Keywords: claim construction, intrinsic evidence, extrinsic evidence, expert testimony, literal infringement, doctrine of equivalents

Goldenberg v. Cytogen Inc.
71 U.S.P.Q.2d 1255 (Fed. Cir. 2004)
Decided June 23, 2004

I. Facts

Goldenberg and Immunomedics asserted that Cytogen infringed U.S. Patent No. 4,460,559. The '559 patent relates to a method for detecting and localizing tumors by targeting "intracellular marker substances" that are produced or associated with tumor cells. The claimed method includes injecting a subject with a radioactively highlighted antibody specific to the intercellular marker substance, which when scanned, reveals the location of concentrations of the intracellular marker substance within the body, thus facilitating the detection and localization of a tumor within the body.

Cytogen manufactures and sells ProstaScint. ProstaScint contains an antibody that is specific to prostate specific membrane antigen (PSMA), and PSMA is a transmembrane antigen that extends through the cell membrane and that has both intracellular and extracellular domains. The binding site, or "epitope," for the ProstaScint antibody is located on a terminal of PSMA that is on the interior of the cell wall. To use ProstaScint, the radiolabeled antibody is injected into a patient, who is then photographed with a camera designed to detect radiation. Because the ProstaScint antibody targets and binds to PSMA, images from the radiation-detecting camera reveal concentrations of the antibody/antigen combination and, by association, the location of the PSMA-producing tumor.

At the district court, the only disputed term in the claims was "intracellular marker substance," which the parties agreed has no commonly accepted meaning. Accordingly, the district court turned to the specification of the '559 patent and noted that the specification did not expressly define the term "intracellular marker substance." However, the district court noted that the specification discussed the need for a method of tumor localization not confined to cell surface antigens and that the specification contained repeated distinctions drawn between intracellular and cell surface antigens. The district court also relied upon the prosecution history and, specifically, on an argument in which Goldenberg explained the differences between the claimed invention and the claims of a separate concurrently-filed application in order to avoid a double patenting rejection. Goldenberg explained that the claims did not overlap with claims related to using radiolabeled antibodies that bind to a cell surface antigen. Finally, the court accepted deposition testimony of Dr. Goldenberg, as well as Cytogen's expert, regarding the meaning of the disputed term.

In regard to infringement, Immunomedics argued that PSMA could be both a cell surface and an intracellular marker substance, depending on the location of the targeted binding site. Cytogen argued that the targeted binding site would not change the character of the antigen as being integral to the plasma membrane and, thus, being considered a cell surface antigen.

Based on these factors, the district court concluded that an "intracellular marker substance" should be defined as "an antigen existing within a body cell." The district court further concluded that PSMA was a cell surface antigen and was, therefore, outside the literal scope of claim 1. The district court also found that Goldenberg and Immunomedics had failed as a matter of law to meet the requirements of the "function-way-result" test in its doctrine of equivalents case. Therefore,

the district court granted Cytogen summary judgment of non-infringement for both literal infringement and infringement under the doctrine of equivalents.

II. Issues

1. Did the district court properly construe the meaning of "intracellular marker substance?"

2. Did the district court properly grant summary judgment of no literal infringement?

3. Did the district court properly grant summary judgment of no infringement under the doctrine of equivalents?

III. Discussion

1. Yes. Immunomedics challenged the district court's construction by arguing that neither the claim nor the written description require a marker substance to be an entire antigen or that the marker substance be wholly within a cell. To the contrary, Immunomedics argued that the intrinsic evidence actually precludes such an interpretation by permitting sub-units of antigens to qualify as marker substances. Specifically, Immunomedics noted that both the claims and the written description refer specifically to the beta sub-unit of the HCG antigen as a suitable intracellular marker substance.

Cytogen countered by noting that HCG is a dimeric antigen, which means that it is composed of two individual sub-units. While the alpha sub-unit is common to several hormones, the beta sub-unit is unique to HCG. Due to this uniqueness, the beta sub-unit is actually a separate antigen and not a "portion" of an antigen. Cytogen further noted that neither the specification nor the prosecution history suggests that an "intracellular marker substance" includes epitopes as Immunomedics would now have the claimed term construed.

Based on a review of the arguments and the evidence, the Federal Circuit affirmed the district court's claim construction that an intracellular marker substance should be defined as an antigen, but clarified that molecular sub-units such as those present in the HCG antigen should qualify as "antigens" under this construction. The Federal Circuit also agreed with the district court's conclusion that the marker substance must be wholly internal to the cell. Cytogen correctly noted that none of the twenty-six example antigens provided in the '559 patent associates in any way with the membrane of the cells in which they are found. Each of the listed structures is completely internal to the cell. The prosecution history further supports this understanding by specifically explaining that HCG is a "cytoplasmic antigen."

2. Yes. The Federal Circuit affirmed the district court's holding of summary judgment of no literal infringement. The Federal Circuit noted that PSMA is a transmembrane antigen that extends both inside and outside of the cell membrane. Despite the intracellular portion, the claims do not provide for "portions" of antigens to qualify as maker substances. Therefore, because PSMA is not an "intracellular marker substance," PSMA does not literally fall within the scope of the claims. However, the Federal Circuit noted that its holding differs somewhat from the district court's holding in that the district court granted summary judgment because it found that PSMA is a cell surface antigen and, thus, not an intracellular antigen. As noted in the discussion below, the Federal Circuit, apparently, believes this to be an error in fact, because the Federal Circuit defines PSMA as transmembrane antigen, which does not fall within the class of either a cell surface antigen or an intracellular antigen.

The Federal Circuit also noted that the district court had relied on the prosecution history of a patent that had issued from a CIP of the separate concurrently filed application discussed during

the prosecution history of the ‘559 patent. The district court analyzed the concurrently filed application at the point it was distinguished from the application that issued as the ‘559 patent, and the district court also analyzed statements contained in the new matter that was added in the CIP. In regard to the former analysis, the Federal Circuit agreed that the response distinguishing the present claims from the claims in the co-pending application for the purpose of overcoming the double patenting rejection constituted part of the prosecution history of the ‘559 patent and, therefore, was properly relied upon by the district court in construing the claims of the ‘559 patent. However, in regard to the latter analysis, the Federal Circuit found that the district court erred in relying on the specification of the CIP application to construe the claims of the ‘559 patent. Specifically, the Federal Circuit stated that absent a formal familial relationship or “incorporation during prosecution,” the new matter content of the ‘744 patent is not available to construe the claims of the ‘559 patent.

3. No. The Federal Circuit agreed with the district court that PSMA is not an “intracellular marker substance.” However, the Federal Circuit did not agree that PSMA must, therefore, be a cell surface antigen. Instead, the Federal Circuit found that transmembrane antigens appear to be a category of their own. The Federal Circuit also relied on the function-way-result evidence provided by Immunomedics. Specifically, Immunomedics alleged that the function of the limitation was to deliver a radioisotope to a cell tumor--a function claimed to be identical to the function ProstaScint antibody. Immunomedics argued that the way that this was accomplished was by binding the radiolabeled antibody to an antigen located within a cell tumor--again equivalent to the ProstaScint antibody. Immunomedics further argued that the processes are substantially the same because both antibodies must cross the cell membrane to bind with the antigen. Accordingly, the Federal Circuit found that Immunomedics had presented a sufficient factual dispute to avoid summary judgment.