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Summaries of Recent Decisions of Interest to the Biotechnology Community

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Edited By:

Melanie Szweras
Subcommittee Chair
Bereskin & Parr LLP
E-mail: mszweras@bereskinparr.com

Nicholas Landau
Subcommittee Vice Chair
Bradley Arant Boult Cummings LLP
E-mail: nlandau@babc.com

C O N T R I B U T O R S

Alice O. Martin
Lynn C. Tyler
Michael R. Brunelle

The AIPLA Biotechnology in the Courts Subcommittee Report is a forum for members of the subcommittee to present summaries and commentary on recent judicial decisions of interest to the biotechnology community. Any view of a contributor expressed in a summary should be understood to reflect only the present consideration and views of the contributor, and should not be attributed to the AIPLA or any of its committees, the contributor's firm, employer, or past or present clients, to other contributors, or to the editor. To request an electronic copy of the Report, or if you are interested in summarizing a case for a future edition, please contact Melanie Szweras at mszweras@bereskinparr.com.

CONTRIBUTORS:

Alice O. Martin is a partner in the Chicago office of Barnes & Thornburg LLP. She is a member of the Intellectual Property Department where she concentrates on international patent prosecution, litigation opinions and due diligence investigations. Dr. Martin's practice covers biotechnology, agriculture-plants and animals, medical compositions and devices, laboratory equipment, genetics, treatments and assays for various diseases, surgical techniques, tissue culture methods, stage equipment, computer systems, business methods and waste management and monitoring.

Dr. Martin was a member of the National Institutes of Health Study Sections and has written more than 100 articles for scientific and legal publications and delivered more than 50 presentations nationally and internationally on scientific and legal issues. She was recommended by her peers as a Leading Lawyer in Intellectual Property Law and was selected for inclusion in *The Best Lawyers in America*® in 2013 and 2014 in the fields of biotechnology law and intellectual property. Dr. Martin was also listed as a Top-Rated Lawyer for intellectual property in the 2012 *Chicago Tribune* magazine, an AV Martindale-Hubbell selection-based listing. In addition, Dr. Martin was recently recognized by American Lawyer Media and Martindale-Hubbell as a 2013 "Top Rated Lawyer in Intellectual Property."

Dr. Martin received her M.S. in genetics from the University of Michigan in 1963 and her Ph.D. in biology (genetics) in 1969 from Case Western Reserve University. She received her J.D. from Loyola University School of Law, Chicago in 1989.

Prior to practicing law, Dr. Martin was a Professor of Obstetrics and Gynecology at Northwestern University Medical School as well as a certified Medical Geneticist and Cytogenetics Laboratory director at Northwestern Memorial Hospitals.

Lynn C. Tyler is a partner and registered patent attorney in the Intellectual Property Department of Barnes & Thornburg LLP in Indianapolis. He concentrates his practice in litigation of intellectual property matters, representing clients at all stages of the process.

Mr. Tyler has been listed in *Best Lawyers in America*® since 2009, more recently in multiple categories, and was recognized as the Indianapolis Patent Litigator of the Year for 2014. He is the author of several published articles on issues of intellectual property or federal procedure in a variety of peer-reviewed publications. In 2010, one of his articles won the prestigious Burton Award for Legal Achievement. The first of his two articles on inequitable conduct has been cited by two Federal Circuit Judges in published opinions.

Mr. Tyler graduated *summa cum laude* in 1981 from the University of Notre Dame and in 1984 received his J.D. *magna cum laude* from the University of Michigan Law School. In 2007, he received a M.S. in Biology from Purdue University (Indianapolis campus).

Mr. Tyler's civic activities include being a co-founder, past president, and volunteer for the Neighborhood Christian Legal Clinic. For his work on behalf of the Clinic, he

received the Indianapolis Bar Association's Pro Bono Award in 2002 and was a co-recipient of the firm's inaugural Joseph A. Maley Pro Bono Award in 2009.

Michael R. Brunelle is an associate in the Indianapolis, Indiana office of Barnes & Thornburg LLP, and a member of the firm's Intellectual Property Department. He concentrates his practice on intellectual property litigation.

Mr. Brunelle received his B.S. in chemical engineering from Purdue University in 2004. He received his J.D. magna cum laude in 2008 from Indiana University School of Law – Bloomington. During law school, Mr. Brunelle served as a managing editor of the Indiana Law Journal, as executive problem editor of the Sherman Minton Moot Court Board, and was selected for membership in the Order of the Coif.

Prior to attending law school, Mr. Brunelle worked as a process engineer at Tate & Lyle North America, a specialty starch producer in Lafayette, Indiana.

Mr. Brunelle is a member of the Indiana State Bar Association, and is admitted to practice in the state of Indiana as well as the U.S. District Courts for the Northern and Southern Districts of Indiana, the Western District of Michigan, and the U.S. Court of Appeals for the Federal Circuit.

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Case Summaries

I. *Bayer CropScience AG v. Dow AgroSciences LLC.*, Case No. 2013-1002 (Fed. Cir. Sept. 3, 2013)

Reported by: Alice O. Martin, Lynn C. Tyler, and Michael Brunelle

Summary

Major players in the biotech crop industry, including Bayer CropScience ("Bayer"), Dow AgroSciences ("Dow"), Monsanto, and Pioneer (DuPont), have had, and continue to have, several patent litigation battles. The Federal Circuit likely put an end to one of those battles recently when it affirmed the entry of summary judgment in favor of Dow and against Bayer on the latter's claim for infringement of U.S. Patent No. 6,153,401 ("the '401 patent"). The court rejected Bayer's proposed, broad claim construction and, as a result, it was undisputed that Dow did not infringe the '401 patent.

Invention

The '401 patent is directed to genetically modified plants that are resistant to a commonly used herbicide called 2,4-dicholorphenoxyacetic acid or simply "2,4-D." Claim 1, the only independent claim in the '401 patent, reads:

> 1. A recombinant gene, comprising
>
> a DNA sequence encoding a polypeptide having the biological activity of a 2,4-D monooxygenase which is capable of being expressed in a plant operably linked to
>
> a heterologous promoter capable of promoting the expression in a plant of a structural gene operably linked thereto.

Procedural History

In December, 2010 Bayer filed suit against Dow, alleging that certain 2,4-D resistant seeds infringed the '401 patent. The district court held a *Markman* hearing, during which it heard witness testimony, and received cross-motions for summary judgment. The district court limited its construction of claim 1 to the phrase, "the biological activity of 2,4-D monooxygenase" and concluded that the established scientific meaning of "monooxygenase" involves an enzyme that catalyzes a reaction in which one oxygen atom of an oxygen molecule goes to water. The court defined the entire phrase to mean, "the enzymatic activity of an enzyme, in a biological system, that causes a reaction with 2,4-D, and two molecules of oxygen, where one molecule [sic – atom] of oxygen is added to 2,4-D and the other ultimately forms water."

Under the district court's construction, the parties agreed that Dow's seeds did not infringe the '401 patent, so the district court entered the summary judgment. The district court also indicated that if it had accepted the broad construction proposed by Bayer, it would have entered summary judgment for Dow that claim 1 was invalid for failure to satisfy the written description requirement under § 112.

Court's Decision

Factual background

In the late 1980s, Bayer filed the application that eventually led to the '401 patent. Bayer scientists had discovered that certain soil bacteria could grow on 2,4-D. The resistant bacteria first convert 2,4-D into 2,4-dicholophenol ("2,4-DCP"). Bayer's inventors were the first to isolate, clone, and characterize a gene that encoded an enzyme that converted 2,4-D to 2,4-DCP. The '401 patent sets forth the nucleotide sequence of the gene in Figure 10, the only gene identified in the '401 patent.

The inventors used a "growth test," described in the specification, to isolate the relevant gene. The steps of the growth test were (1) creating a mutant strain of the bacterium that lacked the ability to grow on 2,4-D, (2) fragmenting the DNA of a non-mutant strain, which could grow on 2,4-D, (3) inserting the fragments into cells of the mutant strain with no more than one fragment per cell, and (4) placing the cells on 2,4-D. They identified the cells that grew and sequenced the fragments in those cells.

Although the inventors were able to identify the Figure 10 sequence, they did not fully understand the enzymatic reaction that converted 2,4-D to 2,4-DCP. They knew that the reaction used a molecule of oxygen and that one of the oxygen atoms combined with 2,4-CD to create an unstable product which then spontaneously splits apart into 2,4-DCP and another compound. The inventors assumed (along with the apparently prevailing view) that the other oxygen atom was used to form water. Enzymes that catalyze a reaction in which one oxygen atom ends up in water and the other ends up in a different product were called "monooxygenases."

In 1993, other scientists discovered that the second oxygen atom in the reaction catalyzed by Bayer's enzyme did not end up in water and, thus, the enzyme was not a monooxygenase. Bayer was aware of this discovery but did not change its then-pending patent application. Instead, Bayer allowed the patent to issue seven years later using the term monooxygenase to describe the enzyme.

Dow's accused products use two genes, both of which code for dioxygenases (enzymes that catalyze a reaction in which both oxygen atoms end up in products other than water).

Court's opinion

The case turned on the construction of "the biological activity of 2,4-D monooxygenase" in claim 1. Bayer proposed a broad, functional construction of "bringing about the cleavage of the side change of 2,4-D." The panel of the U.S. Court of Appeals for the Federal Circuit rejected this construction as (1) inconsistent with the claim language and (2) so broad as to create serious validity issues.

According to the court, "monooxygenase" has long had a clear meaning of an enzyme that catalyzes a reaction in which one oxygen atom is incorporated into water and the second is incorporated into some other compound. Thus, 2,4-D monooxygenase is simply a way of stating that the monooxygenase acts on 2,4-D. The natural reading of "the biological activity of" means the activity that makes the enzyme a *mono*oxygenase. This is the ordinary scientific meaning of the words.

According to the court, Bayer's proposal deprived the word "monooxygenase" of its accepted meaning and thus the court required that either the '401 patent or its prosecution history made clear that Bayer was not using the term according to that meaning. Instead, the court found that "Bayer's usage [of "monooxygenase"] in the intrinsic record is at the very best inconsistent." The court observed that, because Bayer had assumed that one of the oxygen's went into water, the specification used monooxygenase according to its ordinary meaning.

Bayer also argued that the phrase "biological activity" in the '401 patent means "bringing about the cleavage of the side chain of 2,4-D." There are only two occurrences of the phrase in the specification, and Bayer relied heavily on the first. The court found, however, that the first use did not purport to be, and was not in the form of, a definition. The court found that the second use actually worked against Bayer's argument. In short, the specification and prosecution history were not sufficiently clear to deprive the claim language of its accepted meaning.

Turning to the validity issues raised by Bayer's proposed construction, the court first reiterated the general rule from *Phillips v. AWH Corp*., 415 F.3d 1303 (Fed. Cir. 2005), that "validity analysis is [not] a regular component of claim construction." The court departed from that general rule in this case, however, because the district court and the parties created an extensive record on the issue at the same time as they created the claim construction record. The court then noted Bayer's proposed construction covered a broad class of enzymes that cleaved the side chain of 2,4-D, but the specification disclosed only a single gene sequence coding for such an enzyme. The "growth test" did not substitute for the failure to provide structural identification for the broad class of enzymes swept up within Bayer's proposed definition.

Because Bayer rested its case on the adoption of its proposed construction, once the court rejected the construction, its work was done.

Commentary

As is often (but not always) true, our knowledge of this case is limited to the four corners of the court's opinion (disclosure: that is true even though our firm represents Dow AgroSciences in other matters, including patent matters). With that limited knowledge, it is perhaps not surprising that we have several questions based on the opinion. The opinion does not discuss the parties infringement positions in any detail, apparently because Bayer conceded non-infringement if its construction was not adopted. Although the court states at one point that the '401 patent is directed to genetically modified plants, as shown above, claim 1 is literally directed to a recombinant gene. Thus, one question is whether Dow produced its accused seeds by transforming plants with a recombinant gene(s) that caused 2,4-D resistance? If not, for example if the 2,4-D resistance arose from genes mutated naturally or chemically or which arose from breeding, would the Dow seeds infringe the claim?

The case raises some questions about prosecution strategy also. The opinion states that "Bayer" knew that neither of the oxygen atoms was incorporated into water, yet did not change the "monooxygenase" term in the seven years before the '401 patent issued. One question is: Who at Bayer knew? An inventor or someone else involved in the prosecution? For purposes of inequitable conduct, it would be irrelevant if someone knew but did not have a duty of disclosure. Unless the person was involved in the prosecution, why is it relevant here? If the person(s) was/were involved in prosecution, why didn't they change the claim language and any relevant parts of the specification? Were they concerned about adding new matter and possibly losing the original priority date? If so, was the concern (presumably) based on intervening art? Were they damned either way? With these facts, why litigate?

If Bayer had been able to overcome the liability hurdles, it is also easy to imagine difficult damages issues that would have arisen in this case. The relationship between one gene and the plant which incorporates it is similar to the relationship between a processor and the computer which incorporates it, a relationship which was the subject of Judge Rader's well-known opinion in *Cornell Univ. v. Hewlett-Packard Co.*, 609 F. Supp. 2d 279 (N.D.N.Y. 2009) (Rader, J. sitting as district judge by designation). The extent to which the trait produced by the claimed recombinant gene, as opposed to other traits of the resulting plant, generated demand for the accused seeds could present difficult issues under the entire market value rule and/or reasonable royalty analysis.

II. *Aria Diagnostics, Inc. v. Sequenom, Inc.*, Case No. 2012-1531 (Fed. Cir. 2013)

Reported by: Lynn C. Tyler and Michael R. Brunelle

Summary

Aria (now Ariosa) sought a declaratory judgment in the Northern District of California that its Harmony genetic defect test did not infringe any claim of U.S. Patent No. 6,258,540, which was exclusively licensed by Sequenom. In response, Sequenom sought a preliminary injunction, but its request was subsequently denied by the district court. The Federal Circuit vacated and remanded the district court's claim construction and the district court's denial of Sequenom's motion for preliminary injunction based on its finding of a substantial question of non-infringement. In addition, the Federal Circuit provided guidance as to the remaining preliminary injunction factors for the district court's consideration on remand.

Claim

The Federal Circuit treated claim 1 of the '540 patent as exemplary:

> A method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises
>
> amplifying a paternally inherited nucleic acid from the serum or plasma sample and
>
> detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample.

'540 patent, col. 23, ll. 61–67.

Background

Sequenom's '540 patent discloses non-invasive methods to identify fetal genetic defects (such as Down's, Edwards, Patau, and other defects caused by chromosome trisomy) by analyzing maternal plasma or serum. "The '540 patent discloses that non-nucleated free-floating fetal DNA (the cffDNA) exists in maternal blood. The specification explains that not only does analysis of cffDNA permit more efficient determination of genetic defects (for example, trisomy of chromosome 21) but that a pregnant woman carrying a fetus with certain genetic defects will have more cffDNA in her blood than do women with normal fetuses. In other words, the '540 patent claims methods to detect fetal genetic characteristics by analyzing cffDNA obtained from a maternal blood sample. These new tests presented fewer risks and a more dependable rate of abnormality detection." *Slip op*. at 3.

Decision

Aria and Sequenom first disputed the appropriate standard for construing claims during preliminary injunction proceedings. The Federal Circuit recognized the flexibility on this point. *Slip op.* at 4 (citing *Chamberlain Group, Inc. v. Lear Corp.*, 516 F.3d 1331, 1340 (Fed. Cir. 2008) ("a correct claim construction is almost always a prerequisite for imposition of a preliminary injunction") and *Int'l Cmty. Materials v. Ricoh Co.*, 108 F.3d 316, 318-19 (Fed. Cir. 1997) ("We do not regard it as our function [in preliminary injunction appeals] to definitively construe" claims or to review claim construction "as if from final judgment")). The Court declined, however, to reach this question, finding that even under the more relaxed standard the district court had erred in its claim construction and therefore it had erred in its finding of a substantial question of non-infringement.

The Federal Circuit then addressed the district court's constructions of the claim terms "paternally inherited nucleic acid" and "amplifying." The district court had concluded that "paternally inherited nucleic acid" meant "DNA sequence known [in advance] to be received only from the father which is not possessed by the mother." The district court had not actually included the "in advance" phrase, but the parties agreed on appeal that the district court's construction required that the sequence be known in advance. The district court construed "amplifying" to mean "increasing the concentration of a paternally inherited nucleic acid relative to the other DNA in the sample."

The Federal Circuit found that for each limitation the district court had improperly imported limitations into its constructions that were neither included in the claim language nor clearly and unequivocally required by the patent's specification or prosecution history. The Court concluded that the paternal DNA did not have to be known in advance and that amplifying did not require increasing the proportion of the paternal DNA with respect to any other DNA. Based on these findings, the Court reversed the district court's conclusion that Aria had demonstrated a substantial question of non-infringement.

Next, the Federal Circuit addressed the district court's finding that there was a substantial question of whether the subject matter of the claims constituted eligible subject matter. The district court reached this conclusion without the benefit of the Supreme Court's decision of *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013), where the Court held that product claims directed to isolated DNA segments are not eligible subject matter, but that product claims directed to synthetic cDNA are patent eligible. Rather than addressing the substance of the district court's finding on this issue, the Federal Circuit remanded so that the court could consider both the new claim construction findings and the *Myriad* decision.

Finally, the Federal Circuit addressed the district court's recitation and analysis of the remaining preliminary injunction factors. The Court agreed with the district court's holding that in addition to showing a likelihood of success on the merits, Sequenom was also required to demonstrate that it was likely to suffer irreparable harm, that the balance of equities tipped in its favor, and that an injunction was in the public interest. The

district court only briefly addressed these additional factors, because it had found that Sequenom did not meet its burden on the likelihood of success prong; however, the Federal Circuit found that the district court had erred in its analysis and therefore remanded with additional guidance.

Regarding irreparable harm, the district court found that Sequenom's alleged price erosion and its loss of market share were not irreparable. It reasoned that if Sequenom was proven correct that the '540 patent and its MaterniT21 test would set new standards of care, then Sequenom could recover the market and receive damages to compensate for the infringement. The Federal Circuit found this assumption insufficient, instead suggesting that this conclusion would have to be proven by competent evidence. "In the face of that kind of universal assumption, patents would lose their character as an exclusive right as articulated by the Constitution and become at best a judicially imposed and monitored compulsory license." *Slip op.* at 13.

With respect to the balance of hardships, the district court had found that this factor weighed against a preliminary injunction because an injunction would put Aria out of business. The Federal Circuit noted that such evidence may weigh against imposition of an injunction, citing *Intel Corp. v. ULSI Sys. Tech., Inc.*, 995 F.2d 1566, 1568, 1570 (Fed. Cir. 1993), but that this fact alone did not control the analysis on this factor. *Slip op.* at 14. The Federal Circuit noted that the district court had made no findings as to the harm that Sequenom might suffer were the injunction not entered, such as harm to Sequenom's research and development and investment in the technology.

The district court also criticized Sequenom's proof of harm for not taking into account a third party's test, but the Federal Circuit noted that the district court had also found that the third party's test did not yet compete in the same market but rather may do so in the future. The Court added that "the fact that other infringers may be in the marketplace does not negate irreparable harm." *Pfizer, Inc. v. Teva Pharm. USA, Inc.*, 429 F.3d 1364, 1381 (Fed. Cir. 2005).

Lastly, the district court found that the public interest favored denial of a preliminary injunction where Sequenom marketed its tests only to women over 35 and at high risk both of having a fetus with Down's Syndrome and of losing a fetus through invasive testing, but Aria marketed its products to both high- and low-risk women. The Federal Circuit noted that after the preliminary injunction hearing, it had taken judicial notice "that an expert organization had warned that cffDNA tests should not, yet, be used in low-risk women" and that on remand the district court was free to consider that evidence (any other new evidence) pertaining to the public interest factor. *See* Am. Coll. of Obstetricians and Gynecologists Comm. on Genetics, *Noninvasive Prenatal Testing for Fetal Aneuploidy*, Op. No. 545 (Dec. 2012).

Commentary

In recent years and perhaps in light of *eBay, Inc. v. MercExchange, LLC*, 547 U.S. 288 (2006), courts have appeared less willing to grant, and patent owners less willing to

seek, a preliminary injunction. *Aria*, however, shows that this path may still be a viable option. And, if the patent owner wants to allege willfulness (and seek enhanced damages and/or attorneys' fees) based in part on post-filing conduct, the preliminary injunction route may be a necessity in light of *In re Seagate Technology, LLC*, 497 F.3d 1360, 1374 (Fed. Cir. 2007) (en banc) ("By contrast, when an accused infringer's post-filing conduct is reckless, a patentee can move for a preliminary injunction, which generally provides an adequate remedy for combating post-filing willful infringement."). In *Aria*, the Federal Circuit certainly made some pro-patentee comments on the irreparable harm, balance of harms, and public interest factors.

Aria also includes some lessons for district courts and litigants involved in preliminary injunction matters. From the Federal Circuit's opinion, it appears that the district court, having sided with *Aria* on the likelihood of success issue, did not thoroughly address the other preliminary injunction factors. Because the Federal Circuit disagreed with the district court on the likelihood of success, the district court will now apparently have to hold another hearing and issue another opinion. A more thorough analysis of all the factors originally *may* have prevented the need for this additional work. Along the same lines, litigants given the opportunity to submit proposed orders or findings and conclusions should also address all of the factors thoroughly to help the district court make its order "appeal proof" to the extent the court incorporates a party's arguments. We have not reviewed the parties' submissions in this case and do not intend any criticism. We are simply offering a suggestion to future litigants.