Federal Circuit affirms invalidity of functional claims to antibody genus for lack of written description in *Abbvie v. Janssen*

In *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, a Federal Circuit panel majority affirmed a jury verdict of invalidity of Abbvie's asserted patent claims for lack of written description of the claimed subject matter, functionally-defined genera of anti-interleukin-12 antibodies.[1] Abbvie had asserted infringement by Janssen's Stelara® (ustekinumab) antibody product (indicated for the treatment of psoriasis). As detailed below, the majority found that substantial evidence supported the finding that the corresponding patent specifications did not disclose species sufficiently representative of the claimed genera and that Abbvie had not established a structure-function correlation for the claimed antibodies.[2] The Federal Circuit also reviewed various rulings by the district court.[3] This Bulletin focuses on the written description issue.

Facts

Abbvie's U.S. Patent Nos. 6,914,128 and 7,504,485 relate to "fully human antibodies that bind to and neutralize the activity of human interleukin 12 ('IL-12')." IL-12 is a naturally occurring signalling protein. An excess can cause psoriasis and rheumatoid arthritis.[4]

Antibodies are naturally occurring proteins that bind with specificity to another substance, or antigen. A single antibody consists of a pair of identical, longer ("heavy") amino acid chains and a pair of identical, shorter ("light") amino acid chains. Each chain comprises two regions or sections, one constant and one variable. Each variable region has three subregions called complementarity determining regions ("CDRs"). The CDRs bind to the antigen. There are seven families of heavy chain variable regions, designated V_H1 to V_H7, and two classes of light chain variable regions, designated Kappa (κ) and Lambda (λ).[5]

Fully human antibodies to human antigens such as IL-12 do not occur naturally but possess desirable characteristics.[6] At the time of filing, the person of ordinary skill in the art knew generally how to develop and prepare genetically engineered, fully human antibodies that recognize a specific antigen of choice.[7]

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[1] *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, Nos. 2013-1338 and 2013-1346, 2014 U.S. App. LEXIS 12372 (July 1, 2014).
[2] *Id.* at *38-*39. The concurrence agreed that the finding of invalidity should be affirmed but on the grounds of obviousness. It would not have reached the written description issue. *See id.* at *51-*52.
[3] Abbvie appealed rulings on evidence, jury instructions, and whether collateral estoppel (arising from the appeal of a USPTO interference decision to the district court) should have applied. *See id.* at *4.
[4] *See AbbVie*, 2014 U.S. App. LEXIS 12372, at *6.
[5] *See id.* at *5-*6.
[6] *See id.* at *6-*7.
[7] *See id.* at *7.

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Abbvie developed a group of related, fully human anti-IL-12 antibodies that bind to and neutralize the activity of IL-12.[8] The '128 and '485 patents, which have the same written description and claim priority to the same provisional application, have claims that recite genera that encompass those antibodies.[9] Claim 29 of the '128 patent, representative of the asserted claims, reads as follows:

> 29. A neutralizing isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a k_{off} rate constant of $1x10^{-2}$ s^{-1} or less, as determined by surface plasmon resonance.[10]

The claim term k_{off} refers to the rate at which an antibody and antigen dissociate after binding and is a measure of the antibody's affinity for the antigen. A lower k_{off} indicates a stronger affinity.[11] The inventors prepared anti-IL-12 antibodies that had k_{off} values ranging from about 0.1 s^{-1} to as low as about $1x10^{-5}$ s^{-1}.[12] Claim 29 thus encompasses a genus of antibodies the k_{off} of which ranges over at least about four orders of magnitude.

The patent specifications disclosed anti-IL-12 antibodies that were at least 90% similar to each other in amino acid sequence, had identical CDR lengths, had the epitope binding site on the bottom, and had V_H3 heavy chains and lambda light chains.[13] Although the district court found that the accused antibody (Stelara®) met the claims' functional limitations,[14] that antibody had only 50% sequence similarity to the species that the patents disclosed, had a different CDR length, had an epitope binding site on the side, not the bottom, and had V_H5 heavy chains and kappa light chains.[15]

Federal Circuit's Reasoning with Respect to Written Description

The majority set forth the law of written description generally and as it applies to generic and functional claims. The written description requirement constrains the claiming of subject matter that has not been invented.[16] Whether a specification supports a generic claim depends on several factors, "including 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."[17] Further, "[w]hen a patent claims a genus using functional language to define a desired result, the specification must demonstrate that the applicant has made a generic invention that achieves the claimed result and do so by showing that the applicant has invented species sufficient to support a claim to the

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[8] *See id.* at *7-*8.
[9] *See id.* at *8-*10.
[10] *See id.* at *9, '128 patent at col. 386, ll. 55-59, and Certificate of Correction (June 13, 2006) at 1.
[11] *See AbbVie*, 2014 U.S. App. LEXIS 12372, at *6.
[12] '128 patent at col. 32, ll. 56-57.
[13] *See AbbVie*, 2014 U.S. App. LEXIS 12372, at *8, *14.
[14] *See id.* at *12.
[15] *See id.* at *14 and *34.
[16] *See id.* at *29.
[17] *Id.* at *31 (internal quotations omitted).

functionally-defined genus."[18] The specification must disclose either a representative number of species within the genus or structural features that the genus members share so that the person of ordinary skill in the art "can visualize or recognize the members of the genus."[19]

Abbvie conceded at trial that the patents do not disclose structural features common to the species of the claimed genus.[20] Further, the majority concluded that "ample evidence" supported the conclusion that the disclosed species were very similar to one another and did not represent the broad, claimed genus. All of the disclosed antibodies were derived from the same lead antibody (designated "Joe-9"), had V_H3 heavy chains and lambda light chains, and shared at least 90% sequence similarity in the variable regions. Two hundred of the disclosed antibodies differed from a single, lead antibody by only one amino acid. The patents did not describe an example of, or the possibility of, a fully human anti-IL-12 antibody with heavy and light chains other than V_H3 and lambda.[21]

Yet the claimed genus encompasses the Stelara® antibody despite the considerable structural differences between the disclosed antibodies and the Stelara® antibody, enumerated above.[22] Besides having different heavy and light chains, the difference in sequence was more than enough to potentially result in different antigen binding specificity, "thus illustrating the significant structural differences between Stelara and the Joe-9 antibodies and the unpredictability of the field of invention."[23] Thus, the patents' claims encompassed but failed to describe a species representative of antibodies that are structurally similar to the Stelara® antibody. Further, there was no evidence that the person of ordinary skill in the art "could make predictable changes to the described antibodies to arrive at other antibodies such as Stelara."[24]

Abbvie's attempt to exclude structure from the analysis and instead to rely on the functional k_{off} limitation failed because Abbvie failed to demonstrate an established correlation between antibody structure and antibody function (binding to IL-12). Abbvie itself used a trial and error approach to increase IL-12 binding affinity by changing individual amino acids of a lead antibody.[25] It would have been difficult "to predict what would be covered by the functionally claimed genus."[26] The majority therefore concluded that substantial evidence supported the jury verdict of invalidity for lack of written description.[27]

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[18] *Id.* at *31 (internal quotations omitted).
[19] *Id.* at *32 (internal quotations omitted).
[20] *See id.* at *32.
[21] *Id.* at 34.
[22] *See id.* at *34-*35.
[23] *Id.* at *35.
[24] *Id.* at *36.
[25] *See id.* at *36-*38.
[26] *Id.* at *37-38.
[27] *See id.* at *39.

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