United States Court of Appeals for the Federal Circuit

UCB, INC.,
Plaintiff-Appellee

v.

YEDA RESEARCH AND DEVELOPMENT CO., LTD.,
Defendant-Appellant

2015-1957

Appeal from the United States District Court for the Eastern District of Virginia in No. 1:14-cv-01038-LMB-TCB, Judge Leonie M. Brinkema.

Decided: September 8, 2016

JAMES TRAINOR, White & Case LLP, New York, NY, argued for plaintiff-appellee. Also represented by CHRISTOPHER J. GLANCY, ADAM GAHTAN, ROBERT COUNIHAN, DIMITRIOS T. DRIVAS, JOHN PADRO.

NICHOLAS P. GROOMBRIDGE, Paul, Weiss, Rifkind, Wharton & Garrison LLP, New York, NY, argued for defendant-appellant. Also represented by REBECCA FETT, CATHERINE NYARADY, DANIEL KLEIN, WILLIAM S. O'HARE III.

Before NEWMAN, LOURIE, and CHEN, *Circuit Judges.*

NEWMAN, *Circuit Judge.*

In this declaratory judgment action, UCB, Inc. sued Yeda Research and Development Co. in the United States District Court for the Eastern District of Virginia, requesting a declaration that UCB's Cimzia® brand antibody does not infringe Yeda's U.S. Patent No. 6,090,923 ("the '923 Patent"); UCB also sought a declaration that the '923 Patent is invalid. Yeda counterclaimed for infringement. The district court granted summary judgment of non-infringement, holding that, based on the specification and prosecution history, the monoclonal antibodies claimed in the '923 patent are not infringed by the chimeric or humanized antibodies of the Cimzia® product.[1] We affirm the district court's judgment.

BACKGROUND

The '923 Patent describes and claims a monoclonal antibody that binds a defined human cytotoxin. Claim 1 is representative:

> 1. A monoclonal antibody which specifically binds a human cytotoxin having a molecular weight of about 17,500 as determined by polyacrylamide gel electrophoresis, said cytotoxin being obtainable from stimulated human monocytes, said cytotoxin being further characterized by exhibiting a cytotoxic effect on cycloheximide-sensitized SV-80 cells and by being obtainable in a state of enhanced purity by adsorption of the cytotoxin from an impure preparation onto controlled pore glass

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[1] *UCB, Inc. v. Yeda Research and Dev. Co.*, 117 F. Supp. 3d 755 (E.D. Va. 2015) ("Dist. Ct. Op.").

> beads, and subsequent desorption of the cytotoxin in a state of enhanced purity.

'923 Patent, col. 6, ll. 54-63. The question is whether the monoclonal antibody of claim 1 includes chimeric or humanized antibodies, when the patent specification describes only murine (mouse) monoclonal antibodies. Yeda argues that since chimeric monoclonal antibodies were known at the time the '923 priority application was filed in 1984, the claims should be construed to cover such chimeric antibodies, as well as humanized antibodies. UCB responds that the prosecution history prohibits coverage of chimeric and humanized antibodies, and that claim 1 cannot be construed to cover those types of antibodies.

The '923 specification states that the "CT [cytotoxin] can be isolated by the use of monoclonal antibodies against such CT which can be obtained from mice injected with partially purified or crude preparations of CT." Col. 1, l. 66–col. 2, l. 1. The specification states that "a monoclonal antibody specific for CT . . . is produced by such hybridoma cell lines and is used for isolating CT in substantially homogenous purified form." Col. 2, ll. 6–9. The specification presents examples of isolating, partially purifying, and characterizing the cytotoxin, raising and purifying the mouse monoclonal antibody, and using this mouse antibody to bind the cytotoxin.

The claims as originally filed described the antibody as a "monoclonal antibody," but during a lengthy prosecution Yeda first limited all the claims to murine antibodies, and then sought to remove this limitation, stating:

> New claims 41 and 42 are being submitted herewith in order to present claims identical to presently appearing claims 38 and 39 without requiring that the monoclonal antibodies be murine monoclonal antibodies. Arguments have previously been made in this prosecution history that

> the recitation of "murine" with respect to the monoclonal antibody helps to distinguish the present claims over the references such as Matthews and Wallace which disclose obtaining rabbit polyclonal antibodies. However, it is now believed that recitation of "murine" is unduly limiting and that claims 41 and 42 are allowable for the same reasons as argued in applicants' amendment of April 21, 1998 with respect to claims 38 and 39.

Amendment letter of June 30, 1998 at 2.

The examiner rejected the new claims 41 and 42, on the ground that the specification did not "provide enablement for the claimed 'monoclonal antibodies' from a broad range of species." Office Action of Sept. 10, 1998 at 3. Yeda then argued that "the term should encompass chimeric monoclonal antibodies," stating:

> The term "monoclonal antibody" is defined . . . as "an antibody produced by culturing a single type of cell", which "consists of a single species of immunoglobulin molecules." We do not believe that the term necessitates that the monoclonal antibody be produced by the original hybridoma cell; the term should encompass chimeric monoclonal antibodies produced by a genetically engineered cell line.

Amendment letter of March 10, 1999 at 3 (footnote omitted). The applicants' letter continued:

> Applicants are particularly interested in protecting chimeric forms of their anti-cytotoxin mouse monoclonal antibodies. One of the reasons for their insistence on not limiting the claims to "mouse" monoclonal antibodies is uncertainty as to whether that would literally cover a humanized or chimeric derivative of a mouse monoclonal antibody. Any suggestions by the Examiner as to

> how to reconcile Applicants' concerns with the Examiner's concerns as to enablement would be greatly appreciated.

Id. at 5–6. The amendment also added proposed claims 45-48, all of which expressly encompassed chimeric antibodies.

Thus Yeda argued to the Examiner that humanized or chimeric derivatives of mouse monoclonal antibodies were contemplated, and should be included in the claims. Yeda submitted the declaration of Dr. Hartmut Engelmann, stating that it was within the level of skill at the application date to produce monoclonal antibodies from species other than murine. Engelmann Declaration, May 18, 1999 at 2. The Declaration also cited two references that preceded the effective filing date, describing mouse-human chimeric antibodies. *Id.* at 3–4.

The Examiner withdrew the rejection for lack of enablement "in view of the applicant's arguments and the declaration of Hartmut Engelmann." Office Action of June 7, 1999 at 3. However, the Examiner rejected the proposed new claims 45-48, which were specific to "rat, hamster and human antibodies and chimeras thereof" and to "chimeras of" mouse monoclonal antibodies and "non-murine" monoclonal antibodies; the Examiner stated that these claims added new matter and were not supported in the specification. *Id.* The Examiner did not respond to Yeda's request for assistance in protecting the use of chimeric or humanized antibodies in the claimed subject matter.

Yeda then cancelled all the claims that Yeda had proposed to specify chimeric antibodies. The claim that became patent claim 1, filed as claim 41, did not mention chimeric antibodies, and had not been amended during prosecution with respect to that aspect. On UCB's motion for summary judgment, the district court held that this history prohibits construction of claim 1 to cover human-

ized and mouse-human chimeric antibodies, and thus the court granted summary judgment of non-infringement.

DISCUSSION

The issue on summary judgment was presented as a question of claim construction. Claim construction is a matter of law, based on underlying facts. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831 (2015). Summary judgment may be appropriate when there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law. Fed. R. Civ. P. 56; *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247–48 (1986).

The district court construed "monoclonal antibody," as used in the '923 patent specification and claims, to mean "a homogenous population of a single type of antibody produced via hybridoma and not including chimeric or humanized antibodies." Dist. Ct. Op. at 774. We agree that the prosecution history requires this construction, for the scope now sought by Yeda was requested of the Examiner, and refused on the ground of new matter. Yeda argues that present claim 1 was never rejected on this ground; Yeda states that only the specific species claims were deemed by the Examiner to contain new matter.

The district court held that all the claims, correctly construed, exclude chimeric or humanized antibodies, the court stating that "[e]xamination of the prosecution history reveals that for the first ten years of prosecution, neither Yeda nor the examiner understood the term 'monoclonal antibodies' to include chimeric or humanized antibodies. Like the evidence in the specification, the prosecution history weighs towards a construction of 'monoclonal antibodies' which does not include chimeric or humanized antibodies." Dist. Ct. Op. at 770. On this ground, the court found non-infringement.

Yeda argues that the district court erred in construing the claims to find non-infringement, instead of construing the claims objectively. Yeda states that the "claims should not be construed with the goal of including or excluding the accused product." Yeda Br. 38. Yeda points out that claim 1 does not mention any particular monoclonal antibody or species of chimera, and should not be limited to the examples in the specification. Yeda states that every embodiment need not be specifically described and claimed to be within the scope of a generic term in a claim.

Yeda is correct in that generic terms in claims are construed in light of that which is already known. However, the content of the specification and actions and arguments during prosecution must also be considered, in defining the scope of a generic term in a claim. *See Advance Transformer Co. v. Levinson*, 837 F.2d 1081, 1083 (Fed. Cir. 1988) ("Positions taken in order to obtain allowance of an applicant's claims are pertinent to an understanding and interpretation of the claims that are granted by the PTO . . . and may work an estoppel as against a subsequent different or broader interpretation.").

During prosecution, Yeda submitted new claims specific to "rat, hamster and human antibodies and chimeras thereof" as well as claims specifically encompassing "chimeras of" mouse monoclonal antibodies and "nonmurine" monoclonal antibodies. Yeda argued that its invention is not limited to murine antibodies to human cytotoxin, and "should encompass chimeric monoclonal antibodies produced by a genetically engineered cell line." Amendment Letter of March 10, 1999 at 2, 3. The Examiner rejected the proposed claims on the ground of new matter not supported in the specification. Yeda then withdrew the proposed specific claims, and the application was passed to issuance. The district court held that Yeda cannot now obtain a claim construction that recovers claim scope that was yielded in order to obtain issu-

ance of the patent, and construed the claims as excluding chimeric and humanized antibodies.

Yeda argues that this construction is incorrect at least as to claim 1, which recites "monoclonal antibody" but does not specify any specific form or source of antibody. Yeda states that chimeric or humanized monoclonal antibodies were known at the time its priority application was filed, December 20, 1984, and thus should be included in the monoclonal antibodies of claim 1. Yeda presented a publication of Morrison dated November 1, 1984, that describes chimeric antibodies, and cited a December 8, 1984, Nobel Prize speech by César Milstein referring to chimeric antibodies. The district court responded to these arguments, stating: "At best, these references establish that scientists knew of chimeric antibodies in November 1984. Establishing that chimeric antibodies existed in 1984, however, is different from establishing that a person of ordinary skill in the art would have understood chimeric antibodies to be monoclonal antibodies in 1984." Dist. Ct. Op. at 772.

The district court concluded that "the extrinsic evidence relied upon by Yeda's experts does not support the conclusion that the understanding of 'monoclonal antibodies' in 1984 included either chimeric or humanized antibodies." *Id.* The district court found that "for the first ten years of prosecution, neither Yeda nor the examiner understood the term 'monoclonal antibodies' to include chimeric or humanized antibodies." *Id.* at 770. The district court held that Yeda's unsuccessful attempt to claim chimeras in the pending application, with acquiescence in the examiner's rejection on the ground of new matter not supported by the specification, prohibited now obtaining a claim construction that chimeric antibodies, or equivalents thereof, are described in the specification and included in the claims.

Yeda argues that absent a narrowing amendment to the proposed claim that is now claim 1, there can be no prosecution estoppel to the scope of claim 1, merely because some proposed different claims were rejected by the examiner and then dropped by the applicant. That is not a correct general principle. Although each claim in a patent warrants independent consideration in light of its particular facts and history, the general rule is that a patent applicant cannot later obtain scope that was requested during prosecution, rejected by the Examiner, and then withdrawn by the applicant.

Such estoppel was reasonably applied to claim 1 by the district court, although claim 1 had not been amended. In *Builders Concrete, Inc. v. Bremerton Concrete Products Co.*, 757 F.2d 255, 259 (Fed. Cir. 1985), the court rejected the argument that "file wrapper estoppel cannot arise without an amendment," and explained that the "position must be evaluated in the context of this specific case." In *Wang Laboratories, Inc. v. Mitsubishi Electronics America, Inc.*, 103 F.3d 1571, 1578 (Fed. Cir. 1997), the court again explained: "We examine the statements and actions of the patentee before the PTO during prosecution . . . and ask what a competitor reasonably may conclude the patentee surrendered to gain issuance of the patent." (internal citations omitted).

We conclude that the district court correctly applied the law, and we affirm the holding that Yeda is estopped from including chimeric and humanized antibodies within the scope of the monoclonal antibodies claimed in the '923 Patent.

AFFIRMED