United States Court of Appeals for the Federal Circuit

03-1158, -1159

CHIRON CORPORATION,

Plaintiff-Appellant,

v.

GENENTECH, INC.,

Defendant-Cross Appellant.

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Appealed from: United States District Court for the Eastern District of California

Judge William B. Shubb

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DECIDED: March 30, 2004

Before RADER, Circuit Judge, ARCHER, Senior Circuit Judge, and BRYSON, Circuit Judge.

Opinion for the court filed by Circuit Judge RADER. Concurring opinion filed by Circuit Judge BRYSON.

RADER, Circuit Judge.

After a jury trial, the United States District Court for the Eastern District of California entered judgment in favor of Genentech that all claims of U.S. Patent No. 6,054,561 are invalid under 35 U.S.C. § 102 because none of the asserted claims is entitled to priority to a series of applications filed in 1984, 1985, and 1986. Chiron Corp. v. Genentech, Inc., No. Civ. S-00-1252 WBS GGH (Sept. 9 & Oct. 23, 2002). Because Chiron did not adequately disclose or support the subject matter of its '561 patent in its 1984, 1985, or 1986 applications, this court

affirms the district court's denial of a motion for judgment as a matter of law (JMOL) and motion for a new trial.

I.

The '561 patent claims particular monoclonal antibodies. Specifically, independent claim 19 states:[1] "A monoclonal antibody that binds to human c-erbB-2 antigen."

According to modern understanding, a monoclonal antibody is a composition with a homogeneous antibody population. An antibody is a protein generated by the immune system that is capable of recognizing and binding to a specific antigen. Described in terms of its structure, an antibody is a Y-shaped protein consisting of four amino acid chains, two heavy and two light. In a simplified model sufficient for this appeal, each antibody has primarily two regions: a variable region and a constant region. The variable region, located on the ends of the arms of the Y, binds to and interacts with the target antigen. This variable region includes a complementary determining region (CDR) that recognizes and binds to a specific binding site on a

[1] Chiron also relies upon independent claims 1 and 9.

Claim 1 recites:

> A monoclonal antibody that binds to a human breast cancer antigen that is also bound by monoclonal antibody 454C11 which is produced by the hybridoma deposited with the American Type Culture Collection having Accession No. HB 8484.

Claim 9 recites:

> A monoclonal antibody that binds to a human breast cancer antigen that is also bound by monoclonal antibody 520C9 which is produced by the hybridoma deposited with the American Type Culture Collection having Accession No. HB 8696.

particular antigen. The constant region, located on the tail of the Y, is recognized by and interacts with the immune system.

A target antigen generally has numerous binding sites, also called epitopes, recognized by CDRs on multiple antibodies. Each antibody that specifically binds to a different epitope has a different structure. Thus, one antigen may have more than one corresponding antibody. In this case, claim 19 of the '561 patent reads on monoclonal antibodies that bind to human c-erbB-2 antigen (also named HER2) – an antigen associated with breast cancer cells.

There are various methods of producing monoclonal antibodies. One method uses hybridoma technology, which refers to a cloned cell line that produces a single type of antibody. The hybridoma method uses the cells of various species, including mice, hamsters, rats, and humans. Murine antibodies – derived from mouse cells – are particularly important for this invention.

Another method uses genetic engineering including recombinant DNA techniques. Monoclonal antibodies made from these techniques include, among others, chimeric antibodies and humanized antibodies. A chimeric antibody combines DNA encoding regions from more than one type of species. For example, a chimeric antibody may derive the variable region from a mouse and the constant region from a human. A humanized antibody comes predominantly from a human, even though it contains nonhuman portions. Like a chimeric antibody, a humanized antibody may contain a completely human constant region. But unlike a chimeric antibody, the variable region may be partially derived from a human. The nonhuman, synthetic portions of a humanized antibody often come from CDRs in murine antibodies. In any

event, these regions are crucial to allow the antibody to recognize and bind to a specific antigen.

As noted, murine antibodies play an important role in these technologies. While useful for diagnostics and short-term therapies, murine antibodies cannot be administered to people long-term without increasing the risk of a deleterious immunogenic response. This response, called Human Anti-Mouse Antibody (HAMA), occurs when a human immune system recognizes the murine antibody as foreign and attacks it. A HAMA response can cause toxic shock or even death.

Chimeric and humanized antibodies reduce the likelihood of a HAMA response by minimizing the nonhuman portions of administered antibodies. Furthermore, chimeric and humanized antibodies have the additional benefit of activating secondary human immune responses, such as antibody dependent cellular cytoxicity.

In the early 1980s, scientists at Chiron's predecessor corporation, Cetus Corp., (collectively, Chiron) began investigating monoclonal antibodies that target human breast cancer antigens. As noted above, the antigen that facilitates diagnosis and treatment of breast cancer was eventually named HER2. This investigational work led to a series of patent applications. The inventors filed their first application on February 8, 1984. Within a year, on January 11, 1985, they filed a continuation-in-part (CIP) application claiming priority based on that first 1984 application. The inventors filed another CIP application on May 21, 1986. Eventually, the application that led to the '561 patent was filed as another CIP on June 7, 1995. This appeal focuses on the '561 patent's claims to priority based on the applications filed in 1984, 1985, and 1986.

The 1984 application discloses one monoclonal antibody (454C11) that binds to HER2. The 454C11 is a murine antibody produced by the hybridoma method. While the application discloses the deposit of the hybridoma that produced the monoclonal antibody, the application does not identify the structure, function, or molecular weight of the antigen. Because the first publication that disclosed chimeric antibody technology did not appear until four months after this filing, it is not surprising that the 1984 application does not disclose any chimeric antibodies. Similarly, the first publication to disclose humanized antibodies appeared in May 1986. Thus, for good reason, this 1984 application also does not mention any humanized antibodies.

The 1985 application discloses six additional monoclonal antibodies that bind to HER2, all of which are murine antibodies. The disclosure also refers to the deposit of an additional hybridoma for one of these monoclonal antibodies, 520C9. While the application provides an approximate antigen molecular weight of 210 kilodaltons,[2] the application does not describe the identity, structure, or function of the antigen. The application does, however, note that six of the seven antibodies likely bind to the same epitope. By the time of this application, chimeric antibody technology was known in this art field. Although the application does not specifically disclose chimeric or humanized antibodies, it adds the following disclosure:

> As used herein the term "monoclonal antibody" means an antibody composition having a homogeneous antibody population. It is not intended to be limited as regards the source of the antibody or the manner in which it is made.

The 1986 application discloses six additional murine antibodies that bind to HER2 and the deposit for three additional hybridomas. Thus, this application discloses

[2] The HER2 antigen is now known to have a molecular weight of 185 kilodaltons.

a total of thirteen murine antibodies and deposits for five of their corresponding hybridomas, including those corresponding to 454C11 and 520C9. The application discloses that these antibodies likely bind to at least three different epitopes on HER2. Although still not identifying the antigen by name, the application discloses that its molecular weight is approximately 200 kilodaltons. Although the 1986 application makes no specific mention of chimeric or humanized antibodies, it quotes again the statement that the term monoclonal antibody "is not intended to be limited as regards the source of the antibody or the manner in which it is made."

When the '561 patent issued, Chiron sued Genentech over sales of Herceptin®, a humanized antibody useful for the long-term treatment of breast cancer. Herceptin binds to the HER2 antigen and thus inhibits the growth of cancerous cells. Because Herceptin is a humanized antibody, it minimizes any HAMA response in patients.

Before trial, the district court broadly construed the claims of the '561 patent to embrace chimeric and humanized antibodies in addition to the murine antibodies that bind to HER2. Chiron Corp. v. Genentech, Inc., 266 F. Supp. 2d 1172 (E.D. Cal. 2002). Accordingly, the district court subsequently granted Chiron's motion for partial summary judgment of infringement. Chiron Corp. v. Genentech, Inc., No. Civ. S-00-1252 WBS GGH, 2002 U.S. Dist. LEXIS 19126 (E.D. Cal. June 24, 2002). Also before trial, the parties stipulated that the '561 patent would be invalid under § 102 based on intervening prior art if the patent were not entitled to claim priority to the filing date of any one of the 1984, 1985, and 1986 applications. Thus, the thirteen-day jury trial adjudicated only whether any of the priority applications satisfy the written description and enablement requirements of 35 U.S.C. § 112, first paragraph. Specifically the trial determined

whether the 1980s applications adequately disclosed, and thus supported, the claim to chimeric and humanized antibodies claimed in the '561 patent (with its filing date in 1995). The jury determined that Genentech proved by clear and convincing evidence that none of the applications satisfy both the written description and the enablement requirement for the subject matter in the '561 patent's claims. The verdict form, however, did not require the jury to specify the particular requirement of §112 left unfulfilled by each disclosure of the priority applications. After trial, the district court denied Chiron's motions for JMOL and a new trial.

Chiron appeals the denial of its post-trial motions, and Genentech conditionally "cross-appeals" the district court's claim construction. Although styled as a cross-appeal, this court treats this claim construction issue as an alternative ground for affirming the judgment. A cross-appeal is only proper if "a party seeks to enlarge its own rights under the judgment or to lessen the rights of its adversary under the judgment." Bailey v. Dart Container Corp. of Mich., 292 F.3d 1360, 1362 (Fed. Cir. 2002). This court has jurisdiction under 28 U.S.C. § 1295.

II.

A trial court should grant a motion for JMOL if substantial evidence does not support the jury's factual findings, presumed or express, or if those factual findings cannot support the legal conclusions implied from the jury's verdict. Kearns v. Chrysler Corp., 32 F.3d 1541, 1547-48 (Fed. Cir. 1994). This court reviews a district court's denial of a JMOL motion without deference. Sextant Avionique, S.A. v. Analog Devices, Inc., 172 F.3d 817, 824 (Fed. Cir. 1999).

Section 120 of title 35 provides: "An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States . . . shall have the same effect, as to such invention, as though filed on the date of the prior application." Accordingly, the '561 patent may only claim priority to an earlier application if the earlier application fulfills the requirements of § 112, first paragraph. In turn, that paragraph requires, in part, that the application "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." 35 U.S.C. § 112, ¶1.

This court has interpreted this passage as setting forth two requirements: written description and enablement. Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1330 (Fed. Cir. 2003). As explained further below, this court affirms because neither the 1985 nor the 1986 application enables the claims of the '561 patent. The 1984 application does not support the new matter added to the '561 patent and thus does not satisfy the written description requirement.

Whether the earlier applications enable the claims of the '561 patent is a question of law based on underlying facts. In re Wands, 858 F.2d 731, 735 (Fed. Cir. 1988). This court reviews the underlying factual findings for clear error and the legal component of enablement without deference. Plant Genetic Sys. N.V. v. DeKalb Genetics Corp., 315 F.3d 1335, 1339 (Fed. Cir. 2003). Because the '561 patent is presumed valid, clear and convincing evidence must support a conclusion of invalidity.

See 35 U.S.C. §282; Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1375 (Fed. Cir. 1986).

The applications in this case satisfy the enablement requirement only if one skilled in the art, after reading their disclosures, could practice the invention claimed in the '561 patent without undue experimentation. Wands, 858 F.2d at 736-37. "But the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.'" PPG Indus., Inc. v. Guardian Indus., Corp., 75 F.3d 1558, 1564 (Fed. Cir. 1996) (quoting Atlas Powder Co. v. E.I. DuPont de Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984)).

Moreover, the prior application must enable one of ordinary skill in the art to practice "the full scope of the claimed invention." In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Clarifying this principle, this court has explained: "That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art." AK Steel Corp. v. Sollac, 344 F.3d 1234, 1244 (Fed. Cir. 2003). Thus, "[t]he enabling disclosure of the specification [must] be commensurate in scope with the claim under consideration." In re Hyatt, 708 F.2d 712, 714 (Fed. Cir. 1983).

Whether the earlier applications enable the claims of the '561 patent is determined as of the filing date of each application. See Plant Genetic Sys., 315 F.3d at 1339. As noted above, a patent disclosure need not enable information within the

knowledge of an ordinarily skilled artisan. Thus, a patentee preferably omits from the disclosure any routine technology that is well known at the time of application. See Hybritech, 802 F.2d at 1384. At the other end of the knowledge continuum, a patent document cannot enable technology that arises after the date of application. The law does not expect an applicant to disclose knowledge invented or developed after the filing date. Such disclosure would be impossible. See In re Hogan, 559 F.2d 595, 605-06 (CCPA 1977). Nascent technology, however, must be enabled with a "specific and useful teaching." Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1368 (Fed. Cir. 1997). The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology. See, e.g., J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc., 534 U.S. 124, 142 (2001).

"Because a patent specification must enable the full scope of a claimed invention, an enablement inquiry typically begins with a construction of the claims." AK Steel, 344 F.3d at 1241 (citation omitted). In this case, neither party challenges the district court's claim construction in the first instance. As a precaution, Genentech posits a "cross-appeal" on claim construction in the event this court reverses the denials of Chiron's post-trial motions. Because Genentech's arguments regarding claim construction are alternative grounds for affirming the verdict, Bailey, 292 F.3d 1360, this court proceeds on the premise that the claim construction is correct. The district court's claim construction reads the claims of the '561 patent to embrace not only murine antibodies but also chimeric and humanized antibodies that bind to HER2.

At the outset, this court focuses primarily on chimeric antibodies. If the applications in this case do not enable or provide new matter support for chimeric antibodies, this court need not proceed to examine humanized antibodies. The trial record shows that genetically engineered antibodies, specifically chimeric antibodies, first appeared as a successful technology in the literature of this art field in May 1984, four months after the February filing date of the first application. Because the first publication documenting the successful creation of chimeric antibodies occurred after the filing of the 1984 application, this sequence of events shows that this new technology arose after the filing date and thus was, by definition, outside the bounds of the enablement requirement. See Hogan, 559 F.2d at 605-06.

The district court in this case attempted to justify the jury's enablement verdict on the basis that the 1984 applicants might have known about chimeric antibodies before the initial publication on that subject. The trial court cited speculative testimony in the trial about the hypothetical possibility that information may leak out in advance of an initial publication on an important academic topic. At no point did the record show that Chiron scientists actually knew of chimeric antibodies before their filing, only that it was hypothetically possible for them to have acquired some advance knowledge. Even if the record shows that scientists routinely discuss their work with others in the same art field before publication, ethics would suggest impropriety in publishing that information in advance of the actual originator of the ideas. In any event, as noted, the enablement requirement does not extend to technology that arises after the time of filing. Plant Genetic Sys., 315 F.3d at 1340-41. In sum, the district court erred to the extent that it

attempted to create an obligation for Chiron scientists to enable nonexistent technology in the 1984 filing.

In the context of the 1984 application, the trial court and this court need not rely on enablement to support the jury's verdict. The jury may have found that the 1984 application does not provide any support for the new matter, chimeric antibodies, claimed in the '561 patent. Because chimeric antibody technology did not even exist at the time of the 1984 filing, the record conclusively supports that the Chiron scientists did not possess and disclose this technology in the February 1984 filing. See Union Oil Co. of Cal. v. Atl. Richfield Co., 208 F.3d 989, 998 (Fed. Cir. 2000) (A jury determined "that, as of the filing date, the inventor conveyed with reasonable clarity to those of skill in the art that he was in possession of the subject matter of the claims."). Thus, the '561 patent cannot claim priority based on the 1984 application because it fails to comply with the written description requirement.

The written description requirement prevents applicants from using the amendment process to update their disclosures (claims or specifications) during their pendency before the patent office. Otherwise applicants could add new matter to their disclosures and date them back to their original filing date, thus defeating an accurate accounting of the priority of invention. See 35 U.S.C. § 132. Priority is always a vital issue in patent prosecution procedures – often determining entitlement to an invention. In 1967, this court's predecessor began to enforce priority as a component of the 35 U.S.C. § 112, first paragraph, written description requirement. In re Ruschig, 379 F.2d 990 (CCPA 1967). In the context of a new claim added "[a]bout a year after the present application was filed," the Ruschig court sought to determine "whether [the new] claim

13 is supported by the disclosure of appellants' application." Id. at 991. As later explained, "[t]he function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him." In re Wertheim, 541 F.2d 257, 262 (CCPA 1976). In this case, the Chiron scientists, by definition, could not have possession of, and disclose, the subject matter of chimeric antibodies that did not even exist at the time of the 1984 application. Thus, axiomatically, Chiron cannot satisfy the written description requirement for the new matter appearing in the '561 patent, namely chimeric antibodies. See, e.g., In re Kaslow, 707 F.2d 1366, 1375 (Fed. Cir. 1983) ("The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language." (citation omitted)).

Turning next to the 1985 and 1986 applications, this court examines compliance with the enablement requirement. For these applications, the jury was entitled to determine as a matter of fact that chimeric antibodies were not future technology, but were nascent technology requiring a "specific and useful teaching." Genentech, 108 F.3d at 1368. This question, in turn, depends on evidence that undue experimentation would be required to make and use the chimeric antibodies claimed by the '561 patent. Of course, undue experimentation "is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." Wands, 858 F.2d at 737. These factual considerations include "(1) the quantity of experimentation

necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." Id.

Evidence presented to the jury showed that creation of genetically engineered antibodies, such as chimeric antibodies, required significant experimentation in 1985 and 1986 because those antibodies were unpredictable at that early stage of development. The record also shows that only a few laboratories contained the necessary equipment to make these new antibodies – another indication of the excessive experimentation necessary to make and use that technology at that time. The 1985 and 1986 applications provide no disclosure of either how to make and use chimeric antibodies or working examples of chimeric antibodies within the scope of the '561 patent's claims.

Moreover, as mentioned above, "[t]he enabling disclosure of the specification [must] be commensurate in scope with the claim under consideration." Hyatt, 708 F.2d at 714. Here, the scope of the claim includes not only murine but also chimeric antibodies. While Chiron's applications certainly enable murine antibodies, they do not enable chimeric antibodies. Although an aspect of the claimed invention included the binding of an antibody to a breast cancer antigen, Chiron's disclosure fell short of providing a "specific and useful teaching," Genentech, 108 F.3d at 1368, of all antibodies within the scope of the claim.

By the filing date of the 1986 application, Chiron contends that chimeric antibodies were so well known that they had become routine technology. Chiron

particularly highlights a number of publications before the 1986 application that disclosed methods of making chimeric antibodies. Accordingly, Chiron argues that the 1986 application need not specifically enable chimeric antibodies, because technicians of ordinary skill in this art could make and use them by that time without undue experimentation. Substantial evidence, however, supports the jury's implicit finding that the technology was still nascent at the time of the 1986 application (as well as, of course, at the time of the 1985 application) and thus would have still required undue experimentation.

In particular, Genentech's expert, Dr. French, testified that making chimeric antibodies was not routine technology in 1985 or 1986. Dr. French also testified that, by 1986, only a few laboratories had the capacity and expertise necessary to make genetically engineered antibodies. Dr. Larrick, another one of Genentech's experts, testified that polymerase chain reaction (PCR), a technique that facilitated the manufacture of genetically engineered antibodies including chimeric antibodies, did not become widespread until sometime between 1986 and 1988. Although PCR is not necessary to make chimeric antibodies, PCR diminishes the difficulties associated with manufacturing genetically engineered antibodies. Furthermore, by 1989, an article authored by a pioneer in the field described techniques of chimeric antibodies as "obviously those of a very young and very ambitious field." Sherie L. Morrison, Genetically Engineered (Chimeric) Antibodies, 24 Hosp. Practice (No. 10) 65, 75 (Oct. 15, 1989). The article further noted: "We are all new to the game." Thus, substantial evidence supports the finding that chimeric antibodies were still a nascent technology at the time the 1985 and 1986 applications were filed. Accordingly, the record amply

supports the jury's conclusion that the 1985 and 1986 applications do not enable the claims of the '561 patent without undue experimentation.

While agreeing with the conclusion that the '561 patent may not claim priority to the 1984 application, the concurrence reads Hogan and Plant Genetics as allowing an inquiry into whether an application must enable future technology. This court cannot avoid the precedent of Hogan, which is binding unless overruled en banc, by virtue of the more recent Plant Genetics. See Allergan, Inc. v. Alcon Labs, Inc., 324 F.3d 1322, 1332-34 (Fed. Cir. 2003). But even if earlier precedent could be disregarded, this court does not read Plant Genetics to hold that an application must enable unknown, future technology. Plant Genetics states:

> We do not read Hogan as allowing an inventor to claim what was specifically desired but difficult to obtain at the time the application was filed, unless the patent discloses how to make and use it. In Hogan, amorphous propylene, on the record before the court, was not known or in existence when the application was filed. In the present case, however, monocots existed in 1987 and stably-transformed monocot cells were highly desirable. PGS indeed asserts that monocot cells were already being stably transformed. Thus, monocots and stably transformed monocot cells were not an unknown concept that came into existence only after 1987. But stably transformed monocot cells were difficult to produce, and the '236 patent gave no instruction how.

315 F.3d at 1340 (emphasis added). Thus, Plant Genetics distinguishes Hogan because stably transformed monocots were nascent technology when the application was filed, unlike the unknown and nonexistent amorphous propylene in the prior case. In the present case, chimeric antibodies, like the amorphous propylene in Hogan, did not even appear for the first time until several months after the 1984 application.

Because the '561 patent is invalid for the reasons noted above, this court need not reach the question of claim construction. This case poses a particular challenge for accurate assessment of the meaning of the claim terms. In this case, the meaning of

"monoclonal antibody" may not have been stagnant between the earlier applications and the '561 patent. The ordinary usage of "monoclonal antibody" in the early 1980s was narrow. For example, one treatise defines "monoclonal antibody" in these narrow terms: "Antibody secreted by a hybridoma clone. Because each such clone is derived from a single B cell, all of the antibody molecules it makes are identical." Bruce Alberts et al., Molecular Biology of the Cell G-15 (3d ed. 1994); accord Bruce Alberts et al., Molecular Biology of the Cell 182-84 (1983). Indeed, another textbook expressly equated "monoclonal antibody" with "hybridoma antibody." Leroy E. Hood et al., Immunology 20 (1984). Thus, the term "monoclonal antibody" in 1984 apparently referred to antibodies made with hybridoma and was not broad enough to encompass chimeric antibodies. See Alan Munro, Uses of Chimaeric Antibodies, 312 Nature 597 (1984) (differentiating monoclonal antibodies from chimeric antibodies). Accordingly, when the earliest priority application was filed, "monoclonal antibody" apparently referred only to a hybridoma-derived antibody. The 1984 application did not expressly redefine the term.[3]

The '561 patent, however, included a definition for "monoclonal antibody":

> The term "antibody" encompasses polyclonal and monoclonal antibody preparations, as well as preparations including hybrid antibodies, altered antibodies, chimeric antibodies and, [sic] humanized antibodies.
>
> As used herein, the term "monoclonal antibody" refers to an antibody composition having a homogeneous antibody population. The term is not limited regarding the species or source of the antibody, nor is it intended

[3] The additional disclosure of the 1985 and 1986 applications, which stated that "monoclonal antibody" "is not intended to be limited as regards the source of the antibody or the manner in which it is made," may have had some broadening effect on the ordinary meaning of the term. This court, however, need not decide that issue. In any event, the 1984 application did not exercise the lexicographer's option of expressly defining the disputed term.

> to be limited by the manner in which it is made. The term encompasses whole immunoglobulins.

'561 patent, col. 8, ll. 36-45. Thus, the '561 patent defined "monoclonal antibody" to include chimeric and humanized antibodies. Still only a portion of this updated meaning of "monoclonal antibody" can claim priority to the earliest application. If required to engage in claim construction, therefore, this court would face a dilemma: Either construe the term according to the meaning of the earliest application but contrary to the explicit definition in the '561 patent or construe the term according to the explicit definition in the '561 patent but broader than the disclosure of the earliest application. Again, the latter alternative would run afoul of the prohibition against importing new matter into later patent documents. As noted, however, the record amply supports the jury's verdict of invalidity without reaching this complex claim construction question.

III.

A trial court should grant a motion for a new trial if (1) the jury instructions were erroneous or inadequate, (2) the court made incorrect and prejudicial admissibility rulings, or (3) the verdict is contrary to the great weight of the evidence. Murphy v. Long Beach, 914 F.2d 183, 186 (9th Cir. 1990); Chalmers v. City of Los Angeles, 762 F.2d 753, 761 (9th Cir. 1985). Chiron asserts that it is entitled to a new trial based on the first and second avenues. This court reviews the denial of a new trial motion after a jury verdict for an abuse of discretion. Advanced Cardiovascular Sys., Inc. v. Medtronic, Inc., 265 F.3d 1294, 1308 (Fed. Cir. 2001); De Saracho v. Custom Food Mach., Inc., 206 F.3d 874, 880 (9th Cir. 2000).

With respect to the jury instructions, Chiron assigns error to four separate rulings. This court reviews jury instructions in their entirety and "only orders a new trial when

errors in the instructions as a whole clearly misled the jury." Delta-X Corp. v. Baker Hughes Prod. Tools, Inc., 984 F.2d 410, 415 (Fed. Cir. 1993). Furthermore, Chiron "must show both fatal flaws in the jury instructions and a request for alternative instructions which could have corrected the flaws." Id.

First, Chiron argues that the district court erred by instructing the jury on Genentech's burden of proof without also adding an instruction on the presumption of the '561 patent's validity. This court disagrees, because the presumption of validity and heightened burden of proving invalidity "are static and in reality different expressions of the same thing – a single hurdle to be cleared." Am. Hoist & Derrick Co. v. Sowa & Sons, Inc., 725 F.2d 1350, 1360 (Fed. Cir. 1984); see also Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319 (Fed. Cir. 2003). Moreover, this court has explained: "[T]he presumption is one of law, not fact, and does not constitute 'evidence' to be weighed against the challenger's evidence." Avia Group Int'l Inc. v. L.A. Gear Cal., Inc., 853 F.2d 1557, 1562 (Fed. Cir. 1988). Therefore, the district court did not err in declining to include a jury instruction on the presumption of validity because the jury applied the correct "clear and convincing evidence" standard.

Second, Chiron argues that the district court erred by instructing the jury on the law of written description. In particular, Chiron complains that three instructions – the first and third of which were not grouped with the written description instructions – collectively may have directed the jury to find the '561 patent invalid if the earlier applications did not describe every embodiment known to skilled artisans as of the filing dates. The first instruction set forth the construction of "monoclonal antibody." The second instruction stated: "An application satisfies the written description requirement if

persons of ordinary skill in the art at the time the application was filed would recognize from the application that the inventor actually invented the full scope of the invention as finally claimed in the patent." The third instruction set forth that the jury would "determine whether the forms referred to in the definition of 'monoclonal antibody' were or were not known in the art at the time the 1984, 1985, and 1986 applications were filed." This court rejects Chiron's challenge, because the district court instructed the jury on the proper standard for the written description requirement in the second instruction. Even though the second instruction did not echo the precise language of this court's cases, this court has stated that "compliance with § 112 has always required sufficient information in the original disclosure to show that the inventor possessed the invention at the time of the original filing." Moba, 325 F.3d at 1320. The district court's instruction embodies the principle of this court's statement in Moba. The district court need not use identical language to this court's opinions in its instructions.

Separately, Chiron challenges another instruction on written description, which the district court based on Gentry Gallery, Inc. v. Berkline Corp., 134 F.3d 1473 (Fed. Cir. 1998), and Cooper Cameron Corp. v. Kvaerner Oilfield Products, Inc., 291 F.3d 1317 (Fed. Cir. 2002). In particular, the court instructed the jury:

> One way Genentech can meet its burden of proving that an earlier application fails to satisfy the written description requirement is to show, by clear and convincing evidence, that the entirety of the specification of an earlier application would clearly indicate to persons of ordinary skill in the art that the invention described in that application is of a much narrower scope than the invention ultimately claimed in the '561 patent.
>
> In considering this issue, the particular question you must decide is whether the 1984, 1985 or 1986 applications clearly indicate to a person of ordinary skill in the art that the invention described is . . . narrower in scope than the claims of the '561 patent at issue.

Chiron argues that this instruction invited the jury to apply a test that does not correspond to this court's written description law. This court again rejects Chiron's argument. Once again, though using different words, the district court's instruction captures the essence of the written description doctrine that a patent cannot claim priority to earlier applications if it includes new matter not present in those earlier disclosures. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Therefore, this court finds no error in the jury instructions on written description.

Third, Chiron argues that the district court erred by instructing the jury on the law of enablement. In particular, Chiron complains that the district court erred in rejecting the following two proposed instructions:

> The patent application need only enable what it is claimed. Features or characteristics that are not claimed need not be enabled. In this case, the novel aspect of the invention claimed in the '561 patent concerns monoclonal antibodies capable of binding to a specific breast cancer antigen.
>
> To meet the enablement requirement, an application need not enable every way of making the claimed invention. An application meets the enablement requirement if it enables even one way of making the claimed invention.

This court rejects the notion that the district court erred by declining to include these instructions. The district court provided a succinct and correct summary of the law of enablement that Chiron does not challenge. A trial court need not further instruct the jury on what enablement does not require. Cf. Novo Nordisk A/S v. Becton Dickinson & Co., 304 F.3d 1216, 1219-20 (Fed. Cir. 2002) (affirming a district court's refusal to include an instruction that "obvious to try" is not a correct obviousness standard).

Lastly, Chiron argues that the district court erred by instructing the jury that the validity of the dependent claims stands or falls with the validity of the independent claims. Chiron correctly cites the general rule that "a party challenging the validity of a claim, absent a pretrial agreement or stipulation, must submit evidence supporting a conclusion of invalidity of each claim the challenger seeks to destroy." Shelcore, Inc. v. Durham Indus., Inc., 745 F.2d 621, 625 (Fed. Cir. 1984) (emphasis in original). The district court clearly recognized and understood that general rule. The district court, however, also recognized that, in this case, the validity challenges to the independent claims coincided with the validity challenges to the dependent claims; the sameness of the inquiries permitted the treatment of all claims at once. Cf. Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc., 166 F.3d 1190, 1198 (Fed. Cir. 1999) (holding that, under the facts of that case, the dependent claims were invalid solely because their independent claim was invalid). Moreover, the district court's instruction eliminated the potential for an inconsistent verdict; this court commends such foresight. This court, therefore, holds that the district court did not err in instructing the jury, particularly when those instructions are examined as a whole and read in context.

With respect to the prejudicial evidence, Chiron assigns error to three rulings. This court will reverse the district court's denial of a new trial motion based on evidentiary rulings only if Chiron establishes both that the rulings were an abuse of discretion and that it suffered substantial prejudice. Ruvalcaba v. Los Angeles, 64 F.3d 1323, 1328 (9th Cir. 1995); Advanced Cardiovascular, 265 F.3d at 1308; United States v. 99.66 Acres of Land, 970 F.2d 651, 658 (9th Cir. 1992).

First, Chiron argues that the district court erred in admitting evidence regarding the accused drug product Herceptin and regarding the absence of a commercial embodiment by Chiron. This court rejects Chiron's argument, because these facts related to Genentech's defenses. For example, post-1986 evidence, including evidence regarding Herceptin, may show what was known about making and using humanized antibodies in 1986. The absence of a commercial embodiment by Chiron also bears on whether chimeric or humanized antibodies within the scope of the claims of the '561 patent were routine technology. Accordingly, that evidence is relevant to enablement. Moreover, the district court issued a limiting instruction on the evidence relating to Herceptin, which stated that the jury may consider it helpful in deciding whether the 1986 application meets the enablement and written description requirements. Chiron also takes issue with Genentech's mention of this evidence in its closing argument. See Union Carbide Chems. & Plastics Tech. Corp. v. Shell Oil Co., 308 F.3d 1167, 1183-84 (Fed. Cir. 2002). But Chiron points to no evidence of jury prejudice as a result of the identified statements, which were buried in a seventy-seven page transcript of Genentech's closing argument. See Hemmings v. Tidyman's Inc., 285 F.3d 1174, 1194 (9th Cir. 2002) (explaining that an isolated comment during sixty-six page closing argument did not warrant a new trial). Accordingly, this court declines to assign reversible error in denying a new trial based on this evidence.

Second, Chiron argues that the district court erred in admitting evidence relating to unclaimed features, such as binding to particular epitopes or specific therapeutic effects. Chiron particularly objects to evidence regarding the extent of the HAMA response caused by murine antibodies. This court rejects Chiron's argument, because

the district court recognized that testimony regarding the HAMA response and epitope binding was relevant to the claimed features of the monoclonal antibodies. Unless the claim construction is incorrect (which Chiron does not assert), this testimony is relevant.

Finally, Chiron argues that the district court erred in excluding previously admitted documents from the prosecution of a related application assigned to Genentech (the Drebin/Greene application). This court rejects Chiron's argument. Chiron first proffered this evidence, which related to the '561 patent's priority date, before declaration of an interference between the '561 patent and the Drebin/Greene application. When the Board of Patent Appeals and Interferences issued a Notice of Interference, the district court decided that it would strike prior evidence introduced by Chiron and informed Chiron that it would be "inclined" to grant a mistrial. But when the court directly asked Chiron whether it was making a motion for a mistrial, Chiron expressly declined to do so. Accordingly, the district court did not err in declining Chiron's post-trial motion for a new trial based on Chiron's introduction of evidence that was later stricken. Thus, none of these alleged errors warrants reversing the district court's denial of a new trial.

IV.

Because substantial evidence supported the jury's verdict that the '561 patent cannot claim priority to any of the 1984, 1985, and 1986 applications and because the district court did not err in denying Chiron's motion for a new trial, this court affirms the judgment of the district court.

COSTS

Each party shall bear its own costs.

AFFIRMED

United States Court of Appeals for the Federal Circuit

03-1158, -1159

CHIRON CORPORATION,

Plaintiff-Appellant,

v.

GENENTECH, INC.,

Defendant-Cross Appellant.

BRYSON, Circuit Judge, concurring.

I concur in the judgment and in most of the court's opinion. With respect to the issue of priority, I agree that because of a failure to satisfy the written description requirement, Chiron is not entitled to priority back to 1984 for claims broadly construed to incorporate chimeric antibodies. I disagree with the court, however, in holding that the district court erred when it sustained the jury's verdict that the 1984 application did not enable the chimeric antibodies claimed in the '561 patent. I would uphold the jury's verdict in that regard. In my view, the jury permissibly concluded that the 1984 application, like the 1985 and 1986 applications, did not enable chimeric antibodies.

Citing In re Hogan, 559 F.2d 595 (CCPA 1977), the court holds that because it would be impossible for an applicant "to disclose knowledge invented or developed after the filing date" of the application, and because "the creation of chimeric antibodies first occurred after the 1984 application," the timing of the application and the development of chimeric antibody technology "precluded any enablement analysis at all." To be sure,

the enablement issue as to the 1984 application does not affect the outcome of this case, because the court properly finds that the 1984 application failed to satisfy the written description requirement and the patentee therefore was not entitled to priority as of the date of the 1984 application. Nonetheless, I do not agree that the enablement requirement is inapplicable to the 1984 application.

Section 112, paragraph 1, of the Patent Act requires that an applicant who wishes to claim property rights in an invention must bear the burden of demonstrating enablement by showing the public how to make and use the invention. As applied to this case, that principle would require the 1984 application to enable the invention claimed in that application. In my view, In re Hogan does not prevent us from reaching that conclusion.

In Hogan, the PTO rejected certain claims for lack of enablement after concluding that, in light of post-application developments, the claim scope was broad enough to read on certain embodiments that were not enabled by the application. The Court of Customs and Patent Appeals reversed, holding that it was enough that the application enabled the claims as construed in light of the state of the art at the time of filing. As the court explained, "if appellants' 1953 application provided sufficient enablement, considering all available evidence (whenever that evidence became available) of the 1953 state of the art, i.e., of the condition of knowledge about all art-related facts existing in 1953, then the fact of that enablement was established for all time and a later change in the state of the art cannot change it." 559 F.2d at 605.

I have no quarrel with the holding of Hogan—that enablement must be judged in light of the state of the art at the time of the application. What must be guarded against,

in my view, is to interpret Hogan to hold that claims that are enabled by the original application may be construed broadly enough to encompass technology that is not developed until later and was not enabled by the original application. Although there is language in Hogan that could be read to support such a result, this court has recently (and properly, in my view) expressed reservations about reading Hogan that broadly. See Plant Genetic Sys., N.V. v. DeKalb Genetics Corp., 315 F.3d 1335, 1340-41 (Fed. Cir. 2003).

In Plant Genetic Systems, the court explained that Hogan "simply held that one could not use a later-existing state of the art to invalidate a patent that was enabled for what it claimed at the time of filing." 315 F.3d at 1340. This makes perfect sense because, as the Hogan court explained, "The use of a subsequently-existing improvement to show lack of enablement in an earlier-filed application on the basic invention would preclude issuance of a patent to the inventor of the thing improved, and in the case of issued patents, would invalidate all claims . . . therein." 559 F.2d at 606. The court in Hogan did not take the additional step of holding that the claims in that case should be construed to encompass the later-arising technology. In fact, Hogan explicitly declined to construe the claims at issue in that case, although the court suggested in dictum that the scope of the claims might be broad enough to encompass the later-arising technology that was at issue. Id. The court in Plant Genetic Systems noted that the technology that was developed after the application was filed (and thus was not enabled by the application) fell within the scope of the claims if the claims were broadly construed, but added that "the claims (albeit with a narrower scope) might be nevertheless enabled in view of the state of the art then existing." 315 F.3d at 1341

(emphasis added). Plant Genetic Systems further cautioned against using "the dicta from Hogan" to "expand the coverage of claims, yet create a new, lower standard of enablement." Id.

I think the proper approach, suggested in the concurring opinion in Hogan and in Plant Genetic Systems, is to address cases of new technology by construing claims, where possible, as they would have been understood by one of skill in the art at the time of the invention, and not construing them to reach the as-yet-undeveloped technology that the applicant did not enable. That approach preserves the benefits of patent protection for the invention that the applicant has actually conceived and enabled, without extending those benefits for an invention that the applicant may not have conceived and certainly has not enabled.

In this case, however, the patentee is not seeking to preserve the validity of its claims by construing them in accordance with the state of the technology at the time of the invention. Instead, Chiron is arguing that the 1984 application provides support for claims covering technology that was not in existence at that time. In that setting, where the claims are accorded a scope that exceeds the scope of the enablement, I would hold that the claims are not entitled to priority as of 1984, not only because of a failure to satisfy the written description requirement, but also because the 1984 application does not enable the asserted claims. I would therefore uphold the jury's verdict of lack of enablement not only as to the 1985 and 1986 applications, but as to the 1984 application as well.