UNITED STATES DISTRICT COURT FOR THE DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, vs. F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, AND HOFFMANN-LA ROCHE INC., Defendants.	CIVIL ACTION No.: 05-cv-12237WGY U.S. District Judge William G. Young **ORAL ARGUMENT SCHEDULED FOR JULY 17, 2007**

DEFENDANTS' REPLY IN FURTHER SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT THAT AMGEN IS ESTOPPED FROM ASSERTING INFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS FOR THE ASSERTED CLAIMS OF THE '933 AND '422 PATENTS

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

I. INTRODUCTION

On July 3, 2007, Defendants' (hereinafter "Roche") filed a summary judgment motion requesting that this Court bar Amgen from asserting the doctrine of equivalents for certain limitations contained in Amgen's asserted patent claims in U.S. Patent Nos. 5,547,933 ("the '933 patent") and 5,955,422 ("the '422 patent") (DI 620, 621 and 622). On July 13, 2007, Amgen filed its opposition papers with this Court (DI 716 and 718).[1] Roche submits this Reply to rebut mischaracterizations and misconceptions created by Amgen's submissions.

II. The '933 patent

Roche's summary judgment submissions lay out the simple fact that during the long and tortured prosecution of the '933 patent claims, Amgen significantly cancelled, amended and made statements regarding its claims that, when reasonably read, can lead to only one conclusion, *i.e.*, the asserted product claims of the '933 patent were issued as a result of a number of narrowing amendments. For example, while the pending claims were once directed to polypeptides that had "part or all of the primary structural conformation" of human erythropoietin, or polypeptides that were "sufficiently duplicative" of the structure of human erythropoietin, the Patent Office rejected these types of claims based on their lack of support from the specification. Amgen wanted broad claims to cover EPO-like polypeptides that did not require the exact amino acid sequence of human erythropoietin. However, Amgen had to cancel these broad claims in favor of narrower ones where the polypeptides are defined specifically as

[1] For the purpose of this Reply, papers submitted including Roche's Memorandum In Support of its Summary Judgment Motion (Docket No. 621), Roche's Rule 56.1 Statement in Support of its Motion (Docket No. 622), Amgen's Opposition (Docket No. 716), and Amgen's Response to Roche's Rule 56.1 Statement (Docket No. 718) will be referred to as (a) Def. Br., (b) Def. Facts, (c) Pl. Op. Br., and (d) Pl. Facts, respectively.

human erythropoietin expressed by the claimed process. Thus, the '933 patent claims glycoprotein products "expressed" by a mammalian cell as a result of placing an "exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin" into that mammalian cell. Those claimed expression products cannot be anything other than human EPO, and do not include EPO-like products.

In response Roche, Amgen attempts to blur the prosecution estoppel issues. Roche will address the following allegations made by Amgen:

- Roche's motion is "unripe"[2]
- Roche's motion "ignores the Court's claim construction"[3]
- Roche distorts and mischaracterizes the '933 patent prosecution[4]
- Roche fails to identify any feature of its accused product that falls outside the literal scope of the asserted claims[5]

In an attempt to have only the summary judgment motions decided which it feels are important, Amgen alleges that this motion is not ripe. That Amgen would contend that Roche fails to identify any feature falling outside the literal scope of the claims is absurd. Roche submitted numerous expert reports and filed extensive briefs and expert declarations outlining its non-infringement position. Most recently, Roche filed a proposed Surreply in further support of

[2] Pl. Op. Br. at p.2 (Docket No. 716).

[3] *Id.*

[4] *Id.*

[5] *Id.* at p.3.

its Opposition to Amgen's Motion for Summary Judgment of Infringement.[6] Those papers all demonstrate that CERA is a new chemical entity having erythropoietic activity that does not have the amino acid sequence of human EPO and does not meet the limitations of the asserted claims. CERA is chemically synthesized and *inter alia,* does not possess the sequence elements required by the Court's construction of "human erythropoietin." Moreover, CERA is not the product of expression of a mammalian cell claimed in the '933 patent. That said, if the Court finds that CERA does not literally infringe Amgen's claims, which it properly should, Amgen will surely attempt to broaden the asserted claims' scope by asserting infringement under the doctrine of equivalents. Therefore, this motion is ripe and should be decided now.

Roche does not "ignore" the Court's claim construction as Amgen alleges, but points out that the doctrine of equivalents should not be allowed for products made using anything other than "a DNA sequence encoding human erythropoietin" that are products "of the expression in a mammalian host cell of an exogenous DNA sequence." CERA, the product of a chemical reaction, cannot be the expression product of a mammalian cell.

Amgen seeks to distort the Court's July 3, 2007 Markman decision to suggest that the product of expression as claimed in the '933 patent contemplates the addition of other molecules outside of what is produced by the cell. However, this is untrue. The Court found that the expression product "means that the glycoprotein was produced in a cell and recovered from the cell culture."[7] Because the '933 claims are product-by-process claims, it is the cellular process

[6] Defendants' proposed Surreply in Support of Its Opposition to Amgen's Motion for Summary Judgment of Infringement of '422 Claim 1, '933 Claim 3, and '698 Claim 6 (Docket No. 721).

[7] Markman Order at p. 32 (Docket No. 613).

that defines the claimed structure.[8] The CERA structure does not satisfy that requirement under the Court's construction; the structure of CERA is one that cannot be produced in a cell and isolated from a cell. Amgen argues that nothing in claim 3 excludes the presence or absence of additional structures like peg to the claimed non-naturally occurring glycoprotein product.[9] Yet, the Court's claim construction clarifying the meaning of "expression" does precisely that. The synthetic amino acid residues found in CERA are not and indeed cannot be produced, or recovered, from the cell culture.

A fair reading of the prosecution history of the '933 patent (which includes, *inter alia,* the '874 and 178 applications)[10], examples of which are included in Def. Br. at pp. 4-9. and Def. Facts at ¶¶ 6-24, clearly demonstrates the obstacles that Amgen encountered in obtaining its '933 asserted patent claims, and the areas of claim scope Amgen was not allowed and relented on. Amgen can not seriously deny that the '933 patent prosecution history explicitly limits the scope of its claims to products made by a specific process and that those claims do not cover EPO-like products.

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[8] *Tropix v. Lumigen, Inc.*, 851 F. Supp. 25 (D. Mass. 1994).

[9] Pl. Op. Br. at p.13 (Docket No. 716).

[10] It appears that the only application Amgen would like the Court to consider is the '178 application. In Pl. Op. Br. at p. 3, in attempting to separate the '874 application from this Court's consideration Amgen states: "The truth [stating Roche is untruthful], however, is quite different. In actual fact, the '178 application from which the '933 patent issued ***always*** included claims to 'polypeptide products of the expression of a DNA sequence encoding erythropoietin.'" Amgen conveniently left out the original claims filed in the prior application, part of the '933 patent prosecution history, where clearly that limitation does not appear.

Inexplicably, Amgen argues that the asserted '933 patent claims are not product-by-process claims.[11] The truth is that Amgen could not distinguish its claim scope from naturally occurring human EPO until it explicitly stated that "all product claims in the subject application [the '178 application] are now product by process claims ...,"[12] and "it is in fact 'evident that the process of production defines the product."[13]

Amgen complains that, even if Roche is correct that prosecution history estoppel applies to the '933 patent claims, that Roche seeks to import a limitation into that claim language that does not exists.[14] Specifically, Amgen states that Roche is importing the limitation that the claimed product must be the direct product of the expression of a mammalian host cell of an exogenous DNA sequence.[15] Amgen misstates Roche's position. CERA is not a product that can be expressed by a mammalian cell at **all**. CERA is neither the direct **nor** the indirect product of the expression of a mammalian cell. It is a completely different product than the expression product claimed by the '933 claims, possessing substantially different properties. Moreover, if Amgen improperly asserts that CERA is an equivalent to the product "of the expression of a mammalian host cell of an exogenous DNA sequence" encoding human EPO, in that this

[11] Pl. Op. Br. at pp. 11-12 (Docket No. 716).

[12] Def. Br. at p. 6 (Docket No. 621).

[13] *Id*. at p. 8 (Docket No. 621).

[14] Amgen has not made any attempt to rebut the presumption of prosecution history estoppel. Therefore, if the Court finds that the presumption of prosecution history estoppel attaches to limitations of Amgen's asserted claims, in that Amgen has offered no explanation to rebut that presumption, Amgen should be precluded from doing so.

[15] Pl. Op. Br. at pp. 12-13 (Docket No. 716).

limitation was added to narrow the '933 claims during prosecution, Amgen is legally barred from asserting any scope of equivalents.

Amgen asserts that the amendments within the '933 patent application were not narrowing amendments because they merely clarified the "particular biological activities and physical properties" of the defined polypeptides.[16] This is nonsense. It completely ignores the fact that Amgen had to withdraw claims directed to polypeptides "having part or all of the primary ***structural conformation***" of natural erythropoietin and claims directed to polypeptides having a "***primary structural conformation sufficiently duplicative*** of that of a naturally-occurring human erythropoietin."[17] If the Patent Office was merely concerned about the definiteness of particular biological activities, then why were these broad limitations drawn towards structure rejected by the Patent Office and abandoned by Amgen?

Moreover, even assuming Amgen is correct that these amendments were undertaken to define more particularly the "biological" and "physical" properties of the defined properties (they were not), this would still support Roche's motion because this would have constituted a narrowing amendment where the properties of the polypeptide eventually became defined by being the human erythropoietin product of the expression process.

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[16] Pl. Op. Br. at p. 6 (Docket No. 716).

[17] Def. Br. at p. 4 (Docket No. 621); Declaration of Keith E. Toms in Support of Defendants' Motion for Summary Judgment that Amgen is Estopped from Asserting Infringement Under the Doctrine of Equivalents for the Asserted Claims of the '933 and '422 Patents ("Toms Decl."), Ex. 1 at 97, 101, 102 (emphasis added) (Docket No. 623). *See also Mycogen Plant Science, Inc. v. Monsanto Co.*, 261 F.3d 1345, 1349-50 (Fed. Cir. 2001); *Festo Corp. v Shohetsu Kinzoku Kogyo Kabushiki Co.*, 05-1492, 2007 U.S. App. LEXIS 15942, *1 (Fed. Cir. Jul. 5, 2007) (estoppel where claims were cancelled and new claims added).

Amgen's "other arguments" completely miss the point. Simply stated, the asserted claims of the '933 patent only cover a glycoprotein product "expressed" by a mammalian cell as a result of placing an "exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin" into that mammalian cell. EPO analogs, fragments or synthetic peptides are clearly outside the scope of Lin's alleged invention as evidenced by the prosecution history.[18] In short, any product which is not the product of the expression of a mammalian cell should not be covered by the claims. During prosecution of claims directed to analogs, fragments or synthetic peptides, Amgen was forced to limit the scope of its claims for patentability purposes. Any attempt by Amgen to cover any product that is not the product of the expression of a mammalian cell, like CERA, should not be allowed as a matter of law.

III. The '422 Patent

As to the '422 patent, Amgen practically concedes that there was a narrowing amendment during its prosecution. As pointed out in Roche's moving brief, Amgen was forced to add the source limitation "purified from mammalian cells grown in culture" as a way of overcoming the prior art, which disclosed natural human erythropoietin. While Amgen lamely attempts to counter Roche's position by pointing out that the original claim already had the limitation to a "recombinant" erythropoietin, it utterly ignores the irrefutable evidence of the file histories. The Patent Office actually determined that the term "recombinant" was indefinite because it was

[18] Def. Br. at pp. 4-10 (Docket No. 621).

unclear how it would "modify the physical erythropoietin composition."[19] As a result, Amgen amended the claim in an effort to narrow the claim to overcome the Patent Office's rejection.[20]

Moreover, Amgen complains that Roche "conflates" EPO and its product (pharmaceutical composition) claim. Pl. Op. Br. at pp. 18-19. As stated in Def. Br. (at p. 14-15), the erythropoietin contained in the pharmaceutical composition of claim 1 of the '422 patent "is purified from mammalian cells grown in culture." *Id*. at p. 14. Therefore, Amgen should be estopped from asserting infringement under the doctrine of equivalents for all products containing erythropoietic agents **not** purified from mammalian cells grown in culture. CERA is such a molecule.

IV. CONCLUSION

Based upon the foregoing Reply and Roche's moving papers, Roche respectfully requests that its Motion For Summary Judgment That Amgen is Estopped From Asserting Infringement Under The Doctrine of Equivalents of the Asserted Claims of the '933 and '422 Patent be granted.

[19] Toms Decl., Ex. 12 at 2 (Docket No. 623).

[20] As pointed out in Roche's opening brief, Roche does not agree that the source limitation in the '422 patent claim 1 imparts structural or functional limits on the human erythopoietin element recited in the claim. Def. Br. at p. 2 n 1 (Docket No. 621). Notwithstanding the legal point that in some circumstances a source limitation may do so "where such limitations are the best means to distinguish a claimed product over prior art." Markman Order at p. 18 (Docket No. 613).

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Respectfully submitted,

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