33 Biotechnology Law Report 209
Number 6, 2014

DOI: 10.1089/blr.2014.9970

Original Articles

Claim Construction Cannot Save a Modified Gene Invention Claimed with a Scientifically Debatable Biological Mechanism: A Lesson from *Bayer CropScience AG v. Dow AgroSciences LLC*, 728 F.3d 1324 (Fed. Cir. 2013)

By PING-HSUN CHEN

Bayer CropScience AG owns U.S. Patent No. 6,153,401, which claims a genetically modified plant that incorporates a *tfdA* gene.[1] Because of the product of this gene, the plant can resist a weed herbicide, 2,4-dichlorophenoxyacetic acid (2,4-D).[2] The biological action associated with the *tfdA* gene is degradation of 2,4-D into 2,4-dichlorophenol (2,4-DCP) by an enzyme encoded by the *tfdA* gene.[3] This enzyme was mistakenly known as a "monooxygenase" among the scientific community when Bayer was developing the invention.[4]

"Monooxygenase" means that an enzyme catalyzes a reaction involving an oxygen molecule wherein one oxygen atom is incorporated into water, whereas the other oxygen atom is incorporated into a product other than water.[5] Early in the project, Bayer's researchers knew only that the enzymatic reaction performed by the product of a *tfdA* gene creates an unstable, hydroxylated 2,4-D, which is then decomposed into two compounds, 2,4-DCP and glyoxylate.[6] Although not knowing where the second oxygen atom ended up, the team believed that "monooxygenase" was the correct term for describing the invention.[7] So when the application was filed in 1989, Bayer used "monooxygenase" to describe the biological activity of the product of a *tfdA* gene.[8] However, in 1993, two researchers published an article showing that "dioxygenase" was the correct term.[9] "Dioxygenase" means that enzymes catalyze a reaction where an oxygen molecule is involved and both oxygen atoms are incorporated into products other than water.[10] Because the experiment of the 1993 article demonstrated that the second oxygen atom becomes carbon dioxide, the scientific community began to realize that the enzymatic reaction initiated by a *dad* gene is a dioxygenase.[11] After noticing the 1993 article, Bayer did not amend the specification or claims.[12] In 2000, the '401 patent was issued.[13]

In December 2012, Bayer initiated a lawsuit against Dow AgroSciences LLC and asserted that Dow's Enlist E3™ soybean seeds infringe the '401 patent.[14] Claim 1 of this patent was a representative claim and reads as follows:

The author is Assistant Professor of the Graduate Institute of Intellectual Property, National Taipei University of Technology, Taipei, Taiwan. E-mail: cstr@ntut.edu.tw

[1] *See Bayer CropScience AG v. Dow AgroSciences LLC*, 728 F.3d 1324, 1325 (Fed. Cir. 2013)(hereinafter *Bayer II*).
[2] *Id.*
[3] *Id.*
[4] *Id.* at 1326.
[5] *Id.*
[6] *Id.*
[7] *Id.*
[8] *Id.*
[9] *Id.* (quoting the article written by Fumiyasu Fukumori and Robert P. Hausinger [*see* footnote 11]).
[10] *Id.*
[11] *Id.* (quoting Fukumori F, Hausinger RP. *Alcaligenes eutrophus* JMP134 "2,4-dichlorophenoxyacetate monooxygenase" is an α-ketoglutarate-dependent dioxygenase. J Bacteriol 1993;175:2083–2085; *available at* www.ncbi.nlm.nih.gov/pmc/articles/PMC204309/pdf/jbacter00049-0229.pdf)
[12] *See Bayer II*, 728 F.3d at 1326.
[13] *Id.*
[14] *See id.* at 1327; *see also* Dow AgroSciences, *Dow AgroSciences Wins Second Case Brought by Bayer CropScience Involving Enlist™ Technology*, Oct. 8, 2013. Press release; *available at* http://newsroom.dowagro.com/press-release/dow-agrosciences-wins-second-case-brought-bayer-cropscience-involving-enlist-technolog#sthash.QdgFwF0T.dpuf (last visited June 26, 2014).

> A recombinant gene, comprising a DNA sequence encoding *a polypeptide having the biological activity of 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.[15] [Emphasis added.]

Claim 1 does not recite "a *tfdA* gene," which is described in the '401 patent, but it uses "a polypeptide having the biological activity of 2,4–D monooxygenase" to describe "a *tfdA* gene." So, Claim 1 covers more than what was actually invented. On the other hand, Dow's seeds do not include a *tfdA* gene, but they have *aad-1* and *aad-12* genes, which create enzymes causing a dioxygenase of 2,4-D.[16]

The limitation at dispute was "biological activity of 2,4-D monooxygenase."[17] "2,4-D monooxygenase" was scientifically wrong because the enzymatic reaction should have referred to "dioxygenase."[18] If the "biological activity" limitation had recited "biological activity of 2,4-D dioxygenase," the '401 patent would have covered Dow's seeds because Claim 1 does not specify a particular gene that triggers "dioxygenase." Unfortunately, the use of "monooxygenase" made Claim 1 unable to cover Dow's seeds. Nonetheless, to establish infringement, Bayer construed the "biological activity" limitation to mean "[t]he biochemical (enzymatic) conversion of 2,4-D into 2,4-DCP through the cleavage of the side chain of 2,4-D" or, alternatively, "a polypeptide having the biological activity of bringing about the cleavage of the side chain of 2, 4-D."[19] Bayer's claim interpretation was broad enough to cover "dioxygenase" as well as Dow's seeds.[20]

The district court rejected Bayer's claim construction and adopted Dow's version: "the biochemical reactions that occur and the reaction products that form, in a biological system in the presence of a 2, 4-D monooxygenase enzyme and 2,4-D."[21] Following Dow's version, among other things, the district court held a summary judgment of non-infringement in favor of Dow.[22] Bayer then appealed to the Federal Circuit, which affirmed the district court's construction and summary judgment of non-infringement.[23]

This article is intended to explore the unique situation occurring in *Bayer II*[24] where an applicant invents something while using incorrect terms to describe the invention because she is misled by the scientific community. The claimed subject was scientifically true at the time of filing, but became scientifically false by the time of infringement.

This article begins by discussing the risk of claiming a debatable enzymatic reaction. Because the disputed claim focuses on an enzymatic reaction rather than the product made by such a reaction, Bayer handed the fate of its patent to the uncertainty of science. Second, this article analyzes the claim construction conducted by the Federal Circuit. An alternative construction is proposed to save Bayer from not being able to protect its own product by its patent. Third, this article discusses how to fix a scientific mistake when the application is pending. Last, this article examines whether claiming a genus to cover a species is possible in the context of monooxygenases and dioxygenases.

CLAIMING A DEBATABLE ENZYMATIC REACTION

Development of U.S. Patent No. 6,153,401

Before the application for the '401 patent was filed, the bacterium *Alcaligenes eutrophus* was known to degrade 2,4-D through a monooxygenase encoded by a *tfdA* gene.[25] When Bayer was developing the patented plant, one inventor, Dr. Wolfgang R. Streber, conducted an experiment showing that classifying a *tfdA* gene-initiated enzyme as a monooxygenase was incorrect.[26] Bayer chose not to fully investigate the scientific truth

---

[15] *See Bayer CropScience AG v. Dow AgroSciences LLC*, 2012 WL 4498527, at *3 (D. Del. Sept. 27, 2012) (emphasis added) [hereinafter *Bayer I*].
[16] *See Bayer II*, 728 F.3d at 1327.
[17] *Id.*
[18] *See Bayer I*, 2012 WL 4498527, at *2.
[19] *Bayer I* at *3
[20] *See Bayer II*, 728 F.3d at 1330.
[21] *Bayer I*, 2012 WL 4498527, at *3.
[22] *Id.* at *8.
[23] *See Bayer II*, 728 F.3d at 1325.
[24] *Bayer CropScience AG v. Dow AgroSciences LLC*, 728 F.3d 1324 (Fed. Cir. 2013).
[25] *See, e.g.*, Streber WR, Timmis KN, Zenk MH. Analysis, cloning, and high-level expression of 2,4-dichlorophenoxyacetate monooxygenase gene *tfdA* of *Alcaligenes eutrophus* JMP134. J Bacteriol 1987;169:2950; *available at* www.ncbi.nlm.nih.gov/pmc/articles/PMC212332/pdf/jbacter00197-0050.pdf; Perkins EJ, Lurquin PF. Duplication of a 2,4-dichlorophenoxyacetic acid monooxygenase gene in *Alcaligenes eutrophus* JMP134(pJP4). J Bacteriol 1988;170:5669; *available at* www.ncbi.nlm.nih.gov/pmc/articles/PMC211667/pdf/jbacter00190-0277.pdf; Stenström J. Kinetics of decomposition of 2,4-dichlorophenoxyacetic acid by *Alcaligenes eutrophus* JMP134 and in Soil. Environ Toxicol Water Qual 1989;4:405–24; Bayley et al. Engineering 2,4-D resistance into cotton. Theoret Appl Genet 1992;83:645.
[26] *See Bayer I*, 2012 WL 4498527, at *2 n. 4.

behind the performance of a *tfdA* gene.[27] Instead, Bayer adopted the term "monooxygenase," accepted by the science community at that time, to describe the enzymatic reaction caused by a *tfdA* gene throughout the specification of the '401 patent.[28]

The Federal Circuit, in *Newman v. Quigg*, has held that "it is *not a requirement* of patentability that *an inventor* correctly set forth, or *even know, how or why the invention works*"[29] (emphasis added). So, to acquire a patent for a gene-modified plant with a special function, Bayer does not need to know the scientific theory behind the function; accordingly, the investigation of the enzymatic mechanism caused by a *tfdA* gene is not necessary.[30] However, Bayer uses "a polypeptide having the biological activity of 2,4-D monooxygenase" to broaden the claim scope to cover all genes that can create an enzyme to decompose 2,4-D through a monooxygenase. Bayer then has to ask whether science is on its side.

Enablement Requirement

35 USC §112(a) provides:

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

The provision requires the specification of a patent to meet the enablement requirement.[31] The Federal Circuit, in *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, held that "the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'"[32]

The *Wands* factors govern the issue of "undue experimentation" and 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.[33]

As the Federal Circuit has held in *In re Wands*, "[w]hether undue experimentation is needed, is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations."[34] So, none of the *Wands* factors are dispositive by themselves.

Assume that "2,4-D monooxygenase" is scientifically true. The '401 patent may pass the determination of the *Wands* factors if Bayer can provide "extensive testimony from qualified experts, with exploration of the technology in light of the knowledge and publications at the time the patent application was filed."[35] In addition, the patent involves bacteria. As the Federal Circuit has held, in *Ajinomoto Co. v. Archer-Daniels-Midland Co.*, "[t]he deposit of biological organisms for public availability satisfies the enablement requirement for materials that are not amenable to written description or that constitute unique biological materials which cannot be duplicated."[36] Because the '401 patent refers to the deposits of the microorganisms applied,[37] the enablement requirement should be satisfied. But the reality is that "2,4-D monooxygenase" is scientifically incorrect. Thus, the specification of the '401 patent will never enable others to make and use the claimed plant.

---

[27] *See id.* at *6–*7 (suggesting that Bayer knew the methodology of distinguishing monooxygenase and dioxygenase).
[28] *See Bayer II*, 728 F.3d at 1329–30.
[29] *Newman v. Quigg*, 877 F.2d 1575, 1581–82 (Fed. Cir. 1989)(internal citations omitted)(emphasis added)(describing the utility requirement). Quoted by *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014)(describing the enablement requirement).
[30] *See* Jeffrey L. Light, *Note, Broadening the Scope of Biotechnology Inventions by Disclosing a Scientific Theory*, 3 CHI.-KENT J. INTELL. PROP. 87, 113 (2003).
[31] *See* Denise W. DeFranco and Ashley A. Weaver, *Written Description and Enablement: One Requirement or Two?* 15 FED. CIRCUIT B.J. 101, 102 (2005).
[32] *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334 (Fed. Cir. 2003).
[33] *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).
[34] *Id.*
[35] *Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345 (Fed. Cir. 2000).
[36] *Id.* at 1345–46.
[37] *See* U.S. Patent No. 6,153,401 cols.9–10; *see also Bayer I*, 2012 WL 4498527, at *9.

The unique situation Bayer encounters here is a debatable enzymatic reaction or an enzymatic reaction subject to future challenges or continuous debates. Before the application was filed in 1989, "*Alcaligenes eutrophus*" was believed to create a monooxygenase through a *tfdA* gene to transform 2,4-D into 2,4-DCP.[38] This belief was challenged by the paper published in 1993.[39] Bayer's failure to amend the claim or specification after learning of the 1993 paper was criticized by the Federal Circuit and became one of the grounds for rejecting Bayer's claim construction.[40] In a 1997 paper, the authors still referred to "2,4-D monooxygenase" when discussing a *tfdA* gene.[41] Therefore, even at that time Bayer learned an aspect from the 1993 paper, it would have been reasonable for Bayer not to consider a dioxygenase as a scientific truth.

Role of Expert Witnesses

When interpreting the disputed phrase "biological activity of 2,4-D monooxygenase," the district court relied on expert testimony and dictionary definitions to agree with Dow's claim construction.[42] The district court even used the words of Bayer's expert to argue against Bayer's claim construction.[43]

The Federal Circuit has required district courts to find out the original and customary meaning of a claim.[44] Many of the district court judges who have handled patent cases are reported to rely on expert testimony and dictionaries to conduct claim construction.[45] The use of expert testimony or dictionaries is necessary for judges to construe scientific or technical terms.[46] The Supreme Court, in *Markman v. Westview Instruments, Inc.,*[47] has confirmed that claim construction is a question of law subject to the judge's determination.[48] However, the complexity of technology or science may turn claim construction into a question of fact, enabling a judge to delegate the power to construe a claim to technical experts.

CLAIM CONSTRUCTION OF "BIOLOGICAL ACTIVITY OF 2,4-D MONOOXYGENASE"

Federal Circuit's Interpretation

The Federal Circuit disagreed with Bayer's interpretation of "the biological activity of 2,4-D monooxygenase" as "bringing about the cleavage of the side chain of 2,4-D" because Bayer's construction has "serious textual difficulties."[49] Although not directly mentioned in the opinion, the rule of claim construction has been well settled under Federal Circuit case law.[50] Under *Phillips v. AWH Corp.*,[51] claim construction relies on both intrinsic and extrinsic evidence.[52] Intrinsic evidence includes claims, specifications, and prosecution history.[53] Extrinsic evidence covers expert testimony, inventor testimony, dictionaries, and treatises.[54] Here, the Federal Circuit primarily used claim language to reach its interpretation and cited the specification and prosecution history as supporting evidence.

The Federal Circuit's interpretation can be broken down into three levels.[55] First, monooxygenase" means "an enzyme catalyzing a reaction in which one oxygen atom is incorporated into water and the second is incorporated into something other than water."[56] Second, "2,4-D monooxygenase" means "the standard way of conveying what the monooxygenase acts on, namely, 2,4-D."[57] Third, "the biological activity of" means "the activity that makes the identified enzyme a monooxygenase that acts on 2,4-D: the attachment

---

[38]*See Bayer II*, 728 F.3d at 1325–26.
[39]*Id.* at 1326.
[40]*Id.* at 1328.
[41]*See* Kapaun JA, Cheng Z-M. Plant regeneration from leaf tissues of Siberian elm. HortScience 1997;32:301; *available at* http://hortsci.ashspublications.org/content/32/2/301.full.pdf
[42]*See Bayer I*, 2012 WL 4498527, at *4.
[43]*Id.* at *4–*8.
[44]*See* Etan S. Chatlynne, *On Measuring the Expertise of Patent-Pilot Judges: Encouraging Enhancement of Claim-Construction Uniformity*, 12 J. Marshall Rev. Intell. Prop. L. 309, 311 (2013).
[45]*See* Rebecca N. Eyre et al., Patent Claim Construction: A Survey of Federal District Judges 20 (2008), *available at* www.fjc.gov/public/pdf.nsf/lookup/patclaim.pdf/$file/patclaim.pdf/
[46]*See* Paul R. Gugliuzza, *The Federal Circuit as a Federal Court*, 54 Wm. & Mary L. Rev. 1791, 1832 (2013).
[47]*Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996).
[48]*Id.* at 372.
[49]*See Bayer II*, 728 F.3d at 1328.
[50]*See* Christian E. Mammen, *Patent Claim Construction as a Form of Legal Interpretation*, 12 J. Marshall Rev. Intell. Prop. L. 40, 48 (2012)(discussing *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005)).
[51]*Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005).
[52]*See* Mammen, *supra* n. 50, at 48.
[53]*Id*
[54]*Id.* at 48–49.
[55]*See Bayer II*, 728 F.3d at 1328.
[56]*Id.*
[57]*Id.*

of one oxygen atom to the 2,4-D molecule to trigger cleaving with the other atom of O_2 going to water."[58] The Federal Circuit's interpretation simply reflects "the ordinary meaning of [the] words [of the full phrase] 'the biological activity of 2,4-D monooxygenase.'"[59]

Although its methodology was called "a facially straightforward textual analysis,"[60] the Federal Circuit's construction of "monooxygenase" actually was based on an "agreement" between Bayer and Dow.[61] When the case was heard by the district court, both parties provided expert witnesses for the *Markman* hearing on claim construction.[62] Based on the expert testimony from both sides, the district court held that "a "2,4-D monooxygenase" is an enzyme that causes a reaction with 2,4-D and two atoms of oxygen, where one atom of oxygen is added to 2,4-D and the other ultimately forms water."[63] So, the "agreement" the Federal Circuit relied on was in fact derived from extrinsic evidence.

Federal Circuit's Critiques of Bayer's Interpretation

The Federal Circuit criticized Bayer's interpretation in two aspects,[64] both based on the intrinsic evidence of the '401 patent.

The first critique relates to "2,4-D monooxygenase."[65] The Federal Circuit found that Bayer's version of "2,4-D monooxygenase" was "merely 'oxygenase'" or "a proper name of a particular enzyme (or class) without any descriptive meaning."[66] Adopting Bayer's view would deprive "monooxygenase" of its "scientifically accepted descriptive content."[67] The Federal Circuit also worried that the deprivation would violate "[f]amiliar claim-contruction policies regarding public notice and patentee drafting duties."[68] In addition, the Federal Circuit expressed the view that Bayer should be responsible for its mistake: Bayer chose to trust its unverified belief in "monooxygenase" without amending the term even after learning the truth while the application was pending.[69] Moreover, the Federal Circuit found that Bayer's use of "monooxygenase" in the specification or prosecution history would not support the idea that "mono" can be ignored.[70]

The second critique relates to "the biological activity of."[71] Regarding Bayer's version of "biological activity," the Federal Circuit considered it "as referring to *any enzyme* that alters 2,4-D by cleaving its side chain."[72] Bayer based its view on one of the two uses of "biological activity" in the specification.[73] The specifically quoted sentence was "[t]he tfdA gene codes for 2,4-D monooxygenase, a polypeptide having the biological activity of bringing about the cleavage of the side chain of 2,4-D."[74] However, the Federal Circuit characterized the quoted sentence as "not hav[ing] the form of, or otherwise convey[ing] that it is, a definition of 'the biological activity.'"[75] Rather, the Federal Circuit found that the sentence only "describes something that a '2,4-D monooxygenase' does, but it does not say that every enzyme with that function is a '2,4-D monooxygenase.'"[76] Thus, the Federal Circuit refused to transform "the biological activity" along with "2,4-D monooxygenase" into a particular type of enzyme.[77]

Moreover, the Federal Circuit focused on another phrase, "coding for a protein which has the biological activity of the protein encoded by tfda; *e.g.*, its 2,4-D-monooxygenase activity."[78] The Federal Circuit particularly highlighted "*e.g.*" of that phrase and concluded that "[t]he use of '*e.g.*,' rather than '*i.e.*,' strongly suggests that there is more than one 'biological activity.'"[79] Because a *tfda* gene may induce several biological activities, use of "its 2,4-D monooxygenase activity" was considered by the Federal Circuit to suggest that the claimed activity is a monooxygenase.[80] Therefore, the Federal Circuit concluded that the specification refers to a particular biological activity, "2,4-D monooxygenase," rather than a particular enzyme.[81]

---

[58] *Id.*
[59] *Id.*
[60] *Id.*
[61] *Id.* ("As the district court recognized, all agree … .").
[62] *See Bayer I*, 2012 WL 4498527, at *4.
[63] *Id.*
[64] *See Bayer II*, 728 F.3d at 1328.
[65] *Id.*
[66] *Id*
[67] *Id.*
[68] *Id.*
[69] *Id.*
[70] *Id.* at 1328–29.
[71] *Id.*
[72] *Id.* at 1328 (emphasis added).
[73] *Id.* at 1329 ("The specification uses the phrase 'biological activity' just twice.").
[74] *Id.* at 1329–30 (quoting the '401 patent col.2 ll. 25–27 as corrected by a 2012 certification of correction).
[75] *Id.* at 1330.
[76] *Id.*
[77] *Id.* ("More is needed for a term with an established scientific meaning to be redefined in the specification.").
[78] *Id.* (quoting the '401 patent col.2 ll. 65–67)(emphasis added).
[79] *Id.*
[80] *Id.* (emphasis in original).
[81] *Id.*

Written Description

In addition to the textual analysis of the disputed claim language, the Federal Circuit took into consideration the issue of written description.[82] The issue was raised because Bayer's broad claim construction led to Dow's counterclaim of invalidity under the written description doctrine.[83] The district court held that Bayer's claim construction fails to meet the written description requirement.[84] Although not rejecting the district court's ruling, the Federal Circuit did not affirm it because Bayer's claim construction had been denied.[85]

There is some tension between claim construction and validity. The Federal Circuit, in *Chef Am., Inc. v. Lamb-Weston, Inc.,* has held that "courts may not redraft claims, whether to make them operable or to sustain their validity."[86] On the other hand, in *Generation II Orthotics Inc. v. Med. Tech. Inc.*, the Federal Circuit has stated that "claims can only be construed to preserve their validity where the proposed claim construction is 'practicable,' is based on sound claim construction principles, and does not revise or ignore the explicit language of the claims."[87] Here, the Federal Circuit held that the record regarding the issue of written description has created "grave doubts" about the validity of the '401 patent and therefore reinforced its "textual objections to Bayer's proposed construction."[88]

In *Ariad Pharms., Inc. v. Eli Lilly and Co.*, a 2010 *en banc* decision, the Federal Circuit held that to meet the written description requirement, "the description must 'clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'"[89] The question is "whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had *possession* of the claimed subject matter as of the filing date."[90] To establish "possession," courts look into "an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art."[91]

Particularly for generic claims, the Federal Circuit has provided several factors for evaluation, such as "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue."[92] There is no "bright-line rule."[93] It is not necessary that "the number of species that must be disclosed to describe a genus claim, as this number necessarily changes with each invention, and it changes with progress in a field."[94] But "when a patent claims a genus by its function or result, the specification [has to recite] sufficient materials to accomplish that function—a problem that is particularly acute in the biological arts."[95]

Here, Bayer's claim construction was characterized by the Federal Circuit as what "broadly covers *a class of enzymes* defined by their function of causing cleaving of the side chain of 2,4-D."[96] The question, then, was whether the specification discloses sufficient materials to achieve the function.

In *Univ. of Rochester v. G.D. Searle & Co.*, the Federal Circuit reinstated the position that "functional descriptions of genetic material can, in some cases, meet the written description requirement if those functional characteristics are '*coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics*.'"[97] Here, although recognizing "the primacy of *structural identification* for inventions in certain areas like the one at issue here,"[98] the Federal Circuit also considered "the possibility of other means of identification"[99] as long as "such alternative means sufficiently correlate with structure."[100] But the '401 patent failed to pass that "other means" standard.[101]

The Federal Circuit found that the '401 patent "structurally identifies just one gene sequence and the enzyme it encodes."[102] The specification failed to support Bayer's claim construction in two

---

[82] *Id.* at 1330–31.
[83] *Id.* at 1330.
[84] *See Bayer I*, 2012 WL 4498527, at *8–*10.
[85] *See Bayer II*, 728 F.3d at 1331–32.
[86] *Chef Am., Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1374 (Fed. Cir. 2004).
[87] *Generation II Orthotics Inc. v. Med. Tech. Inc.*, 263 F.3d 1356, 1365 (Fed. Cir. 2001).
[88] *See Bayer II*, 728 F.3d at 1330.
[89] *Ariad Pharms., Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010)(citation omitted).
[90] *Id.* (emphasis added).
[91] *Id.*
[92] *Id.* (citation omitted).
[93] *See id.*
[94] *Id.* (citation omitted).
[95] *Id.* at 1352–53.
[96] *See Bayer II*, 728 F.3d at 1331 (emphasis added).
[97] *Univ. of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 925 (Fed. Cir. 2004)(quotation omitted)(emphasis added).
[98] *Bayer II*, 728 F.3d at 1330 (emphasis added).
[99] *Id.*
[100] *Id.* at 1331.
[101] *Id.*
[102] *Id.* at 1330.

aspects. First, the patent provided "the DNA sequence (and hence amino acid sequence) of just one embodiment."[103] The first aspect shows that the Federal Circuit adopted the district court's factual findings. The district court's decision specifically recited Bayer's expert testimony showing that soil may contain billions of microorganisms capable of degrading 2,4-D.[104]

Second, the Federal Circuit held that the "growth test" could not describe its correlation with the shared structure of species enzymes.[105] The specification described the growth test in Example 22.[106] The growth test presented plants with the *tfdA* gene and control plants (without a *tfdA* gene) for testing of their ability to resist to 2,4-D, where the result showed the *tfdA* gene-containing plants can survive in a higher concentration of 2,4-D.[107] At the district court, Bayer provided some scientific evidence supporting the correlation between a *tfdA* gene and "the cleavage of the side chain of 2, 4-D."[108] But the district court found that Bayer failed to point out any place in the specification that described that correlation.[109] The Federal Circuit sided with the district court and found no such correlation.[110]

The decision on the issue of written description was negative for Bayer, but the result was not to invalidate the '401 patent because the issue was discussed only for purposes of the review of the district court's summary judgment of non-infringement.[111] The district court's ruling did not relate to "invalidity," so the Federal Circuit did not "go beyond rejecting Bayer's proposed claim construction."[112] Interestingly, the Federal Circuit also stated that "we need not affirmatively construe the claims in order to affirm the district court's judgment."[113] It seems that the Federal Circuit limited its holding to Bayer's broad claim construction. Therefore, the '401 patent is valid.

Ordinary and Customary Meaning of ''2,4-D Monooxygenase''

When addressing the written description issue, the Federal Circuit at the end stated, "[a]t oral argument in this court, Bayer has sought to mitigate this concern by expressly arguing that any genes not derived from *soil bacteria* would fall outside of the claimed genus."[114] Because that last construction was not presented to the district court or in the opening brief to the Federal Circuit, the Federal Circuit did not go through that alternative construction, which might survive the written description challenge and cover the defendant's product.[115]

It is not clear what the "soil bacteria" version of Bayer's claim construction would have been. It is possible to guess what may be an appropriate claim construction that may recover the misunderstanding of 2,4-D degradation triggered by a *tfdA* gene. The ultimate question is whether the Federal Circuit would have found any alternative construction in favor of Bayer.

The Federal Circuit did not interpret "2,4-D monooxygenase" as a whole, but construed first "monooxygenase" and then "2,4-D monooxygenase." That is, the Federal Circuit focused too much on the ordinary and customary meaning of "monooxygenase." The question, then, is why not look to the ordinary and customary meaning of "2,4-D monooxygenase" alone?

As the Federal Circuit in *Phillips* has recognized, "the specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term."[116] Here, the specification of the '401 patent recites,

> *2,4-D-Monooxygenase is an enzyme catalyzing in many 2,4-D-degrading organisms the first step in the metabolizing of 2,4-dichlorophenoxyacetic acid (2,4-D).* Among the 2,4-D-degrading organisms belong, in particular, *soil bacteria*, such as, for example, *Acinetobacter*, *Alcaligene*s, *Arthrobacter*, *Cyronebacterium* and *Pseudomonas*[117] (emphasis added).

This description suggests that "2,4-D monooxygenase" refers to the first step of an enzymatic reaction caused by a 2,4-D-degrading organism living in the soil. Because "degrading" is used, the term "the first step in the metabolizing" indicates a step of transforming 2,4-D into a nontoxic compound (*e.g.*, 2,4-DCP). Such an enzymatic reaction

---

[103] *Id.* at 1331.
[104] *See Bayer I*, 2012 WL 4498527, at *9–*10.
[105] *See Bayer II*, 728 F.3d at 1331.
[106] *See* '401 patent cols.31–32.
[107] *Id.*
[108] *See Bayer I*, 2012 WL 4498527, at *10.
[109] *Id.*
[110] *See Bayer II*, 728 F.3d at 1331.
[111] *Id.* at 1331–32.
[112] *Id.* at 1331.
[113] *Id.* at 1332.
[114] *Id.* at 1331 (emphasis added).
[115] *Id.*
[116] *Phillips*, 415 F.3d at 1315 (quotation and citation omitted).
[117] '401 Patent col.1 ll.21–27 (emphasis added).

is found in soil bacteria (*e.g.*, *Acinetobacter*, *Alcaligenes*, *Arthrobacter*, *Cyronebacterium*, *Pseudomonas*, and the like). Therefore, "2,4-D monooxygenase" may be interpreted as "an *enzyme* produced by a 2,4-D-degrading soil bacteria and transforming 2,4-D into a nontoxic compound."

The proposed interpretation of "2,4-D monooxygenase" focuses on a 2,4-D-degrading *enzyme* rather than a specific mechanism. This approach may recover Bayer's misunderstanding of a scientific fact. "2,4-D monooxygenase" is considered as a name of an enzyme, and such enzyme is produced by a soil bacterium and causes the degradation of 2,4-D. Although an applicant can act as a lexicographer to define a claim term in the specification,[118] the proposed interpretation is not that case because when the application was filed, "2,4-D monooxygenase" had been a well-accepted term in the field for describing a 2,4-D-degrading organism, such as *Alcaligenes eutrophus*.

Under this approach, it does not matter whether the applicant uses "2,4-D monooxygenase" or "2,4-D dioxygenase." The latter adoption of "2,4-D dioxygenase" can be treated as a name change of "2,4-D monooxygenase," because both terms are intended to describe a enzymatic reaction caused by the same soil bacterium. The name change results from more understanding of the natural phenomenon caused by a particular gene.

"*Arabidopsis*" is an example of a name change in terms of its enzymatic property.[119] In an early study of nitric oxide generation as an important endogenous signaling molecule in *Arabidopsis* (Rock Cress flowers), the researcher found an enzyme that creates NO synthase (NOS) and therefore named it "*AtNOS1*."[120] Later, the NOS function of *AtNOS1* was heavily challenged by other scholars because they could not reproduce the NOS results similar to those in early studies.[121] Based on those challengers' papers finding the co-existence of NO synthesis and accumulation, "*AtNOS1*" was renamed "*Arabidopsis thaliana* nitric oxide associated 1" (*AtNOA1*).[122] However, the story did not end there. After *AtNOA1* was named, several follow-up studies began to propose other possible enzymatic mechanisms.[123] Therefore, the enzymatic function of "*AtNOA1*" remains scientifically debatable.[124]

The "*Arabidopsis*" story tells us that a certain enzyme is understood by scientists to correlate with a chemical reaction leading to a particular product (NO), while the mechanism behind that chemical reaction remains debatable from time to time if there is some new finding. But in any event, the consensus among scientists in the field is still that such an enzyme causes the generation of NO. Likewise, "2,4-D monooxygenase" was used to describe an enzyme that causes 2,4-D degradation. Although followup studies may have shown a different mechanism of 2,4-D degradation, that does not change the correlation between the enzyme and 2,4-D degradation. The replacement of "2,4-D monooxygenase" by "2,4-D dioxygenase" is to clarify the believed truth of the enzymatic reaction caused by the same enzyme.[125] That is only a name change for the enzyme.

Therefore, the phrase "a polypeptide having the biological activity of 2,4-D monooxygenase" in Claim 1 of the '401 patent may be interpreted as "an enzyme which can degrade 2,4-D by transforming it into a non-toxic compound 2,4-DCP." The proposed claim construction saves the '401 patent from being unable to assert infringement against at least some plant which exactly copies its disclosure.

IS "MONOOXYGENASE" A CORRECTABLE ERROR?

Correction Made by the Patent and Trademark Office

The Federal Circuit, in *Bayer CropScience AG v. Dow AgroSciences LLC*, interpreted "2,4-D monooxygenase" by elaborating why Bayer's broad

---

[118] *Phillips*, 415 F.3d at 1316 ("[O]ur cases recognize that the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs.").

[119] *See* Neill S, Bright J, Desikan R, Hancock J, Harrison J, Wilson I. Nitric oxide evolution and perception. J Exp Botany 2008;59:25–27; *available at* http://jxb.oxfordjournals.org/content/59/1/25.full.pdf

[120] *Id.* at 26.

[121] *Id.*

[122] *Id.* at 26–27.

[123] *Id.* at 27.

[124] *Id.*; *see also* Sun LR, Hao FS, Lu BS, Ma LY. AtNOA1 modulates nitric oxide accumulation and stomatal closure induced by salicylic acid in *Arabidopsis*. Plant Signal Behavior 2010;5:1022–23; *available at* www.ncbi.nlm.nih.gov/pmc/articles/PMC3115186/pdf/psb0508_1022.pdf

[125] *See* Hausinger RR Fukumori F. Characterization of the first enzyme in 2,4-dichlorophenoxyacetic acid metabolism. Environ Health Persp 1995;103:37 ("We have shown that the enzyme is not a 2,4-D monooxygenase, as commonly stated in the literature but is rather a ferrous and a ketoglutarate (a-KG)-dependent dioxygenase."); *available at* www.ncbi.nlm.nih.gov/pmc/articles/PMC1519297/pdf/envhper00366-0040.pdf

construction should be rejected. It is possible that in any future lawsuit regarding the '401 patent, "2,4-D monooxygenase" will be treated, not as the name of a particular enzyme, but as a particular enzymatic reaction, which cannot be infringed.

The question then becomes whether Bayer can correct "monooxygenase" as an error under 35 USC §254 or §255. 35 USC §254 provides that a patentee may file a petition with the PTO to correct a mistake in the patent if such a mistake is made by the PTO.[126] Here, §254 is not applicable because Bayer, not the PTO, chose the term "monooxygenase" when the application was filed.

Under 35 USC §255, a patentee may correct an applicant-made error if such an error is "of a clerical or typographical nature, or of minor character."[127] The Federal Circuit, in *Superior Fireplace Co. v. Majestic Products Co.*,[128] has defined "clerical" as "relating to an office clerk or office work,"[129] "typographical" as "relating to the setting of type, printing with type, or the arrangement of matter printed from type,"[130] and "minor" as "lesser in importance" or "seriousness."[131]

Here, "monooxygenase" was a term adopted by scientists in the field for decades, so "monooxygenase" could not be a clerical or typographical error. Additionally, because "dioxygenase" and "monooxygenase" have different meanings in terms of biological activities created by the enzymes, "monooxygenase" cannot be considered a minor error. Therefore, Bayer cannot correct "monooxygenase" and then use the scientifically correct term "dioxygenase" to describe the claimed biological activity.

Correction Made by Courts

Courts may correct a claim error under some circumstances.[132] The Federal Circuit, in *CBT Flint Partners, LLC v. Return Path, Inc.*, held that "a district court may correct an obvious error in a patent claim,"[133] "only if (1) the correction is not subject to reasonable debate based on consideration of the claim language and the specification and (2) the prosecution history does not suggest a different interpretation of the claims."[134] The question is whether "monooxygenase" is an obvious error and whether those two elements are met. The Federal Circuit, in *Ultimax Cement Mfg. Corp. v. CTS Cement Mfg. Corp.*, has held, "[t]hose determinations must be made from the point of view of one skilled in the art."[135]

Here, "monooxygenase" is not an obvious error similar to those which the Federal Circuit has ever encountered.[136] The term "monooxygenase" is not an error because the specification of the '401 patent uses "monooxygenase" to describe a type of enzymatic reaction caused by a *tfdA* gene.[137] "Dioxygenase" exists nowhere in the specification. Therefore, courts will not conclude that the specification supports the argument that "2,4-D monooxygenase" may be corrected as "2,4-D dioxygenase."

Correction Through Continuing Applications

During the prosecution of the '401 patent, the applicant might have a chance to amend the specification and claims to change "monooxygenase" to "dioxygenase." The question is whether "dioxygenase" constitutes new matter. If so, Bayer would have lost the priority date of the original application.[138]

---

[126] *See* 35 USC §254 ("Whenever a mistake in a patent, incurred through the fault of the Patent and Trademark Office, is clearly disclosed by the records of the Office, the Director may issue a certificate of correction stating the fact and nature of such mistake, under seal, without charge, to be recorded in the records of patents.").

[127] *See* 35 USC §255 ("Whenever a mistake of a clerical or typographical nature, or of minor character, which was not the fault of the Patent and Trademark Office, appears in a patent and a showing has been made that such mistake occurred in good faith, the Director may, upon payment of the required fee, issue a certificate of correction, if the correction does not involve such changes in the patent as would constitute new matter or would require re-examination.").

[128] *Superior Fireplace Co. v. Majestic Products Co.*, 270 F.3d 1358 (Fed. Cir. 2001).

[129] *Id.* at 1369 (citing a dictionary).

[130] *Id.* (citing a dictionary).

[131] *Id.* at 1375.

[132] *See* Ping-Hsun Chen, *Judicial Power to Correct Disputed Patent Claims Under the American Patent Case Law: A Comment on Taiwan Intellectual Property Court Civil Judgment (99) Min Zhuan Shang Zi No. 5 (2010)*, 9(1) SOOCHOW L.J. 75, 80–93 (2012).

[133] *CBT Flint Partners, LLC v. Return Path, Inc.*, 654 F.3d 1353, 1358 (Fed. Cir. 2011).

[134] *Id.*

[135] *Ultimax Cement Mfg. Corp. v. CTS Cement Mfg. Corp.*, 587 F.3d 1339, 1353 (Fed. Cir. 2009).

[136] *See*, *e.g.*, *Hoffer v. Microsoft Corp.*, 405 F.3d 1326 (Fed. Cir. 2005)(correcting a claim number recited by a dependent claim); *Ultimax Cement Mfg. Corp. v. CTS Cement Mfg. Corp.*, 587 F.3d 1339 (Fed. Cir. 2009)(adding a common between "f" and "cl" in the term $\{(C_9S_3S_3Ca(f\ cl))_2\}$); *CBT Flint Partners, LLC v. Return Path, Inc.*, 654 F.3d 1353 (Fed. Cir. 2011)(correcting the phrase "detect analyze" by adding "and" between "detect" and "analyze").

[137] *See Bayer II*, 728 F.3d at 1329–30 (citing as references several parts of the specification).

[138] *See Pfizer, Inc. v. Teva Pharms. USA, Inc.*, 518 F.3d 1353, 1361 (Fed. Cir. 2008).

"New matter" is determined by the law of the written description requirement.[139] The question becomes whether the original specification supports "dioxygenase" as an enzymatic reaction created by a *tfdA* gene. The answer is probably "no," because the specification does not provide any experimental results showing a "dioxygenase" mechanism. Therefore, adding "dioxygenase" is new matter.

Alternatively, Bayer would have filed a continuation-in-part (CIP) application to introduce "dioxygenase" as new matter. A CIP is "just what its name implies. It partly continues subject matter disclosed in a prior application, but it adds new subject matter not disclosed in the prior application."[140]

Here, according to the district court's decision, before the application was filed, one inventor of the '401 patent, Dr. Wolfgang R. Streber, conducted some experiments demonstrating that the enzymatic reaction of 2,4-D degradation was not performed by a monooxygenase.[141] Bayer's expert also stated that at that time, the methods for identify "monooxygenase" or "dioxygenase" were known to the scientists in the field.[142] Therefore, the record indicates that Bayer would have had a chance to conduct experiments after the filing date to find out whether a *tfdA* gene encodes a "monooxygenase" or a "dioxygenase." If Bayer had done so, it would have had a chance to file a CIP to include "2,4-D dioxygenase" as a possible biological activity caused by a *tfdA* gene. However, Bayer gave up that chance, leading to a failure to claim a correct enzymatic reaction.

USE OF "2,4-D HYDROXYLASE" OR "2,4-D OXYGENASE"

At the *Markman* hearing, Bayer's expert said that he would have used "2,4-D hydroxylase" to cover both monooxygenases and dioxygenase.[143] In fact, "monooxygenase" and "dioxygenase" may be categorized as the enzymes catalyzing reactions with O_2; "oxidase," which transforms O_2 into hydrogen peroxide or two H_2O molecules, also belongs to this category.[144] Alternatively, "oxygenase" may be used as a group name for "monooxygenase" and "dioxygenase."[145] In any case, to claim a genus (hydroxylase or oxygenase), the specification has to meet the requirements for written description and enablement.

The Federal Circuit, in *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*,[146] held that "to satisfy the written description requirement for a claimed genus, a specification must describe the claimed invention in such a way that a person of skill in the art would understand that the genus that is being claimed has been invented, not just a species of the genus."[147] Thus, the '401 patent may have to describe both 2,4-D monooxygenase and 2,4-D dioxygenase. But the question is how Bayer would have described 2,4-D dioxygenase at the time when the scientific community supported 2,4-D monooxygenase.

Even assuming that when the application for the '401 patent was filed, the scientific community had recognized the possibility of 2,4-D monooxygenase, 2,4-D dioxygenase, or the co-existence of both 2,4-D monooxygenase and 2,4-D dioxygenase, the question is what to do if the enzymatic reaction caused by a *tfdA* gene product is still debatable when the application is pending.

Claiming a 2,4-D hydroxylase or oxygenase means that the specification has to enable both 2,4-D monooxygenase and 2,4-D dioxygenase. If the answer is no, then the enablement requirement cannot be satisfied. Because "monooxygenase" and "dioxygenase" belong to different subgroups of the genus "hydroxylase" or "oxygenase," a *tfdA* gene can create either a "monooxygenase" or a "dioxygenase." Thus, the '401 patent may have to provide a great deal of experimental data to demonstrate that both enzymatic mechanisms can co-exist to transform 2,4-D. However, the time spent conducting experiments may delay the filing. More realistically, the co-existence of a 2,4-D monooxygenase and a 2,4-D dioxygenase is scientifically impossible. Therefore, claiming "2,4-D hydroxylase" or "2,4-D oxygenase" is not an option. Bayer has to choose either a 2,4-D monooxygenase or a 2,4-D dioxygenase.

---

[139] *See Agilent Techs., Inc. v. Affymetrix, Inc.*, 567 F.3d 1366, 1379 (Fed. Cir. 2009)("The written description doctrine prohibits new matter from entering into claim amendments, particularly during the continuation process.").

[140] *Pfizer, Inc. v. Teva Pharms. USA, Inc.*, 518 F.3d 1353, 1359 (Fed. Cir. 2008).

[141] *See Bayer I*, 2012 WL 4498527, at *2 n. 4.

[142] *Id.*

[143] *Id.* at *6.

[144] *See* Knorre DG, Mysina SD. Biochemistry: A Manual for Universities. Nova Science Publishers, 1998, pp 110–1.

[145] *See* Shozo Yamamoto, *The 50th Anniversary of the Discovery of Oxygenases*, 58(5-6) IUBMB LIFE 248, 248 (May–Jun 2006); *available at* http://onlinelibrary.wiley.com/doi/10.1080/15216540600719655/pdf

[146] *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115 (Fed. Cir. 2008).

[147] *Id.* at 1124.

Bayer may have to file a CIP to correct an unintentional scientific mistake of 2,4-D monooxygenase. Or, if Bayer still believes in the truth of 2,4-D monooxygenase, Bayer may keep the original application claiming 2,4-D monooxygenase and simultaneously prosecute a CIP claiming 2,4-D dioxygenase. So, when the scientific debate is finalized, Bayer would have a chance to decide whether to abandon the one the scientists believe is not true.

CONCLUSION

Bayer II teaches us that if a patentee chooses to claim a scientific belief, he may leave his patent vulnerable to a scientific debate whose outcome is uncertain, which may lead to a negative effect on the patent. If a scientific term used to describe his invention is being challenged by some scientists, he has to avoid using that scientific term. Otherwise, if such a term is replaced by a new term, he cannot rely on claim construction to transform the replaced term into the new term.

In the context of claiming an enzymatic reaction, a patentee may choose conduct a full investigation of the enzymatic mechanism to make sure the claimed reaction is scientifically correct. Otherwise, if the claimed enzymatic reaction is proved to be wrong, the patentee will lose the chance to protect his own product. Alternatively, if a patentee wants to take a risk, he may first file an application claiming one version of the debatable enzymatic reaction (for example, monooxygenase) and then file a CIP to claim another version of the reaction. That way, when the scientific debate is finalized, he may have a chance to reserve one patent which claims a scientific truth.

• • •