United States Court of Appeals for the Federal Circuit

INTERVET INC.,
Plaintiff-Appellee,

v.

MERIAL LIMITED AND MERIAL SAS,
Defendants-Appellants.

2009-1568

Appeal from the United States District Court for the District of Columbia in case no. 06-CV-0658, Judge Henry H. Kennedy, Jr.

Decided: August 4, 2010

WILLIAM G. JAMES, II, Kenyon & Kenyon LLP, of Washington, DC, argued for plaintiff-appellee. With him on the brief were JOHN R. HUTCHINS and YARIV WAKS; RICHARD L. DELUCIA and MICHAEL D. LOUGHNANE, of New York, New York. Of counsel was PATRICE P. JEAN, of New York, New York.

J. PATRICK ELSEVIER, Jones Day, of San Diego, California, argued for defendants-appellants. With him on the brief were FRANK G. SMITH, III and KRISTEN L.

MELTON, Alston & Bird LLP, of Atlanta, Georgia; MADISON C. JELLINS, of Palo Alto, California. Of counsel on the brief were JUDY JARECKI-BLACK, Merial Limited, of Duluth, Georgia; EDGAR H. HAUG, and THOMAS J. KOWALSKI, Frommer Lawrence & Haug LLP, of New York, New York.

Before BRYSON, DYK, and PROST, *Circuit Judges*.

Opinion for the court filed by *Circuit Judge* PROST.

Opinion concurring-in-part, dissenting-in-part filed by *Circuit Judge* DYK.

PROST, *Circuit Judge*.

The present patent infringement case arises from a declaratory judgment action brought in the United States District Court for the District of Columbia on April 11, 2006. Plaintiff Intervet Inc. ("Intervet") denies infringing U.S. Patent No. 6,368,601 ("'601 patent"), owned by Defendants Merial Limited and Merial SAS (collectively "Merial"), directed to DNA constructs encoding a type of porcine circovirus. The district court entered summary judgment of noninfringement based on its construction of six disputed claim terms. Merial appeals the district court's claim construction for three of the terms, and, in the alternative, appeals the district court's summary judgment of noninfringement based on the doctrine of equivalents.

Because we agree with Merial that the district court erred in its construction of two disputed claim terms, we reverse the district court's claim construction, vacate the judgment of noninfringement, and remand for a finding of whether the accused device infringes under the claim

construction articulated herein. Additionally, because we agree with Merial that the district court misapplied the law of prosecution history estoppel, we instruct the district court to consider on remand arguments related to literal infringement and to infringement under the doctrine of equivalents, consistent with the analysis herein.

BACKGROUND

Postweaning Multisystemic Wasting Syndrome ("PMWS") is a disease affecting livestock pigs. Researchers at Merial learned that PMWS is associated with a particular type of porcine circovirus.[1] The scientific community was aware of porcine circoviruses prior to Merial's findings. Known porcine circoviruses, however, were not observed to be pathogenic, meaning they did not appear to cause disease in infected pigs. Merial filed for the '601 patent pertaining to the discovery of what it described as a previously unknown pathogenic type of porcine circovirus that the inventors dubbed "PCV-2." PCV-2 stands for "porcine circovirus type II." Merial's patent categorizes previously known, nonpathogenic porcine circoviruses as belonging to "type I" or "PCV-1". The patent identifies a particular known DNA sequence isolated from pig kidney cells called PK/15 as being representative of type I. The '601 patent then identifies five isolated pathogenic porcine circovirus strains as being representative of type II.

The patentee placed the five representative strains on deposit with the United States Patent and Trademark Office ("PTO") as part of the description of the invention. The written patent disclosure provides the full DNA

[1] The prefix "circo" refers to the circular genome of the virus. A porcine circovirus is thus a virus having a circular genome that infects pigs.

sequence for four of these strains, as well as the full sequence of PK/15.

The disclosure explains that the deposited PCV-2 strains had been detected in lesions of pigs with PMWS, but not in healthy pigs. The patent description observes that the sequenced strains exhibit 96% nucleotide homology with each other, and only 76% nucleotide homology with PK/15.[2] The description concludes from these observations that there are two types of porcine circoviruses, and that nonpathogenic "type I," as represented by PK/15, is "thus" distinct from pathogenic "type II," as represented by the five isolated strains. '601 patent col.1 ll.48-62. The disclosure then identifies the subject of the present invention as "the group II porcine circovirus, as defined above, isolated or in the form of purified preparation." *Id.* at col.1 ll.63-65.

The patent disclosure goes on to analyze the sequenced PCV-2 strains in more detail, providing tables comparing the sizes and alignments of the strains. The disclosure then identifies one of the sequenced strains, designated SEQ ID 4, as being further representative of the other strains, and identifies thirteen open reading frames ("ORFs") for PCV-2 using that sequence. The '601 specification identified nine of the thirteen disclosed ORFs that are unique to PCV-2, and four that are present in both PCV-2 and PCV-1.

"ORF" is a commonly used term in molecular genetics that has a standard textbook meaning. An ORF is a portion of a gene that contains a sequence of nucleotide

[2] "Homology" is a measure of the similarity of sequences. Sequences with 96% nucleotide homology, for instance, are 96% identical at the nucleotide level.

bases that may be translated into a protein. Each amino acid of a protein is encoded by a DNA codon. A codon consists of three adjacent nucleotide bases. The first codon in an open reading frame is the "start" codon, which encodes a modified form of methionine. Each amino acid in the polypeptide chain is encoded by a subsequent set of three base pairs, until the translation is terminated at a stop codon that does not itself encode an amino acid, but rather signals the end of translation. Thus, a double-stranded length of DNA can have six different reading frames, depending on the starting base-pair of the first codon and the direction in which the strand is read.[3] The length of an ORF is thus defined by the number of codons that lie between a start codon and a stop codon within the same frame.

Identifying the ORFs of a gene sequence differentiates the portions of the sequence that may encode a protein from the portions that do not encode a protein. It allows those skilled in the art to estimate the size and composition of potential amino acid sequences for the proteins encoded by the gene. Identifying ORFs is especially important in the context of viral or prokaryotic DNA, which can contain several overlapping ORFs in the same gene sequence.

There are two groups of claims in the '601 patent relevant to the present case. The first group can be represented by independent claim 9, which reads:

> 9. A vector comprising an isolated DNA molecule comprising a sequence selected from the group

[3] Two strands times three base pairs per codon equals six reading frames.

> consisting of ORFs 1 to 13 of porcine circovirus type II.

The second group can be represented by independent claim 32, which reads:

> 32. An isolated DNA molecule comprising a nucleotide sequence encoding an epitope which is specific to PCV-2 and not specific to PCV-1.

An epitope is an immunodominant region of a protein, meaning it is the part of an antigen peptide that is recognized by antibodies of the immune system. The patent explains that certain epitopes found among strains of PCV-2 are not present in PCV-1. Thus, the regions of DNA encoding these epitopes are unique to PCV-2. Epitopes unique to PCV-2 are relevant to diagnostics or treatments, because antibodies specific to these epitopes will recognize and bind to the pathogenic PCV-2, but will ignore the benign PCV-1.

Merial's patent claims cover certain vectors and other DNA molecules that contain portions of the PCV-2 gene sequence. These molecules are believed to be useful in diagnosing and vaccinating against PMWS, by stimulating the production and activity of antibodies against PCV-2.

Intervet is an animal healthcare company that manufactures vaccines for livestock. Intervet developed a vaccine called "Porcine Circovirus Vaccine Type 2" that contains a porcine circovirus nucleotide sequence in a vector for treating PMWS in pigs. Merial alleges that Intervet's PMWS vaccine uses an infringing PCV-2 sequence.

At a *Markman* hearing, the United States District Court for the District of Columbia construed six disputed claim terms of the '601 patent. Among these constructions, the district court defined the term "porcine circovirus type II" as consisting of the five nucleotide sequences that Merial placed on deposit with the PTO. The district court construed the term "ORFs 1-13" as the DNA sequences of the thirteen ORFs of SEQ ID 4 listed in the table under Example 13 of the patent. Finally, the district court construed claim 32 in its entirety to refer (in part) to a construct comprising at least one DNA molecule that is unique to one of the five sequences on deposit with the PTO.

The district court then entered summary judgment of noninfringement based on these claim constructions. It was undisputed that Intervet's vaccine contained a nucleotide sequence that was 99.7% homologous to one of the deposited sequences. The accused product was therefore held to be outside the literal claim scope of PCV-2, which required strict identity to one of the five deposited sequences. The district court also held that the doctrine of prosecution history estoppel precluded Merial from arguing that the accused sequence infringed under the doctrine of equivalents.

Merial timely appealed to this court, arguing that the district court erred in its claim construction and erred in applying the doctrine of prosecution history estoppel to Merial's equivalence arguments for the accused product. For the reasons discussed below, we agree with Merial that the district court erred in its claim construction and application of prosecution history estoppel.[4]

---

[4] We do not address the issues of validity and non-patentable subject matter discussed by the dissent

DISCUSSION

Claim Construction

Claim construction is a question of law that is reviewed de novo. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 978 (Fed. Cir. 1995) (en banc). To the extent possible, claim terms are given their ordinary and customary meaning, as they would be understood by one of ordinary skill in the art in question at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc). Idiosyncratic language, highly technical terms, or terms coined by the inventor are best understood by reference to the specification. *Id.* at 1315. Such understanding is informed, as needed, by the prosecution history, if it is in evidence. *Id.* Construing the claims in light of the specification does not, however, imply that limitations discussed in the specification may be read into the claims. It is therefore important not to confuse exemplars or preferred embodiments in the specification that serve to teach and enable the invention with limitations that define the outer boundaries of claim scope. *Id.* at 1323.

It is with an eye to these tenets of claim construction that we review the district court's *Markman* order and conclude the district court erred. We discuss each term in turn.

"Porcine Circovirus Type II"

The district court found that the claim term "porcine circovirus type II" was limited to the five sequences that

---

because these issues were not addressed by the district court or raised on appeal.

were deposited with the PTO as part of the description of the invention. The district court was persuaded by Intervet's arguments that the patent specification defined the invention as being these five sequences, and contained no disclosure from which to infer that any other sequences were also part of the invention.

It is clear enough to us, however, that the patent states that the five deposited strains and listed sequences are "*representative* of" a "*type* of porcine circovirus," and thus do not constitute the entire scope of the invention. '601 patent col.1 ll.60-61 (emphases added). Sequences are representative of the scope of broader genus claims if they indicate that the patentee has invented species sufficient to constitute the genera. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 967 (Fed. Cir. 2002); *In re Smythe*, 480 F.2d 1376, 1383 (C.C.P.A. 1973). Here, the deposited strains are representative species of the larger "type II" genus, where the genus is identified and claimed as the invention.

Claims properly directed to a genus may be adequately supported by the patent disclosure if a sufficient number of species is disclosed so as to properly identify the scope of the genus. *Id.* Here, the patentee has disclosed five species of PCV-2, provided the full sequences for four, and identified the potential coding portions of the sequences. The patentee also provided a counterexample, PCV-1, that by definition lies outside the scope of the claimed genus, as well as a representative species of the counterexample, its sequence, and potential coding portions for the representative.

Neither the claim itself nor the specification provides a homology threshold above or below which a particular PCV strain is properly considered PCV-2 rather than

PCV-1. It refers instead to strains of the invention having "significant serological similarity" and stringent, selective cross-hybridization to the deposited strains over PK/15. The only quantitative boundaries disclosed in the patent are the 96% homology among representative PCV-2 sequences, and the 76% homology between those sequences and the representative of PCV-1.

The patent's stated conclusion that the disclosed PCV-2 sequences "thus" represent a new type of porcine circovirus is based on the pathogenicity of the isolated strains, as well as the observed homology patterns. *See, e.g.*, '601 patent col.5 ll.59-61. This conclusion comports with the way that viruses are typically classified in the relevant art. *Cf.* Universal Virus Database of the International Committee on Taxonomy of Viruses *available at* http://www.ictvdb.rothamsted.ac.uk/. The invention is then defined as being the type II porcine circovirus, which is in turn "as defined above." '601 patent col.5 ll.64. Thus, the pathogenicity and homology patterns are the defining properties of the new type of virus. The claim construction of "porcine circovirus type II" is therefore properly limited to porcine circoviruses that have these two defining properties.

We therefore construe the claim term "porcine circovirus type II" to be "a pathogenic pig virus having a circular genome that is at about 96% or more homologous with the four sequences disclosed in the present specification, and about 76% or less homologous with the PK/15 sequence." Strains that fit this definition would be expected to have strong serological similarity and cross-hybridize to the deposited strains under high stringency conditions. As such, limiting the claim scope according to these properties is not inconsistent with the other descriptive language in the specification.

"ORFs 1-13"

The district court's claim construction of ORFs 1-13 defines the claim scope as consisting of the DNA sequence of the thirteen ORFs enumerated in Example 13 of the patent specification as those ORFs apply to SEQ ID 4. Merial argues that the term should instead read on any translatable length of DNA between a start and stop codon in the PCV-2 gene sequence. Although the district court is correct that the disclosed ORFs define the claim term, the court erred in confining the scope of the term to the precise limits of the representative ORFs listed in Example 13, and the exact DNA sequence of SEQ ID 4.

The ORFs listed in Example 13 are identified as corresponding to one representative PCV-2 sequence, designated in the patent as SEQ ID 4. Although the patent explains that the listed ORFs are identical for some of the deposited strains of PCV-2, it also identifies some variation. The specification explains that the ORFs listed in the table are representative, and one of skill in the art would understand that slight natural variation is to be expected. Indeed, limiting the construction of the term to the exact ORF sequences of SEQ ID 4 would even exclude from the claimed ORFs two of the four sequenced strains of PCV-2, the ORF variations for which sequences are expressly disclosed following the table in Example 13. Thus, we hold that the district court's construction is improperly narrow in scope.

We reject the dissent's position that the specification limits "ORFs 1-13" to the ORFs of the four sequenced strains. The discussion in Example 13, which explains that the limits of ORFs 1 to 13 are "identical" for certain sequenced strains (and not for others), strongly implies that the term "ORFs 1-13" does not refer to a specifically

defined list of limits, but instead contemplates the potential for variation in any given strain of PCV-2. Furthermore, the specification describes the analysis set forth in Example 13 as "representative of the other circovirus strains associated with the multi-systemic wasting syndrome." We have already construed that set of circovirus strains to be broader than just the four sequenced strains, so it would be incongruous to selectively impose the narrower construction here, as the dissent suggests.

We note that because isolates of the same viral type will have essentially the same proteins, they will have the same number of ORFs. The ORFs will be approximately the same size and located in the same relative regions of the genome. By identifying the thirteen ORFs of representative sequence SEQ ID 4, the specification purports to disclose to one of skill in the art the expected ORFs of all PCV-2 isolates. Thus a broader claim construction that allows for some variation in the precise limits of the ORFs and of the underlying DNA sequence is consistent with the expectations of a skilled artisan reading the patent disclosure.

Thus the term ORFs 1-13 is properly construed as "lengths of translatable DNA between pairs of start and stop codons, corresponding to the 13 ORFs identified in the patent specification." ORFs of some PCV-2 strains may not have limits 100% identical to the thirteen illustrated in the patent, but one of skill in the art would readily recognize those ORFs as corresponding to ORFs identified in the patent. Indeed, ORFs 1-13 could correspond to ORFs in other circoviruses, or even other species, as indicated by the examiner's initial rejection of the claim. It is the "of porcine circovirus type II" limitation, rather than Example 13, that confines the claim scope to ORFs of PCV-2.

"Specific to PCV-2 and Not Specific to PCV-1"

The parties below could not agree on what terms of claim 32 were disputed, and the district court decided to construe the claim in its entirety. The district court construed claim 32 to mean "an isolated DNA molecule that includes, but is not necessarily limited to, a DNA sequence which codes for an immunodominant region of a protein, wherein the sequence is from the genome of a PCV-2 circovirus, and not from the genome of a PCV-1 circovirus." The district court explained that due to the "comprising" transition term, the claim may read on molecules that contain sequences that encode epitopes common to PCV-1 and PCV-2, as long as the molecule contains at least one sequence that encodes an epitope unique to PCV-2. We see no error in this construction, and it appears that at the time of the *Markman* hearing, Merial did not see any either.

Merial challenges this construction on appeal because in the district court's subsequent infringement analysis, the court explained that the part of the claim construction specifying that the sequence be "from" the genome of a PCV-2 circovirus, etc., excluded sequences that were physically derived from a non-PCV-2 source. Merial argues that such a manufacturing requirement has no place in a proper analysis of this claim, and is inconsistent with the district court's otherwise correct claim construction. We agree. For purposes of our review of the district court's opinion, we focus our analysis on the term "specific to" in claim 32, since it appears that this term is the hook for the requirement that the sequence be unique to and derived from PCV-2.

As Intervet explains, the term "specific to" is a specialized term of art in immunology that typically refers to

one structure's proclivity for binding to another structure. For example, antibodies will attack a viral antigen if paratopes of those antibodies are "specific to" an epitope in the viral antigen. The specialized definition of this term does not make sense in the context of claim 32, however, because the claimed epitope is not described as binding to porcine circoviruses; it is described as located within a porcine circovirus. The epitope is thus bound by antibodies that are "specific to" PCV-2. In light of the patent description and a general understanding of the relevant art, the claim would be understood by one of skill in the art to be using the term "specific to" in a colloquial or non-technical sense. *Cf. Intervet, Inc. v. Merial Ltd.*, No. 1:06-cv-00658 (D.D.C. Nov. 28, 2007) (claim construction order at 21). As construed, a nucleotide sequence encoding an epitope that is specific to PCV-2 and not specific to PCV-1, as that term is used in claim 32, is a nucleotide sequence that encodes part of a polypeptide sequence of PCV-2, but not part of a polypeptide sequence of PCV-1. More specifically, it encodes at least one epitope found on the PCV-2 virus, but not found on the PCV-1 virus.

The district court found that Intervet's vaccine could not have contained a sequence encoding an epitope specific to PCV-2 because the sequence was derived from a non-PCV-2 source. This analysis may be mooted by our reversal of the district court's claim construction of "PCV-2", since it is no longer clear that the source of the sequence in Intervet's product is not PCV-2. Nevertheless, to the extent that the district court's application of its claim construction requires that the encoded epitope be unique to PCV-2 among all possible antigens, it is erroneous. If the term "specific to PCV-2" meant that the epitope must be found only on PCV-2 and no other antigen, then the subsequent limitation "and not specific to PCV-

1" would be redundant. Thus an infringing epitope may be common to PCV-2 and some other antigen, as long as it is not also common to PCV-1. Whether one isolates the sequence directly from a PCV-2 virus or engineers a sequence obtained from another source such that it encodes a PCV-2 epitope makes no difference to the proper application of the district court's otherwise correct claim construction.

Accordingly, we reverse the district court's claim constructions of the terms "porcine circovirus type II" and "ORFs 1-13," clarify the proper interpretation of the construction of the term "specific to PCV-2 and not specific to PCV-1," and remand the question of infringement for a determination consistent with the claim constructions articulated herein.

Doctrine of Equivalents

The district court found that prosecution history estoppel precluded Merial from invoking the doctrine of equivalents. Merial was thus estopped from arguing that the accused PCV strain was equivalent to the claimed "porcine circovirus type II," as that term was construed by the district court.[5] The district court erred, however, in applying controlling Federal Circuit and Supreme Court law to the prosecution history of the '601 patent. As a result, the scope of the district court's bar on Merial's ability to invoke the doctrine of equivalents was overly broad.

[5] Because we are reversing the judgment of literal infringement, it may not be necessary for the district court to reach the doctrine of equivalents claim, but we are addressing the issue in the event that the district court on remand finds it necessary to decide.

Whether prosecution history estoppel applies to a particular argument, and thus whether the doctrine of equivalents is available for a particular claim limitation, is a question of law. *Bai v. L & L Wings, Inc.*, 160 F.3d 1350, 1354 (Fed. Cir. 1998); *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1460 (Fed. Cir. 1998) (en banc). Where an amendment narrows the scope of the claims, and that amendment is adopted for a substantial reason related to patentability, the amendment gives rise to a presumption of surrender for all equivalents that reside in "the territory between the original claim and the amended claim." *Festo Corp. v Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 740 (2002) (*Festo VIII*). This presumption can be overcome by showing that "at the time of the amendment one skilled in the art could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent." *Id.* at 741. One way to make this showing is to demonstrate that "the rationale underlying the narrowing amendment bore no more than a tangential relation to the equivalent in question." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1368 (Fed. Cir. 2003) (en banc) (*Festo IX*). Although there is no hard-and-fast test for what is and what is not a tangential relation, it is clear that an amendment made to avoid prior art that contains the equivalent in question is not tangential. *See Pioneer Magnetics, Inc. v. Micro Linear Corp.*, 330 F.3d 1352, 1357 (Fed. Cir. 2003).

The applicability of prosecution history estoppel does not completely bar the benefit of the doctrine of equivalents from all litigation related to the amended claim. *See Festo VIII*, 535 U.S. at 737-38 ("There is no reason why a narrowing amendment should be deemed to relinquish equivalents . . . beyond a fair interpretation of what was surrendered.") The scope of the estoppel must fit the

nature of the narrowing amendment. A district court must look to the specifics of the amendment and the rejection that provoked the amendment to determine whether estoppel precludes the particular doctrine of equivalents argument being made.

Merial's independent claim 9 as originally drafted read, "9. A vector comprising an isolated DNA molecule comprising a sequence selected from the group consisting of ORFs 1-13." The examiner rejected this claim, noting that for purposes of the rejection "[t]he ORFs are assumed to be derived from porcine circovirus, but as written, the claims could encompass ORFs from any organism." The claim was then rejected in view of ORFs from PK/15. The inventors disagreed that these ORFs could be derived from any other organism, and argued that the specification defined ORFs 1-13 based on the limits of the ORFs in the PCV-2 genome. Nevertheless, the claim was amended to add the limitation that the ORFs were "of porcine circovirus type II". The examiner then allowed the claim.

We agree with the district court that this amendment was a narrowing amendment, despite Merial's arguments that it was merely clarifying. As noted in the patent specification, four of the thirteen claimed ORFs are present in the "type I" circovirus. The original claim only required that a vector comprise a nucleotide sequence comprising one of the thirteen ORFs. Thus, the claim as originally written read on ORFs of PCV-1, and was properly rejected over PK/15. We therefore also agree with the district court that the amendment was substantially related to patentability.

The amendment thus raises a presumption of surrender for all equivalents that reside in the territory between the identified ORFs of PCV-2 and ORFs of PCV-1, as well

as corresponding ORFs, if any, for any non-porcine organism. Merial is thus estopped from arguing that ORFs of pathogenic circoviruses found in other organisms are equivalent to ORFs of PCV-2. It is also estopped from arguing that ORFs of a pathogenic strain of PCV-1 are equivalent to ORFs of PCV-2, despite the strain having strong homology with PK/15 and weak homology with the representative strains disclosed in the patent. Merial is not, however, estopped from arguing that a pathogenic porcine viral sequence with over 99% nucleotide homology with one of the five representative strains is equivalent to that strain.[6] Such a draconian preclusion would be beyond a fair interpretation of what was surrendered. *Cf. Festo VIII*, 535 U.S. at 737-38. The rationale for the amendment was to narrow the claimed universe of ORFs down to those of PCV-2, and bore only a tangential relation to the question of which DNA sequences are and are not properly characterized as PCV-2. *Cf. Festo IX*, 344 F.3d at 1369.

The district court thus erred in finding that prosecution history estoppel precluded Merial from arguing that the accused product is equivalent to one of the exemplary embodiments of the asserted claim. The district court is thus instructed on remand to compare the accused product with the claims as construed herein for a determination of infringement literally or pursuant to the doctrine of equivalents, if applicable.

---

[6] Merial is thus not estopped from arguing that such a sequence would infringe even though it did not meet the exact homology limitations required for literal infringement of the claims as construed by this court.

CONCLUSION

The district court erred in construing the disputed claims of the patent in suit and in barring the doctrine of equivalents from its infringement analysis. Accordingly, we reverse the district court's claim construction, vacate the entry of summary judgment of noninfringement, and remand to the district court with instructions to determine, consistent with the analysis in this opinion, whether the accused product infringes the asserted claims of the '601 patent.

REVERSED-IN-PART, VACATED-IN-PART, AND REMANDED

United States Court of Appeals for the Federal Circuit

INTERVET INC.,
Plaintiff-Appellee,

v.

MERIAL LIMITED AND MERIAL SAS,
Defendants-Appellants.

2009-1568

Appeal from the United States District Court for the District of Columbia in case no. 06-CV-0658, Judge Henry H. Kennedy, Jr.

DYK, *Circuit Judge*, concurring-in-part and dissenting-in-part.

I agree with the majority's construction of claim 32 of U.S. Patent No. 6,368,601 ("the '601 patent"), but as discussed below, I disagree with its construction of claim 9. I write separately primarily to make clear that in construing the claims, we are not deciding that the claims as construed are limited to patentable subject matter. As we noted in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc), we do not take validity into account in construing claims, unless "the court concludes, after applying all the available tools of claim construction, that the claim is still ambiguous." *Id.* at 1327 (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 911 (Fed.

Cir. 2004) (quotation marks omitted)). That is not the case here.

At least claim 32 of the '601 patent raises substantial issues of patentable subject matter under 35 U.S.C. § 101. That claim is not limited to the use of a particular isolated DNA molecule in a vaccine or other application. Rather, it broadly encompasses "[a]n *isolated DNA molecule* comprising a nucleotide sequence encoding an epitope which is specific to PCV-2 and not specific to PCV-1." '601 patent col.28 ll.40-42 (emphasis added). Neither the district court nor the parties provided a precise definition of "isolated" DNA. In order to analyze the DNA or use it for applications (for example, the production of vaccines), DNA must be extracted from the cell of the living organism and separated from other cell components, such as RNA, protein, lipids, or in the case of plasmid DNA isolation, from chromosomal DNA. *See generally*, Peter B. Kaufman et al., *Handbook of Molecular and Cellular Methods in Biology and Medicine* 1-26 (1995). DNA "isolation" applies generally to the process of extracting DNA from a cell for purposes of genetic analysis. *See* James D. Watson et al., *Molecular Biology of the Gene* 740 (6th ed. 2008); *see also* Kaufman et al., *supra*, at 1-2. Isolation also encompasses techniques for selective amplification or cloning of such fragments, which allows for a large number of fragments to be available for analysis and sequencing. *See* Watson et al., *supra*, at 746. The '601 patent indicates that the isolation of the genomic DNA of the viral strains was performed by a method well known in the art. *See* '601 patent col.10 l.5-col.11 l.43.

The majority interprets "PCV-2" to mean "a pathogenic pig virus having a circular genome that is at about 96% or more homologous with the four sequences disclosed in the present specification, and about 76% or less homologous with the PK/15 sequence," Majority Op. at 9,

reversing the district court's construction limiting PCV-2 to the five viral strains specifically disclosed in the '601 patent. Additionally, the majority construes "specific to PCV-2 and not specific to PCV-1" to read on molecules that contain sequences that encode epitopes[1] common to PCV-1 and PCV-2, as long as the molecule contains at least one sequence that encodes an epitope unique to PCV-2. *Id.* at 11-12. Patent claim 32 reads on an isolated DNA molecule that comprises a nucleotide sequence that encodes an epitope unique to PCV-2, which is defined with respect to its homology with the known PCV-1 virus. Thus, under the majority's claim construction, claim 32 covers DNA sequences that were not in fact isolated by the inventor and are distinct from the five isolated strains disclosed in the '601 patent.

The question is whether the isolated DNA molecule, separate from any applications associated with the isolated nucleotide sequence (for example, the production of a vaccine) is patentable subject matter. Neither the Supreme Court nor this court has directly decided the issue of the patentability of isolated DNA molecules. Although we have upheld the validity of several gene patents, *see, e.g.*, *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995); *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993); *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.3d 1200 (Fed. Cir. 1991), none of our cases directly addresses the question of whether such patents encompass patentable subject matter under 35 U.S.C. § 101. Although the U.S. Patent and Trademark Office ("PTO") believes that at least some of these patents satisfy section 101, *see* Utility Examina-

[1] An epitope is an immunodominant region of a protein, meaning it is the part of an antigen that is recognized by antibodies of the immune system.

tion Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001),[2] thus far the question has evaded judicial review.

I think that such patents do in fact raise serious questions of patentable subject matter. The Supreme Court's recent decision in *Bilski v. Kappos* has reaffirmed that "laws of nature, physical phenomena, and abstract ideas" are not patentable. No. 08-964, slip op. at 5 (U.S. June 28, 2010) (quoting *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980)); *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948). Just as the patentability of abstract ideas would preempt others from using ideas that are in the public domain, *see Bilski*, slip op. at 13, so too would allowing the patenting of naturally occurring substances preempt the use by others of substances that should be freely available to the public. Thus, "a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity." *Chakrabarty*, 447 U.S. at 309. These aspects are properly conceptualized as representing a public domain, "free to

---

[2] In response to comments urging the PTO not to issue patents for genes on the ground that genes are products of nature, the PTO remarked:

> An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally occurring compound.

66 Fed. Reg. at 1093.

all men and reserved exclusively to none." *Id.* (quoting *Funk Bros.*, 333 U.S. at 130) (quotation mark omitted).

In *Funk Brothers*, the Court considered the patentability of a mixture of several naturally-occurring species of bacteria. 333 U.S. at 128-31. The patented product was a mixture of bacteria used in agricultural processes, enabling plants to draw nitrogen from the air and convert it for usage. The inventor discovered that certain strains of the bacteria were effective in combination with one another, and contrary to existing assumptions, did not exert mutually inhibitive effects on each other. The Court held that the invention was not patentable subject matter. *Id.* at 131. The inventor "did not create a state of inhibition or of non-inhibition in the bacteria. Their qualities are the work of nature. Those qualities are of course not patentable." *Id.* at 130. The Court furthermore noted:

> The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none. He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end.

Id.

In *Chakrabarty*, the Court considered whether a human-made microorganism is patentable subject matter under section 101. 447 U.S. at 305. The microorganism in question was a bacterium that had been genetically engineered to break down crude oil. In concluding that the man-made bacteria was patentable, the Court ob-

served that the claim "is not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter." *Id.* at 309. The Court went on to distinguish *Funk Brothers* on the ground that the *Chakrabarty* bacterium possessed "*markedly different characteristics from any found in nature*. . . . His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under § 101." *Id.* at 310 (emphasis added).

Thus, it appears that in order for a product of nature to satisfy section 101, it must be qualitatively different from the product occurring in nature, with "markedly different characteristics from any found in nature." It is far from clear that an "isolated" DNA sequence is qualitatively different from the product occurring in nature such that it would pass the test laid out in *Funk Brothers* and *Chakrabarty*. The mere fact that such a DNA molecule does not occur in isolated form in nature does not, by itself, answer the question. It would be difficult to argue, for instance, that one could patent the leaves of a plant merely because the leaves do not occur in nature in their isolated form.

Finally, I disagree with the majority with respect to its construction of "ORFs 1-13" in claim 9.[3] Merial argues, and the majority appears to accept, the proposition that one of ordinary skill in the art would read the phrase "ORFs 1-13" to read on any translatable length of DNA between a start and stop codon in the PCV-2 sequence that could encode for a protein greater than twenty amino

[3] An Open Reading Frame ("ORF") is a region or length of DNA that contains a sequence of nucleotides that contains the instructions for making proteins. All ORFs begin and end with a set of three nucleotides known respectively as a start and stop codon.

acids in size. In contrast, the district court concluded that the plain language of the claims indicated that ORFs 1-13 were limited to the ORFs in the disclosed isolates.[4]

I agree with the district court that the phrase must be limited to the specific DNA sequences defined as ORFs 1-13 in the '601 patent based on the intrinsic evidence. The majority holds that the district court's construction is improperly narrow in scope because "limiting the construction of the term to the exact ORF sequences of SEQ ID 4 would even exclude from the claimed ORFs two of the four sequenced strains of PCV-2." Majority Op. at 10. I disagree. The specification appears to specifically define "ORFs 1-13" to include the ORFs from all four of the

[4] It is unclear whether the district court's claim construction limited "ORFs 1-13" to the relevant ORFs in Imp. 1010, or whether the phrase also encompasses ORFs 1-13 of the other isolates disclosed in the patent, namely, Imp. 1011-48121, Imp. 1011-48284, and Imp. 999. The court's infringement determination is also unclear. *See Intervet, Inc. v. Merial Ltd.*, 643 F. Supp. 2d 97, 103 (D.D.C. 2009) ("Example 13, however, also states that the positions of the start and end of each ORF refer to the sequence presented in figure 4. Figure 4 contains the precise DNA sequence of one of the five listed strains and thus Example 13, while it does not include the specific DNA sequence of each ORF, refers to a figure from which those specific DNA sequences can be determined. Given this, the Court declines to read the language 'specific DNA sequence' out of its claim construction, and therefore concludes that Intervet's vaccine does not contain one of ORFs 1-13.").

sequenced strains, not just Imp. 1010,[5] represented by SEQ ID 4. The specification provides:

> It was possible to detect 13 open reading frames (or ORFs) of a size greater than 20 amino acids on this sequence (circular genome). *These 13 ORFs are the following*:

'601 patent col.13 ll.33-34 (emphasis added). The specification then proceeds to detail the ORF sizes and stop and start codons for the Imp. 1010 isolate in table form, and describes the stop and start codons for the other three isolates by reference to Imp. 1010:

> The positions of the start and end of each ORF refer to the sequence presented in FIG. No. 4 (SEQ ID No. 4), of the genome of strain 1010. The limits of ORFs 1 to 13 are identical for strain 999. They are also identical for strains 1011-48121 and 1011-48285, except for the ORFs 3 and 13:
>
> ORF3 1432-1549, sense, 108 nt, 35aa
>
> ORF1,3 314-1377, antisense, 705 nt, 234 aa.

Id. col.13 ll.53-61. Thus, "ORFs 1-13" is properly read to include the relevant ORFs on all of the disclosed isolates, because a description of those ORFs follows the assertion that "[t]hese 13 ORFs are the following." *Id.* col.13 ll.33-34. Because the patentee acted as his "own lexicographer and clearly set forth a definition of the disputed claim term," *Edward Lifesciences LLC v. Cook Inc.*, 582 F.3d 1322, 1329 (Fed. Cir. 2009), the definition in the specification controls, *see Phillips*, 415 F.3d at 1321. In my view,

---

[5] The "Imp." designation, an abbreviation for "imported," is a tracking number assigned by the inventors to their pig tissue samples and to any virus they isolated from that tissue.

claim 9 is not literally infringed, and I would also hold that it is not infringed under the doctrine of equivalents.