UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD; ROCHE DIAGNOSTICS GmbH; and HOFFMANN-LA ROCHE INC., Defendants.	CIVIL ACTION No.: 05-CV-12237WGY U.S. District Judge Young

ROCHE'S OPPOSITION TO AMGEN'S BENCH MEMORANDUM FOR FURTHER JURY INSTRUCTION REGARDING INHERENT WRITTEN DESCRIPTION

Amgen's requested instruction regarding "inherent" written description of human EPO (D.I. 1326) will improperly instruct the jury on the relevant legal standard for evaluating the adequacy of Dr. Lin's written description and will also contradict the Federal Circuit's previous findings and Amgen's own express admissions regarding the written description provided by the Lin patent specification. Amgen effectively asks this Court to endorse a baseless inherency argument in an attempt to trump the statutory requirement of §112.

With respect to the Lin specification, the Federal Circuit already has found that "the claimed glycoprotein must have -- at minimum -- all 166 amino acids shown in Figure 6." *Amgen v. HMR/TKT*, 314 F.3d 1313, 1345 (Fed. Cir. 2003). Amgen has admitted that "to subsequently add a description of the later-discovered equivalent — in this case, the fact that the product of example 10 has only, 165 amino acids — would violate the statutory prohibition against adding new matter to the application" because there was no adequate written description.

(D.I. 485-5 - 485-8 at 5 (TRX PCS, AM-ITC 00852567)). Trapped by these findings and admissions, Amgen now seeks to rely on "inherency," for adequate written description of EPO as the 165 amino acid protein isolated from human urine through its proposed jury instruction, which fundamentally misstates the law of inherency.

Inherent disclosure may exist only if it is "the natural result flowing from" the explicit disclosure. *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1379 (Fed. Cir. 2003). The missing descriptive matter must be "necessarily present in the thing described in the reference." *Continental Can Co. v. Monsanto*, 948 F.2d 1264, 1268 (Fed. Cir. 1991); *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1159 (Fed. Cir. 1998) ("the missing descriptive matter must necessarily be present in the parent application's specification."). Inherency "may not be established by probabilities or possibilities." *In re Oelrich*, 666 F.2d 578, 581 (C.C.P.A. 1981) ("The mere fact that a certain thing may result from a given set of circumstances is not sufficient."). Rather, the applicant must show that any absent text is "necessarily comprehended in the description provided." *Hyatt v. Boone*, 146 F.3d 1348, 1354-1355 (Fed. Cir. 1998).

Here, the evidence establishes that Amgen cannot claim that a 165 amino acid sequence is necessarily produced because some mammalian cells covered by the asserted claims express human EPO with the 166 amino acid residues expressly described by the Lin specification. *Amgen v. HMR/TKT*, 287 F.Supp.2d 126, 157 n.14 (D. Mass. 2004).[1] This was plainly admitted by Amgen's expert Dr. Harvey Lodish.[2] In addition, because the construction of claim 1 of the '422 patent allows the human EPO to be taken "from the cells" before secretion as well as from

[1] Only claim 2 of the '868 patent and claim 8 of the '933 patent limits human EPO to the product expressed from CHO cells, which is not necessarily 165 amino acids. The remaining 13 claims asserted by Amgen broadly claim the product of "mammalian cells", "non-human mammalian cells" or "vertebrate cells."

[2] 10/3/07 Trial Tr. at 2317:18-20.

the cell culture medium, *Amgen, Inc. v. F. Hoffmann-La Roche Ltd.*, 494 F. Supp.2d 54, 64 (D. Mass. 2007), the human EPO produced in CHO cells of Example 10 at the very least may have 166 amino acid residues.[3] Thus, the disclosed human EPO is not inherently 165 residues as Amgen now claims. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991)(the "invention is, for purposes of the 'written description' inquiry, ***whatever is now claimed***.") (emphasis in original).

Precedent states that inherency will not support adequate written description where the procedures disclosed in the specification produce the structure expressly disclosed as well as the structure allegedly inherently disclosed. *Chen v. Bouchard*, 347 F.3d 1299, 1305 (Fed. Cir. 2003) (no written description of inherently produced 7,8-cyclopropataxols where specification expressly disclosed 7-a flurotaxol derivatives made by same process). The Lin specification expressly discloses that claimed erythropoietin product is 166 amino acids, not 165 amino acids. The language of the specification is plain on this point: "Figure 6 thus serves to identify the primary structural conformation (amino acid sequence) of mature human EPO as including 166 specified amino acid residues...."[4] Dr. Lodish confirmed the unambiguous nature of this statement when he testified that the primary structure of a protein is the amino acid sequence.[5] Here, even assuming Example 10 of the Lin patent specification inherently produces a product with 165 amino acids under some conditions, Lin expressly described human EPO as 166 amino acids and set forth procedures that will produce a product with 166 amino acids thereby negating any inherency argument.

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[3] Trial Tr. 2315:12-20.

[4] TRX 0001, '933 Patent Col 21 lns. 3-6.

[5] 10/4/07 Trial Tr. at 2402:11-13.

Amgen's proposed instruction also invites legal error by conflating the written description requirement with enablement. The law is clear: adequate written description is a requirement separate and distinct from enablement. *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 921 (Fed. Cir. 2004) ("an invention may be enabled even though it has not been described"). The specification must describe each claim element and "proof of a reduction to practice, absent an adequate written description in the specification of what is reduced to practice, does not serve to describe or identify the invention for purposes of §112, 1." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 969 (Fed. Cir. 2002). That is because the law requires that "adequacy of the written description (i.e., the disclosure) ***is measured from the face of the application***; the requirement is not satisfied if one of ordinary skill in the art must first make the patented invention before he can ascertain the claimed features of that invention." *New Railhead Mfg. LLC v. Vermeer Mfg.*, 298 F.3d 1290, 1295 (Fed. Cir. 2002) (emphasis added).[6] Amgen's proposed instruction, however, improperly asks the jury to consider what one of skill in the art might ascertain regarding the amino acid sequence of the product after making and analyzing the product in 1983-1984. Amgen's position is squarely in conflict with controlling law that requires actual description of each feature that is included as a claim limitation. *Enzo*, 323 F.3d at 969 (A showing of 'possession' is ancillary to the ***statutory mandate*** that '[t]he specification shall contain a written description of the invention,' and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention.")(emphasis in original).

Amgen's proposed jury instruction effectively asks this Court to instruct the jury to

[6] In contrast, the enablement requirement requires that the specification teach one of skill in the art how to make and use the claimed invention as of the date that the patent application was first filed. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999).

disregard overwhelming evidence that shows Dr. Lin did not describe human EPO with the 165 amino acid sequence claimed. The Lin specification admits that the amino acid sequence of EPO isolated from human urine was not known at the time of filing and the specification only provides a partial sequence.[7] Testimony shows that in 1983-1984 no one knew that human EPO may, in some instances, have the 165 amino acid sequence of EPO isolated from human urine.[8] Indeed, Dr. Lin told the public otherwise in his specification, and he clearly did not conceive the 165 amino acid sequence now claimed by Amgen. *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993) ("one cannot describe what one has not conceived"). In fact, documentary evidence shows that Amgen told the FDA in 1986 -- 2 years after the Lin specification was filed -- that the 165 amino acid sequence of its commercial EPO product "reflects new experimental data from ongoing research."[9] Thus, Amgen's proposed instruction is nothing more than an improper attempt to circumvent the evidence elicited at trial demonstrating that there is no adequate written description.

Amgen's proposed instruction is contrary to the established law and will lead the jury to improperly analyze the adequacy of the Dr. Lin's written description. For these reasons, the Court should reject Amgen's requested instruction.

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7 TRX 0001, '933 Patent Col. 8 lns. 41-44 and col. 15 lns. 29-60.

8 Trial Tr. 1230:8-1231:6.

9 TRX 2086, AM-ITC 00065040; *see also* AM-ITC 00065045 ("Correction based on newly acquired data").

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Boston, Massachusetts

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