
>
> 144. [A method for reducing bacterial lipopolysaccharide-induced expression of cytokines in mammalian cells, which method comprises reducing NF-κB activity in the cells so as to reduce bacterial lipopolysaccharide-induced expression of said cytokines in the cells] wherein reducing NF-κB activity comprises reducing binding of NF-κB to NF-κB recognition sites on genes which are transcriptionally regulated by NF-κB.
>
> 145. [A method for reducing bacterial lipopolysaccharide-induced expression of cytokines in mammalian cells, which method comprises

> reducing NF-κB activity in the cells so as to reduce bacterial lipopolysaccharide-induced expression of said cytokines in the cells], carried out on human cells.

Importantly, the district court determined that "reducing NF-κB activity" means "decreasing the function of NF-κB to act as an intracellular messenger that regulates transcription of particular genes, in response to certain stimuli." Ariad Pharms., Inc. v. Eli Lilly & Co., No. 02-cv-11280, 2004 U.S. Dist. LEXIS 3170, at *3 (D. Mass. Mar. 3, 2004). Neither party appealed the district court's claim construction.

Ariad filed its complaint on the day the '516 patent issued, June 25, 2002. During the proceedings, the district court denied Lilly's combined motion to dismiss and motion for summary judgment. Ariad Pharms., Inc. v. Eli Lilly & Co., No. 02-cv-11280, 2003 U.S. Dist. LEXIS 8030 (D. Mass. May 12, 2003). On April 4, 2005, Lilly filed a request for reexamination of the '516 patent. The district court denied Lilly's motion for a stay. Ariad Pharms., Inc. v. Eli Lilly & Co., No. 02-cv-11280, 2005 U.S. Dist. LEXIS 10941 (D. Mass. June 6, 2005). The district court also denied Lilly's renewed motion to stay made on January 17, 2006. There was a fourteen-day jury trial in April, 2006. At the close of Ariad's case-in-chief, Lilly moved for JMOL that the asserted claims were not infringed and were invalid for anticipation, lack of enablement, or lack of written description. The district court denied the JMOL motion without opinion.

On April 28, 2006, the jury rendered a special verdict finding infringement of claims 80 and 95 with respect to Evista and claims 144 and 145 with respect to Xigris. The jury also found that the asserted claims were not invalid for anticipation, lack of enablement, or lack of written description. The court denied Lilly's renewed motion for JMOL or, in the alternative, a new trial, again without opinion. In August 2006, the court

conducted a four-day bench trial on three further defenses offered by Lilly: unpatentable subject matter, inequitable conduct, and prosecution laches. The district court ruled in favor of Ariad on all three issues. Ariad Pharms., Inc., 529 F. Supp. 2d 106.

Lilly timely appeals all of these rulings except the district court's ruling that prosecution laches did not render the '516 patent unenforceable. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

I.

We review the denial of Lilly's motion for JMOL without deference. Cytologix Corp. v. Ventana Med. Sys., Inc., 424 F.3d 1168, 1172 (Fed. Cir. 2005) (applying First Circuit law). Under First Circuit law, JMOL is warranted pursuant to Fed. R. Civ. P. 50(a)(1) where "there is no legally sufficient evidentiary basis for a reasonable jury to find" for the non-moving party. Guilloty Perez v. Pierluisi, 339 F.3d 43, 50 (1st Cir. 2003) (quotations omitted). "A patent is presumed to be valid, and this presumption only can be overcome by clear and convincing evidence to the contrary." Enzo Biochem, Inc. v. Gen-Probe Inc., 424 F.3d 1276, 1281 (Fed. Cir. 2005) (citing WMS Gaming Inc. v. Int'l Game Tech., 184 F.3d 1339, 1355 (Fed. Cir. 1999)); see 35 U.S.C. § 282.

Section 112 of Title 35 provides, in relevant part, that:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § 112, ¶ 1 (emphasis added). The emphasized portion of § 112, the written description requirement, "serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed." Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005). The requirement "serves a teaching function, as a quid pro quo in which the public is given meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time." Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 922 (Fed. Cir. 2004) (quoting Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 970 (Fed. Cir. 2002)); see O'Reilly v. Morse, 56 U.S. (15 How.) 62, 121 (1853) (explaining that a patentee "can lawfully claim only what he has invented and described, and if he claims more his patent is void"); Reiffen v. Microsoft Corp., 214 F.3d 1343, 1345–46 (Fed. Cir. 2000) ("The purpose of [the written description requirement] is to ensure that the scope of the right to exclude . . . does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification.").

"To satisfy the written description requirement, 'the applicant does not have to utilize any particular form of disclosure to describe the subject matter claimed, but the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.'" Carnegie Mellon Univ. v. Hoffmann La Roche Inc., 541 F.3d 1115, 1122 (Fed. Cir. 2008) (quoting In re Alton, 76 F.3d 1168, 1172 (Fed. Cir. 1996)). "In other words, the applicant must 'convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention,' and demonstrate that by disclosure in the specification of the patent." Id.

(quoting Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991)). Such disclosure need not recite the claimed invention in haec verba, but it must do more than merely disclose that which would render the claimed invention obvious. Rochester, 358 F.3d at 923; Regents of the Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1566–67 (Fed. Cir. 1997); see also PowerOasis, Inc. v. T-Mobile USA, Inc., 522 F.3d 1299, 1306–07 (Fed. Cir. 2008) (explaining that § 112, ¶1 "requires that the written description actually or inherently disclose the claim element").

"Whether the written description requirement is satisfied is a fact-based inquiry that will depend on the nature of the claimed invention and the knowledge of one skilled in the art at the time an invention is made and a patent application is filed." Carnegie Mellon, 541 F.3d at 1122 (citing Enzo, 323 F.3d at 963). The written description requirement is not satisfied by "[t]he appearance of mere indistinct words in a specification or a claim, even an original claim. . . . A description of what a material does, rather than of what it is, usually does not suffice." Enzo, 323 F.3d at 968 (citing Eli Lilly, 119 F.3d at 1568); see Rochester, 358 F.3d at 926 ("[G]eneralized language may not suffice if it does not convey the detailed identity of an invention.").

The same is true for both process claims and composition claims. Rochester, 358 F.3d at 926 ("Regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods."). Where the specification provides only constructive examples in lieu of working examples, it must still "describe the claimed subject matter

in terms that establish that the applicant was in possession of the claimed invention, including all of the elements and limitations." Id. (citing Hyatt v. Boone, 146 F.3d 1348, 1353 (Fed. Cir. 1998)).

Of course, what is adequate depends upon the context of the claimed invention. See Capon, 418 F.3d at 1358 ("The written description requirement must be applied in the context of the particular invention and state of the knowledge."). We have articulated a variety of factors to evaluate the adequacy of the disclosure supporting "generic claims to biological subject matter." Id. at 1359. These factors include "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue." Id.

Ariad explains that developing the subject matter of the '516 patent "required years of hard work, great skill, and extraordinary creativity—so much so that the inventors first needed to discover, give names to, and describe previously unknown cellular components as a necessary predicate for their inventions." Lilly offered the undisputed expert testimony of David Latchman that the field of the invention was particularly unpredictable. Thus, this invention was made in a new and unpredictable field where the existing knowledge and prior art was scant. See Capon, 418 F.3d at 1359.

A.

Ariad claims methods comprising the single step of reducing NF-κB activity. Lilly argues that the asserted claims are not supported by written description because the specification of the '516 patent fails to adequately disclose how the claimed reduction of NF-κB activity is achieved. The parties agree that the specification of the '516 patent

hypothesizes three classes of molecules potentially capable of reducing NF-κB activity: specific inhibitors, dominantly interfering molecules, and decoy molecules. Lilly contends that this disclosure amounts to little more than a research plan, and does not satisfy the patentee's quid pro quo as described in Rochester. Ariad responds that Lilly's arguments fail as a matter of law because Ariad did not actually claim the molecules. According to Ariad, because there is no term in the asserted claims that corresponds to the molecules, it is entitled to claim the methods without describing the molecules. Ariad's legal assertion, however, is flawed.

In Rochester, we held very similar method claims invalid for lack of written description. Id. (holding patent invalid because "Rochester did not present any evidence that the ordinarily skilled artisan would be able to identify any compound based on [the specification's] vague functional description"); see also Fiers v. Revel, 984 F.2d 1164, 1170–71 (Fed. Cir. 1993) (holding a claim to a genus of DNA molecules not supported by written description of a method for obtaining the molecules); cf. Eli Lilly, 119 F.3d at 1567–68 (holding claims to a broad genus of genetic material invalid because the specification disclosed only one particular species). Ariad attempts to categorically distinguish Rochester, Fiers, and Eli Lilly, because in those cases, the claims explicitly included the non-described compositions. For example, in Rochester, the method claims recited a broad type of compound that we held was inadequately described in the specification of the patent:

> 1. A method for selectively inhibiting PGHS-2 activity in a human host, comprising administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product to a human host in need of such treatment.

Id. at 918 (emphasis added). Ariad's attempt to distinguish these cases is unavailing. Regardless of whether the asserted claims recite a compound, Ariad still must describe some way of performing the claimed methods, and Ariad admits that the specification suggests only the use of the three classes of molecules to achieve NF-κB reduction. Thus, to satisfy the written description requirement for the asserted claims, the specification must demonstrate that Ariad possessed the claimed methods by sufficiently disclosing molecules capable of reducing NF-κB activity so as to "satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed." Capon, 418 F.3d at 1357.

B.

Alternatively, Ariad argues that the specification of the '516 patent and the expert testimony of Tom Kadesch provided the jury with substantial evidence of adequate written description of the claimed methods. "A determination that a patent is invalid for failure to meet the written description requirement of 35 U.S.C. § 112, ¶ 1 is a question of fact, and we review a jury's determinations of facts relating to compliance with the written description requirement for substantial evidence." PIN/NIP, Inc. v. Platte Chem. Co., 304 F.3d 1235, 1243 (Fed. Cir. 2002) (citing Vas-Cath, 935 F.2d at 1563).

Much of Ariad's written description evidence, however, is legally irrelevant to the question of whether the disclosure of the '516 patent conveys to those skilled in the art that the inventors were in possession of the claimed invention on April 21, 1989—the effective filing date of the '516 patent. The parties disputed the effective filing date of the '516 patent, and in a detailed and well-crafted special verdict form, the jury was

asked to choose between the two possible dates: April 21, 1989 and November 13, 1991. The jury chose 1989 and neither party appealed that determination. Presumably because of uncertainty over the priority date, much of Ariad's evidence was actually directed to the later date. Because written description is determined as of the filing date—April 21, 1989 in this case—evidence of what one of ordinary skill in the art knew in 1990 or 1991 cannot provide substantial evidence to the jury that the asserted claims were supported by adequate written description. See Vas-Cath, 935 F.2d at 1563–64 (holding that a written description analysis occurs "as of the filing date sought").

In accordance with Rochester, the '516 patent must adequately describe the claimed methods for reducing NF-κB activity, including adequate description of the molecules that Ariad admits are necessary to perform the methods. The specification of the '516 patent hypothesizes three classes of molecules potentially capable of reducing NF-κB activity: specific inhibitors, dominantly interfering molecules, and decoy molecules. We review the specification's disclosure of each in turn to determine whether there is substantial evidence to support the jury's verdict that the written description evidenced that the inventor possessed the claimed invention.

Specific inhibitors are molecules that are "able to block (reduce or eliminate) NF-κB binding" to DNA in the nucleus. '516 patent col.37 ll.44–45. The only example of a specific inhibitor given in the specification is I-κB, a naturally occurring molecule whose function is to hold NF-κB in an inactive state until the cell receives certain external influences. Id. at col.37 ll.48–49. Nearly all of Ariad's evidence regarding the disclosure of I-κB relies upon figure 43. Ariad's expert, Dr. Kadesch, testified that figure 43 discloses the sequence of DNA that encodes I-κB and relied on this disclosure with

regard to his opinion that the written description requirement was satisfied by disclosure of specific inhibitor molecules. See Trial Tr. 53; 57–58; 60; 78–85, Apr. 27, 2006. But as Ariad admits, figure 43 was not disclosed until 1991. Because figure 43 was not in the 1989 application, neither it nor Dr. Kadesch's testimony regarding it can offer substantial evidence for the jury determination. See Vas-Cath, 935 F.2d at 1563–64. The only other testimony of Dr. Kadesch with regard to I-κB was that it existed in 1989 and that one of ordinary skill could through experimentation isolate natural I-κB. See Trial Tr. at 62–85. In the context of this invention, a vague functional description and an invitation for further research does not constitute written disclosure of a specific inhibitor.[1] See Eli Lilly, 119 F.3d at 1566 (holding that written description requires more than a "mere wish or plan for obtaining the claimed chemical invention"); see also id. at 1567 ("[A] description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention."). And it certainly does not constitute written disclosure of a method for reducing NF-κB activity using I-κB.

Dominantly interfering molecules are "a truncated form of the NF-κB molecule." '516 patent col.38 l.11. The truncation would "retain[] the DNA binding domain, but lack[] the RNA polymerase activating domain." Id. at col.38 ll.13–14. As such, the dominantly interfering molecule "would recognize and bind to the NF-κB binding site [on nuclear DNA], however, the binding would be unproductive." Id. at col.38 ll.15–17. In other words, the dominantly interfering molecules would block natural NF-κB from

[1] Moreover, the district court found, in the context of its inequitable conduct ruling, that figure 43 is both incorrect and incomplete. Ariad Pharms., 529 F. Supp. 2d at 123–25 (finding those errors material). That the inventors of the '516 patent, among the most skilled artisans in their field in the world at this time, failed to correctly disclose the structure of I-κB even two years after the application was filed is a strong sign that one of skill in the art could not be expected to provide this knowledge in 1989.

inducing the expression of its target genes. The specification provides no example molecules of this class. Moreover, the specification acknowledges that dominantly interfering molecules can work only "if the DNA binding domain and the DNA polymerase domain of NF-κB are spatially distinct in the molecule." Id. at col.38 ll.9–10 (emphasis added). The jury also heard Dr. Kadesch's testimony that "it is a fair representation" that "the '516 patent itself doesn't disclose in its text that the DNA binding domain and the RNA preliminary activating domain of NF-κB are, in fact, separable or spatially distinct." Considering that the inventors of the '516 patent discovered NF-κB, if they did not know whether the two domains are distinct, one of ordinary skill in the art was at best equally ignorant. Perhaps one of ordinary skill could discover this information, but this does not alter our conclusion that the description of the dominantly interfering molecules "just represents a wish, or arguably a plan" for future research. Fiers, 984 F.2d at 1171; see Eli Lilly, 119 F.3d at 1567 (rendering obvious is insufficient for written description). Nor is it sufficient, as Ariad argues, that "skilled workers actually practiced this teaching soon after the 1989 application was filed." See Vas-Cath, 935 F.2d at 1563–64 (holding that a written description analysis occurs "as of the filing date sought").

Decoy molecules are "designed to mimic a region of the gene whose expression would normally be induced by NF-κB. In this case, NF-κB would bind the decoy, and thus, not be available to bind its natural target." '516 patent col.37 ll.51–54. Like the other two classes of molecules, decoy molecules are presented hypothetically, but unlike the other two classes of molecules, the specification proposes example structures for decoy molecules. Id. at col.37 tbl.2. As Dr. Kadesch explained, decoy

molecules are DNA oligonucleotides, and because the specification discloses specific example sequences, there is little doubt that the specification adequately described the actual molecules to one of ordinary skill in the art. Yet this does not answer the question of whether the specification adequately describes using those molecules to reduce NF-κB activity. The full extent of the specification's disclosure of a method that reduces NF-κB activity using decoy molecules is that NF-κB "would bind the decoy" and thereby, "negative regulation can be effected." Id. at col.37 ll.50–54. Prophetic examples are routinely used in the chemical arts, and they certainly can be sufficient to satisfy the written description requirement. But this disclosure is not so much an "example" as it is a mere mention of a desired outcome. As Dr. Latchman pointed out, there is no descriptive link between the table of decoy molecules and reducing NF-κB activity.

Ariad also relies upon "[a] 1990 publication in evidence [that] reported using decoy molecules to reduce NF-κB activity" which was discussed by Dr. Kadesch. Appellee Br. 25–26. Again, because the priority date was determined to be 1989, the disclosure in a later publication cannot, as a matter of law, establish that the inventor in this case possessed using decoy molecules to reduce NF-κB when the patent application was filed in 1989. Dr. Kadesch's reliance on this evidence as support for his opinion is likewise erroneous.[2]

[2] Dr. Kadesch testified that the scientists who conducted the decoy molecule study published in November 1990 would likely have mastered their technique prior to the filing of the '516 patent application in April 1989. Perhaps so, but this fact is not in evidence, and even if it were true, one research group does not necessarily represent the knowledge of one of ordinary skill in the art without further testimony to support that contention.

We reviewed all other portions of Dr. Kadesch's testimony that Ariad contends provided the jury with substantial evidence relating to each of the three classes of molecules, and we deem them insufficient as a matter of law.[3] Indeed, most of the testimony cited by Ariad was irrelevant to the question of whether the inventors were in possession of the claimed invention as of the 1989 priority date. The '516 patent discloses no working or even prophetic examples of methods that reduce NF-κB activity, and no completed syntheses of any of the molecules prophesized to be capable of reducing NF-κB activity. The state of the art at the time of filing was primitive and uncertain, leaving Ariad with an insufficient supply of prior art knowledge with which to fill the gaping holes in its disclosure. See Capon, 418 F.3d at 1358 ("It is well-recognized that in the unpredictable fields of science, it is appropriate to recognize the variability in the science in determining the scope of the coverage to which the inventor is entitled.").

Whatever thin thread of support a jury might find in the decoy-molecule hypothetical simply cannot bear the weight of the vast scope of these generic claims. See LizardTech, Inc. v. Earth Res. Mapping, Inc., 424 F.3d 1336, 1345 (Fed. Cir. 2005) (holding that "[a]fter reading the patent, a person of skill in the art would not understand" the patentee to have invented a generic method where the patent only disclosed one embodiment of it); Reiffen, 214 F.3d at 1345–46 (noting that the "scope of the right to

[3] Dr. Kadesch certainly offered a general conclusion that he thought the inventors were in possession of the claimed invention in 1989. This conclusory testimony, as shown infra, is devoid of any factual content upon which the jury could have relied when considering the specification of the '516 patent, and therefore cannot constitute substantial evidence. Besides, possession of an invention must be shown by written description in the patent application, and that was not shown here. See Rochester, 358 F.3d at 926 ("After all, it is in the patent specification where the written description requirement must be met.").

exclude" must not "overreach the scope of the inventor's contribution to the field of art as described in the patent specification"); Fiers, 984 F.2d at 1171 ("Claiming all DNA[s] that achieve a result without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived."); cf. Carnegie Mellon, 541 F.3d at 1126 (holding that the narrow description of the E. coli polA gene did not adequately support a broad claim to the gene from any bacterial source). Here, the specification at best describes decoy molecule structures and hypothesizes with no accompanying description that they could be used to reduce NF-κB activity. Yet the asserted claims are far broader. We therefore conclude that the jury lacked substantial evidence for its verdict that the asserted claims were supported by adequate written description, and thus hold the asserted claims invalid.

Ariad sought and obtained the broad claims we now hold to be invalid. For its own reasons, Ariad maintained the breadth of these claims through claim construction and into trial. As Judge Rader observed, the situation presented in this case should not often occur, because "[i]n simple terms, a court would properly interpret the claim[s] as limited." Univ. of Rochester v. G.D. Searle & Co., 375 F.3d 1303, 1312 (Fed. Cir. 2004) (dissenting from denial of petition for rehearing en banc). Nonetheless, as it stands, Ariad chose to assert claims that are broad far beyond the scope of the disclosure provided in the specification of the '516 patent. Cf. Liebel-Flarsheim Co. v. Medrad, Inc., 481 F.3d 1371, 1380 (Fed. Cir. 2007) ("The motto, 'beware of what one asks for,' might be applicable here.").

II.

We next turn to Lilly's appeal of the district court's ruling that Lilly failed to establish the affirmative defense of inequitable conduct. "We review the district court's findings on the issues of materiality and intent for clear error. The ultimate decision regarding inequitable conduct is reviewed for abuse of discretion." Rentrop v. Spectranetics Corp., No. 2007-1560, 550 F.3d 1112, 1120 (Fed. Cir. Dec. 18, 2008).

Lilly bears the burden of proving inequitable conduct. Ulead Sys., Inc. v. Lex Computer & Mgmt. Corp., 351 F.3d 1139, 1146 (Fed. Cir. 2003). To successfully prove inequitable conduct, Lilly must present "evidence that the applicant (1) made an affirmative misrepresentation of material fact, failed to disclose material information, or submitted false material information, and (2) intended to deceive the [USPTO]." Cargill, Inc. v. Canbra Foods, Ltd., 476 F.3d 1359, 1364–65 (Fed. Cir. 2007) (citing Impax Labs., Inc. v. Aventis Pharms. Inc., 468 F.3d 1366, 1374 (Fed. Cir. 2006)).

"Further, at least a threshold level of each element—i.e., both materiality and intent to deceive—must be proven by clear and convincing evidence." Star Scientific, Inc. v. R.J. Reynolds Tobacco Co., 537 F.3d 1357, 1365 (Fed. Cir. 2008). "If a threshold level of intent to deceive or materiality is not established by clear and convincing evidence, the district court does not have any discretion to exercise and cannot hold the patent unenforceable regardless of the relative equities or how it might balance them." Id. Lilly alleges that two errors gave rise to inequitable conduct. On appeal, Ariad does not dispute the substance or materiality of the errors. Rather, relying on Digital Control, Inc. v. Charles Machine Works, Lilly challenges the district court's finding that neither error was accompanied by an intent to deceive. 437 F.3d

1309, 1313 (Fed. Cir. 2006) ("[A] greater showing of [materiality] allow[s for] a lesser showing of [intent]."). Unless otherwise noted, the facts are taken from the district court's detailed opinion. Ariad Pharms., Inc., 529 F. Supp. 2d at 121–36.

A.

The first of the two errors underlying Lilly's defense of inequitable conduct relates to figure 43 of the '516 patent. Ariad does not dispute the district court's finding that figure 43 is incorrect. The patent describes figure 43 as "[t]he nucleotide sequence of the I-κB-α gene and the amino acid sequence of I-κB-α." '516 patent col.28 ll.16–17. The district court found that one of ordinary skill in the art would, given the context, infer that the gene in figure 43 is that of a mouse or other mammal. There are two errors in the figure: the sequence is both incomplete and from a chicken as opposed to a mouse or other mammalian organism. The district court further found that the errors were material because during prosecution, Ariad and the examiner relied on figure 43 for certain arguments to overcome § 112 rejections. Ariad does not dispute the materiality of the errors. According to Lilly, the district court clearly erred because Ariad and the prosecuting attorneys were aware of the errors in figure 43 and purposely concealed them from the USPTO at the "crowning moment" of the prosecution of the '516 patent.

Figure 43 was added to the specification of a predecessor application of the '516 patent in 1991. Without detailing the full lineage, it is sufficient to note that several related applications in the family contained figure 43. In 1997, an employee of Ariad, Sharon Hausdorff, informed Lisa Warren, an attorney with Hamilton, Brooks, Smith & Reynolds, P.C., that figure 43 contained errors. Ms. Warren succeeded in deleting figure 43 from at least one application on file with the USPTO. Around the same time,

the prosecution files for the family of applications were transferred to Matthew Vincent at Foley, Hoag & Elliot LLP.

Dr. Vincent delegated the work to Isabelle Clauss. Dr. Clauss handled the "ministerial" actions, including, upon learning of the errors from Ms. Hausdorff, removing figure 43 from two more of the related applications. Although Dr. Vincent testified that he was never aware of the errors in figure 43 during the pendency of the application that led to the '516 patent, Dr. Clauss testified that she had discussed the issue regarding figure 43 with him. The district court credited Dr. Vincent's testimony because Dr. Class was "at best, equivocal" and was uncertain about the timing and substance of the conversations. In 1998, Dr. Vincent filed a response to an office action regarding the '516 patent application. While apparently not referencing figure 43, Dr. Vincent made arguments relating to § 112 that would be furthered by figure 43. Dr. Clauss also filed a similar response in 1999, arguing that the specification of the application disclosed I-κB-encoding DNA. Although she did not reference it explicitly, she could only have been referring to the contents of figure 43.

In 2001, Dr. Vincent moved to Ropes & Gray LLP, taking with him all of the related applications. Dr. Clauss did not move to Ropes & Gray LLP and did no further work on the Ariad patent applications. After this, no further corrections were made, and the '516 patent issued in 2002 with figure 43 included.

The district court did not clearly err by finding no intent to deceive the USPTO by Ms. Hausdorff, Dr. Vincent, or Dr. Clauss. While it is true that "because direct evidence of deceptive intent is rarely available, such intent can be inferred from indirect and circumstantial evidence[,] . . . such evidence must still be clear and convincing, and

inferences drawn from lesser evidence cannot satisfy the deceptive intent requirement." Star Scientific, 537 F.3d at 1366.

Dr. Vincent never knew of the errors. Thus, to the extent that he may have relied on figure 43 in his communications with the USPTO, this is insufficient evidence of intent to deceive. Ms. Hausdorff knew, but there is no other evidence that Ms. Hausdorff had any intent to conceal the errors from the USPTO. To the contrary, she disclosed the errors to her attorneys. She was justified in her expectation that her attorneys would determine the legal significance of the errors and take appropriate actions. Dr. Clauss also knew of the errors, but the district court credited Dr. Clauss's testimony that she was following Foley, Hoag & Elliot LLP's standard practice to make the correction only after the PTO indicated the claims were allowable in any particular related application. That knowledge of the errors was lost when Dr. Vincent moved to Ropes & Gray LLP does not rise to the level of intent to deceive. See Kingsdown Med. Consultants, Ltd. v. Hollister Inc., 863 F.2d 867, 876 (Fed. Cir. 1988) (en banc) (holding even gross negligence insufficient to prove intent to deceive). While Dr. Clauss's 1999 office action response could be the seed of a finding of intent, more evidence of deliberate concealment would be needed and this fact alone does not constitute "clear error" in the district court fact finding.

Lilly argues that the fact that figure 43 was left in the one application that issued as the '516 patent is sufficiently suspicious that it should contribute to a finding of intent. We disagree. It appears that the parties involved endeavored to correct figure 43 throughout the family of applications. These actions do not signal a nefarious plot to leave figure 43 in the one application that would lead to the patent now asserted; rather,

they signal an honest but imperfect attempt to correct mistakes. Certainly, deceptive intent is not "the single most reasonable inference able to be drawn from the evidence." Star Scientific, 537 F.3d at 1366. There is simply no evidence of what Lilly contends is "purposeful concealment" no matter how material the errors might be.

B.

The second of the two errors underlying Lilly's defense of inequitable conduct relates to the failure to submit four references to the USPTO during the prosecution of the '516 patent application. The references were not prior art per se; they were scientific papers published after the filing date of the '516 patent application and authored or co-authored by one of the patent's co-inventors, Albert Baldwin. The references discuss the impact of various compounds on NF-κB activity. According to Lilly, the references are relevant to the issue of whether certain claims are inherently anticipated by these prior art compounds. Ariad does not dispute the district court's finding that the omissions were material. Lilly argues that Ariad intentionally concealed the references, pointing to testimony by Dr. Baldwin that he knew the references were relevant to the subject matter of the '516 patent application. Lilly does not claim that any other person had the requisite intent.

There is no doubt that Dr. Baldwin was aware of the references, because he authored them. He testified as follows:

> Q. Did you at any time consider disclosing your findings regarding Resveratrol in those experiments to the United States Patent Office?
>
> A. I mean I — I considered it, but I — again, I feel like that one would inundate the patent office with every report of — of things that affect NF-κB one way or the other. It's — you can do a search on NF-κB and it's endless.

> Q. Why is it you considered disclosing your findings regarding the effect of Resveratrol in your experiments to the United States Patent Office?
>
> A. Well, we signed — we signed this document that says that was our obligation to do so at some point.

Dr. Baldwin—who is a scientist and not a patent lawyer—was apparently aware of his duty to disclose, and also aware that it could be inappropriate to submit material that might "inundate" the USPTO. His reasons for not submitting the references are plausible, even if ultimately legally incorrect, and Lilly failed to show that deceptive intent was the better explanation for Dr. Baldwin's behavior. Lilly failed to show that Dr. Baldwin had any knowledge of how the statements about the effect of prior art compounds on NF-κB activity made in the references could impact the '516 patent application. Lilly did not show that Dr. Baldwin appreciated the inherent anticipation theory to which the references allegedly pertained. And even if Lilly had shown this knowledge, it did not show that Dr. Baldwin had any knowledge of the historical uses of the prior art compounds. Accordingly, we conclude that the district court did not clearly err by finding no intent to deceive the USPTO on the part of Dr. Baldwin.

C.

Lilly cannot prove deceptive intent by clear and convincing evidence simply by relying on the materiality of the errors. Rather, there must be clear and convincing evidence of "culpable" conduct. Halliburton Co. v. Schlumberger Tech. Corp., 925 F.2d 1435, 1443 (Fed. Cir. 1991) (citing Consol. Aluminum Corp. v. Foseco Int'l Ltd., 910 F.2d 804, 809 (Fed. Cir. 1990)). Digital Control's statement that "a greater showing of [materiality] allow[s for] a lesser showing of [intent]" is not to the contrary. 437 F.3d at 1313. Only after a district court makes independent findings of both materiality and

intent may it weigh the two against each other in its ultimate determination of inequitable conduct. Materiality and intent are different requirements, and absent a finding of deceptive intent, no amount of materiality gives the district court discretion to find inequitable conduct. Star Scientific, 537 F.3d at 1365 ("If a threshold level of intent to deceive or materiality is not established by clear and convincing evidence, the district court does not have any discretion to exercise and cannot hold the patent unenforceable regardless of the relative equities or how it might balance them."); see Aventis Pharma S.A. v. Amphastar Pharms., Inc., 525 F.3d 1334, 1350 (Fed. Cir. 2008) (Rader, J., dissenting) ("Merging intent and materiality at levels far below the Kingsdown rule has revived the inequitable conduct tactic."). "[C]ourts must be vigilant in not permitting the defense [of inequitable conduct] to be applied too lightly." Star Scientific, 537 F.3d at 1366. Because Lilly failed to establish the "threshold level of intent to deceive . . . by clear and convincing evidence," the district correct correctly concluded that the '516 patent was not unenforceable due to inequitable conduct. Id. at 1365.

CONCLUSION

Because we hold that claims 80, 95, 144, and 145 of the '516 patent are invalid for lack of written description, we need not address infringement or the other validity issues on appeal. We affirm the district court's ruling that the '516 patent is not unenforceable due to inequitable conduct. The judgment below is

REVERSED-IN-PART AND AFFIRMED-IN-PART.

United States Court of Appeals for the Federal Circuit

2008-1248

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

Plaintiffs-Appellees,

v.

ELI LILLY AND COMPANY,

Defendant-Appellant.

Appeal from the United States District Court for the District of Massachusetts in case no. 02-CV-11280, Judge Rya W. Zobel.

LINN, Circuit Judge, concurring.

I join the opinion of the court because I concur that it is supported by our precedent. I write separately to emphasize, as I have before, my belief that our engrafting of a separate written description requirement onto section 112, paragraph 1 is misguided. See, e.g., Univ. of Rochester v. G.D. Searle & Co., Inc., 375 F.3d 1303, 1325-27 (Fed. Cir. 2004) (Linn, J., dissenting from denial of rehearing en banc); Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 987-89 (Fed. Cir. 2002) (Linn, J., dissenting from denial of rehearing en banc). As I observed in University of Rochester, section 112, paragraph 1 requires no more of the specification than a disclosure that is sufficient to enable a person having ordinary skill in the art to make and use the invention:

> Section 112 of Title 35 of the United States Code requires a written description of the invention, but the measure of the sufficiency of that written description in meeting the conditions of patentability in paragraph 1 of that statute depends solely on whether it enables any person skilled in the art to which the invention pertains to make and use the claimed invention and sets forth the best mode of carrying out the invention. The question presented by 35 U.S.C. § 112, paragraph 1, is not, "Does the written description disclose what the invention is?" The question is, "Does the written description describe the invention recited in the claims—themselves part of the specification—in terms that are sufficient to enable one of skill in the art to make and use the claimed invention and practice the best mode contemplated by the inventor?" That is the mandate of the statute and is all our precedent demanded prior to Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997).

375 F.3d at 1325.

As both this court and the Supreme Court have recognized, the claims—not the specification—define the invention. See Aro Mfg. Co. v. Convertible Top Replacement Co., 365 U.S. 336, 339 (1961) ("[T]he claims made in the patent are the sole measure of the grant."); see also Johnson & Johnston Assocs. Inc. v. R.E. Serv. Co., 285 F.3d 1046, 1052 (Fed. Cir. 2002) (en banc) ("Consistent with its scope definition and notice functions, the claim requirement presupposes that a patent applicant defines his invention in the claims, not in the specification. After all, the claims, not the specification, provide the measure of the patentee's right to exclude."). The court's invention of a separate written description requirement has "create[d] confusion as to where the public and the courts should look to determine the scope of the patentee's right to exclude," University of Rochester, 375 F.3d at 1326, causing uncertainty "in how inventions are protected, in how the [Patent & Trademark Office] discharges its responsibilities, and in how business is conducted in emerging fields of law," id. at 1327.

Aside from these general observations, I note that the written description requirement does separate mischief in this case. Because the court relies upon this

requirement to reverse the district court, it does not reach the important enablement issue raised by Lilly. As the majority opinion observes, the claims-in-suit broadly claim any method for reducing NF-κB activity in cells, including both known and unknown methods. We have long held that in order to survive the enablement requirement, the specification "must describe the manner and process of making and using the invention so as to enable a person of skill in the art to make and use the full scope of the invention without undue experimentation." LizardTech, Inc. v. Earth Res. Mapping, Inc., 424 F.3d 1336, 1344-45 (Fed. Cir. 2005) (emphasis added); see also Invitrogen Corp. v. Clontech Labs., Inc., 429 F.3d 1052, 1070 (Fed. Cir. 2005). To my knowledge, however, we have not specifically addressed this requirement in relation to the type of claims at issue here—that is, claims written broadly enough to cover any method for achieving a particular result. It may be, as Lilly argues, that such a claim can never be valid, since the specification cannot enable unknown methods. Cf. In re Hyatt, 708 F.2d 712, 714 (Fed. Cir. 1983) (rejecting "single means" claim, as such claims "cover[ ] every conceivable means for achieving the stated result"). This is an important issue that we have left unresolved. It is an issue that we would have been compelled to reach had the case been decided on enablement grounds, a basis found in section 112, instead of on written description grounds, a separate basis not justified under that section or any other provision of the Patent Act.