IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMGEN, INC., Plaintiff, v. F. HOFFMANN-LA ROCHE, LTD, a Swiss Company, ROCHE DIAGNOSTICS GmbH, a German Company and HOFFMANN-LA ROCHE INC., a New Jersey Corporation, Defendants.	Civil Action No. 05-12237 WGY U.S. District Judge Young

SUPPLEMENTAL DIRECTED VERDICT OPPOSITION REGARDING OBVIOUSNESS AND THE OPINIONS OF ROCHE'S EXPERT DR. LOWE RAISED BY AMGEN DURING THE SEPTEMBER 24TH HEARING

I. INTRODUCTION

Defendants Hoffmann-La Roche, Ltd, Roche Diagnostics, GmbH, and Hoffmann-La Roche Inc. ("Roche") submit this supplemental opposition to Plaintiff Amgen Inc.'s ("Amgen") motion for a directed verdict on the issue of obviousness and to specifically address arguments raised by Amgen's counsel at the September 24, 2007 hearing concerning Dr. Lowe's opinions. Amgen's arguments are unavailing for at least the following reasons:

- First, the law of obviousness does not require that the prior art disclose the specific structure of a DNA sequence for purposes of invalidating the asserted claims of the patents-in-suit. The cases Amgen cited by Amgen's counsel were misstated and misapplied. Moreover, here, unlike the claims of Amgen's now expired '008 patent, the asserted claims are directed to proteins, pharmaceutical compositions, and methods of making and using these products.

- Second, to the extent that obviousness of these claims requires chemical structure in the prior art, Roche has submitted substantial evidence that the prior art teaches such structure. Dr. Goldwasser's protein provided the requisite structure that would have allowed one of skill in the art to create a synthetic gene. Moreover, Goldwasser's protein also provided sufficient structure to allow synthesis of DNA probes that could be used to isolate a DNA clone.

- Third, Amgen's position regarding motivation within the prior art is also spurious. Motivation to combine is no longer required after the Supreme Court's decision in *KSR*. Nevertheless, Roche's evidence of motivation is compelling. One need only look at the binding admissions within the background of the patent specification to see that once skilled workers had Goldwasser's protein, they were specifically instructed by the patent background that the preferred and easiest method of cloning a gene would be by sequencing the protein and synthesizing a gene based on that sequence.

- Finally, even assuming that Amgen is correct that the law of obviousness requires a DNA structure for these claims (it is not), Roche presented evidence that Dr. Fritsch, working at Genetics Institute, isolated and expressed the EPO clone in CHO cells before the November 1984 filing date of the patents. Since Amgen has presented no proof on the record that its inventions are entitled to an earlier invention date, Dr. Fritsch's work constitutes invalidating prior art under 35 U.S.C. Sections 102(g) and 103.

II. ARGUMENT

A. The Law of Obviousness

Pursuant to 35 U.S.C. Section 103, a patent may be obtained "if the difference between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time of the invention was made to a person having ordinary skill in the art."

In arguing in favor of a directed verdict on obviousness, Amgen's counsel cited *In re Deuel, 51 F.3d 1552* (Fed. Cir. 1995), *In re Bell*, 991 F.2d 781 (Fed. Cir. 1993) and *Amgen, Inc. v. Chugai Pharmaceutical Co*., 927 F.2d 1200 (Fed. Cir. 1991), as being "spot on" and standing for the proposition that "where the invention that's claimed is a chemical structure like a DNA sequence, it requires that there be in the prior art a DNA sequence that leads one to the claimed sequence." (*See* Trial Tr. 1306:22–1308:18). As demonstrated below, Amgen has thoroughly misstated and misapplied the teaching of these cases which, in fact, fully support Roche's obviousness defense.

Pivotal to the analysis here is the fact that the asserted claims of the patents-in-suit do not recite or require the use of specific DNA sequences. Indeed, claim 1 of the '422 patent makes no mention at all of DNA. The other Amgen patents claim any "DNA encoding human erythropoietin" ('349 patent), any "DNA sequence encoding human erythropoietin" ('933 patent), any "DNA encoding the mature erythropoietin amino acid sequence of FIG. 6" ('698 patent) and any "isolated DNA sequence encoding human erythropoietin" ('868 patent). The specification of Amgen's patents admits that at the time of Dr. Lin's claimed invention, given the amino acid sequence of erythropoietin and the genetic code, one of skill in the art could have routinely made any DNA sequence coding for erythropoietin. (*See, e.g*., col. 3, lines 3-37). It is

not relevant whether one would or would not have been led to a particular EPO DNA sequence such as that found in the human genome.

In addressing the issue of obviousness in *In re Deuel,* the Federal Circuit expressly distinguished between claims to specific DNA sequences encoding a protein (heparin) and claims – such as those at issue here – which cover the use of any DNA sequence encoding the protein. The court reversed the PTO's rejection of claims to the specific DNA sequences on the grounds that the applied prior art references did not "teach or suggest the claimed cDNA molecules." *Deuel*, 51 F.3d at 1560; *see also id*. at 1558-58-9 ("No particular one of these DNAs can be obvious unless there is something in the prior art to lead to the particular DNA and indicate that it should be prepared"; emphasis added). By contrast, the court described co-pending claims that "generally encompass all DNA sequences encoding" the proteins as being "tantamount to the general idea of all genes encoding the protein, all solutions to the problem." *Id.* The court observed that although the prior art only disclosed a partial amino acid sequence, claims to all DNA sequences "might have been obvious from the complete amino acid sequence of the protein, coupled with knowledge of the genetic code":

> Claims 4 and 6 . . . are of a different scope than claims 5 and 7 [to specific DNA sequences]. As is conceded by Deuel, they generically encompass all DNA sequences encoding [the proteins] . . . [and] are thus tantamount to the general idea of all genes encoding the protein, all solutions to the problem. Such an idea might have been obvious from the complete amino acid sequence of the protein, coupled with knowledge of the genetic code, because this information may have enabled a person of ordinary skill in the art to envision the idea of, and, perhaps with the aid of a computer, even identify all members of the claimed genus.

Id. (emphasis added).

As Dr. Lowe testified, given Dr. Goldwasser's EPO, it would have been routine for one of ordinary skill in 1983 to derive the complete EPO protein sequence, and to use the genetic code to obtain the corresponding DNA sequences encoding the protein. (Lowe 177:1–178:22,

206:2–207:11). Accordingly, one of ordinary skill in 1983 would have been able to envision and identify the genus of DNA sequences encoding the EPO protein – i.e., the DNA sequences claimed by Amgen's patents. As the Manual of Patent Examining Procedure explains:

> [I]n the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid [i.e., DNA] sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.

MPEP § 2163.II.A.3.a.ii. (8th ed., rev. 2 2001) (emphasis added); *see also In re Wallach*, 378 F.3d 1330, 1332-34 (Fed. Cir. 2004) ("we see no reason to require a patent applicant to list every possible permutation of the nucleic acid sequences that can encode a particular protein for which the amino acid sequence is disclosed, given the fact that it is, as explained above, a routine matter to convert back and forth between an amino acid sequence and the sequences of the nucleic acid molecules that can encode it"). Thus, as properly applied, *Deuel* works to render the asserted claims – which are to all EPO DNAs, not particular DNAs – obvious.

In re Bell likewise fails to support Amgen's argument. As in *Deuel*, the claims held non-obvious in *Bell* were directed to specific DNA sequences encoding a protein (IGF). The Court made clear that its analysis was based on the fact that the claims were not directed, as they are in Amgen's patents, to the use of any DNA sequence:

> Bell does not claim all of the 10^{36} nucleic acids that might potentially code for IGF. Neither does Bell claim all nucleic acids coding for a protein having the biological activity of IGF. Rather Bell claims only the human nucleic acid sequences coding for IGF.

Bell, 991 F.2d at 784. The Federal Circuit concluded: "Absent anything in the cited prior art suggesting which of the 10^{36} possible sequences . . . corresponds to the IGF gene, the PTO has not met its burden of establishing that the prior art would have suggested the claimed

sequences." *Id*. As in *Deuel*, the claims in *Bell* were held non-obvious because the prior art did not lead one to specific claimed sequences – not because (as Amgen's counsel argues) "there must be in the prior art a composition that is structurally similar to the claimed structure." (Trial Tr. 1307:11-16). Accordingly, Amgen's contention that "it's not that there is a motivation to get to that structure" but that "[t]here must be in the prior art a structure" is simply incorrect. (*See* Trial Tr. 1307:14-16).

Moreover, in *Bell*, in finding the claims non-obvious, the court made much of the fact that cited prior art, which taught a general method for cloning genes, also appeared to "teach away from the claimed invention by emphasizing the importance of unique codons for the amino acids." There is no such "teaching away" in the prior art cited in the instant case.

Amgen's assertion that *Deuel* "survived" *KSR* is based on the Federal Circuit's decision in *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd*., 492 F.3d 1350 (Fed. Cir. 2007). (*See* Trial Tr. 1308:19–1309:2). *Takeda*, however, is inapposite. *Takeda* does not concern itself with whether a particular structure must be in the prior art to invalidate a DNA sequence or sequences. Rather, at issue in *Takeda* was whether a specific new chemical compound would have been obvious to select from "hundreds of millions" of compounds disclosed in the prior art. *Id*. at 1357; *see also id*. at 1360. ("[Defendant's] obviousness argument rested entirely on the court making a preliminary finding that the prior art would have led to the selection of compound b as the lead compound, and [defendant] failed to prove that assertion."). If anything, *Takeda* merely reiterates that one must have a reason to combine prior art references, under the modified teachings of *KSR*. *See id*. at 1356-60. Here, as described in detail below, Roche has presented substantial evidence of a reason to combine Goldwasser's EPO protein with known techniques in the art to generate an EPO clone.

Moreover, despite Amgen's assurances to the contrary, the continued post-*KSR* viability of *Deuel* as applied to specific DNA sequences has indeed been called into question. In *Ex Parte Kubin*, a case more "spot on" than those cited by Amgen, claims to specific DNA sequences were rejected as obvious over the prior art disclosure of methods for isolating a particular protein and methods for isolating cDNA. *See Ex Parte Kubin*, Appeal 2007-0819, Slip Op. at 4 (B.P.A.I. May 31, 2007). Notably, the claims were rejected for obviousness notwithstanding the absence of any structural information in the prior art – no DNA sequence, and no protein sequence. The prior art merely disclosed *methods* for isolating the protein. The applicants argued that: "As in *Deuel*, it is not proper for the [Patent] Office to use the p38 protein . . . together with the [prior art cloning methods] to reject claims drawn to specific sequences." *Id*. The Board of Patent Appeals rejected this argument:

> [T]he Supreme Court recently cast doubt on the viability of *Deuel* to the extent the Federal Circuit rejected an 'obvious to try' test. Under *KSR*, it's now apparent 'obvious to try' may be an appropriate test in more situations than . . . previously contemplated. . . .
>
> This reasoning is applicable here. The "problem" facing those in the art was to isolate NAIL cDNA, and there were a limited number of methodologies available to do so. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. Thus, isolating NAIL cDNA was "the product not of innovation but of ordinary skill and common sense," leading us to conclude NAIL cDNA is not patentable as it would have been obvious to isolate it.

Id. at 8-9.

Lastly, Amgen's reliance on the *Chugai* case is defective for a number of reasons. First, as the Court made clear by its Electronic Order, dated September 18, 2007, Roche is not precluded from arguing the obviousness of the DNA clone based on the *Chugai* decision. Roche did not stand in the shoes of Chugai during that case, and as a matter of law, is not collaterally estopped by that decision.

Second, the claims at issue in *Chugai* were directed to DNA sequences and host cells. In contrast, as stated above, the asserted claims in this case are directed to polypeptides and pharmaceutical compositions, as well as methods for making and using these compositions.[1] In fact, Amgen's insistence of the applicability of the *Chugai* decision only shows that the asserted claims in this case are invalid for obviousness-type double patenting over the now expired DNA and host cells claims of the '008 patent.

Third, the critical date for purposes of prior art of the '008 patent in the *Chugai* decision was 1983. *See Chugai*, 1989 WL 169006 at *39. As detailed below, the critical date in this case is the November 30, 1984 effective filing date of the patents-in-suit. Thus, any findings regarding obviousness in that case are irrelevant here due to, *inter alia*, the advances in the prior art during the intervening time period together with the standard for obviousness under the present law. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007).

Fourth, Amgen's reliance on simultaneous conception and reduction to practice in the *Chugai* case is similarly misplaced because these issues are limited to priority contests involving 35 U.S.C. § 102(g). Goldwasser's protein qualifies as prior art under the combination of Section 102(f) derivation and Section 103 obviousness. As the Federal Circuit has held, "subject matter derived from another not only is itself unpatentable to the party who derived it under § 102(f), but, when combined with other prior art, may make a resulting obvious invention unpatentable ... under a combination of §§ 102(f) and 103." *OddzOn Prods., Inc. v. Just Toys, Inc.*, 122 F.3d

[1] Moreover, in *Chugai*, the Federal Circuit specifically limited its analysis to whether particular cloning techniques were obvious, not whether the EPO DNA sequence itself was obvious:

> We note that both the district court and the parties have focused on the obviousness of a process for making the EPO gene, despite the fact that it is products (genes and host cells) that are claimed in the patent, not processes. We have directed our attention accordingly, and do not consider independently whether the products would have been obvious aside from the alleged obviousness of a method of making them.

927 F.2d at 1207 n.3 (emphasis added).

1396, 1403-04 (Fed. Cir. 1997); *see also Gambro Lundia AB v. Baxter Healthcare Corp*., 110 F.3d 1573, 1576 (Fed. Cir. 1997) (another person need only invent *part* of the invention to qualify under § 102(f)). Prior art pursuant to § 102(f) "does not pertain only to public knowledge, but also applies to private communications between the inventor and another which may never become public." *OddzOn*, 122 F.3d at 1401-2. However, Amgen's faulty legal reasoning regarding conception and reduction to practice contradicts the established precedent of *OddzOn* and its progeny.

B. Goldwasser's Protein Provides Structure

As discussed above, the Federal Circuit in *In re Deuel* and *In re Wallach* has recognized that the existence of proteins within the prior art do provide sufficient structure to make DNA claims obvious. By 1983, routine techniques were available to those of ordinary skill to obtain accurate and complete protein sequence, provided one had access to sufficient amounts of protein. (Lowe 217:23–218:11; TRX 2010). For example, Dr. Lowe testified that in 1980, a paper published in the journal *Science* disclosed a sequencing method "very sensitive in its ability to determine protein sequence." (Lowe 221:2-5; TRX 2018). In 1983, a review article authored by Hunkapiller and Hood discussed the state of the art of protein sequencing, including highly developed techniques for automated "microsequencing". (Lowe 210:1-21, 218:1–219:6; TRX 2010). These papers taught one of ordinary skill that it was possible to obtain the EPO protein sequence using sufficient amounts of purified EPO and "straightforward methods." (Lowe 219:3-6, 177:21-24). Indeed, the Patent Office determined that the EPO protein sequence Amgen scientist Dr. Por Lai obtained by these methods did not constitute an inventive contribution. (Lowe 225:20-24; TRX 2011). Likewise, Dr. Goldwasser testified that if someone in his laboratory had a microsequencer, he could have sequenced EPO. (Goldwasser 531:5-

532:5). However, as Dr. Goldwasser admitted, he was "the only real source in the world for significant amounts of pure EPO," and he only provided it to Amgen. (Goldwasser 526:20-22; *see also* Goldwasser 532:11–535:21, 540:22-23, 544:5–545:5, 546:3-7; Lowe 178:19–179:4; TRX 2035-2037).

Given the sequence derived from Goldwasser's EPO protein, and the standard "codon table" from any biochemistry textbook, one of skill in the art in 1983 would have known to "work backwards" to obtain the corresponding DNA sequences encoding the protein. (Lowe 177:1–178:22, 206:2–207:11). Using these DNA sequences, one of ordinary skill would have known that there were three general methods to obtain an EPO clone, including the "preferred method," the manufacture of a synthetic EPO gene.

C. Roche Presented Substantial Evidence Of Motivation

The Supreme Court's ruling in *KSR* no longer requires that the prior art provide a specific motivation to combine particular references. The Court stated:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp . . . . any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.[2]

KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1742 (2007),

Here however, Roche presented substantial evidence within the prior art of a specific motivation to combine Goldwasser's EPO protein with known techniques in the art to generate an EPO clone. In fact, one need only look to the Background of the patents to elicit this motivation. As the Federal Circuit recently stated "Admissions in the specification regarding

[2] Additionally, for purposes of determining whether it would be obvious to combine elements into a claim, a "person of ordinary skill is also a person of ordinary creativity, not an automaton." *Id.*

prior art are binding on the patentee for purposes of a later inquiry into obviousness." *PharmaStem Therapeutics, Inc. v. ViaCell, Inc..,* 491 F.3d 1342, 1362 (Fed. Cir. 2007) (citing *Constant v. Advanced Micro Devices, Inc.,* 848 F.2d 1560, 1570 (Fed. Cir. 1988). The Background of the patents clearly state that the prior art demonstrated three methods of cloning a gene.

> At the risk of over-simplification, it can be stated that three alternative principal methods can be employed: (1) the "isolation" of double-stranded DNA sequence from the genomic DNA of the donor; (2) the chemical manufacture of a DNA sequence providing a code for a polypeptide of interest; and (3) the in vitro synthesis of a double-stranded DNA sequence by enzymatic "reverse transcription" of mRNA isolated from donor cells.

'933 patent, Background, col. 3, ln. 3-11 (TRX 0001).

The patent then plainly states that the preferred method of cloning a gene is the second method, where the gene can be chemically synthesized when the amino acid sequence of the protein is known.

> Manufacture of DNA sequences is **frequently the method of choice** when the entire sequence of amino acid residues of the desired polypeptide product is known. DNA manufacturing procedures of co-owned, co-pending U.S. patent application Ser. No. 483,451, by Alton, et al., (filed Apr. 15, 1983 and corresponding to PCT U.S.83/00605, published Nov. 24, 1983 as WO83/04053), for example, **provide a superior means for accomplishing such highly desirable results** as: providing for the presence of alternate codons commonly found in genes which are highly expressed in the host organism selected for expression (e.g., providing yeast or E.coli "preference" codons); avoiding the presence of untranslated "intron" sequences (commonly present in mammalian genomic DNA sequences and mRNA transcripts thereof) which are not readily processed by procaryotic host cells; avoiding expression of undesired "leader" polypeptide sequences commonly coded for by genomic DNA and cDNA sequences but frequently not readily cleaved from the polypeptide of interest by bacterial or yeast host cells; **providing for ready insertion** of the DNA in convenient expression vectors in association with desired promoter/regulator and terminator sequences; and **providing for**

> **ready construction of genes** coding for polypeptide fragments and analogs of the desired polypeptides.

'933 patent, Background, col. 3, ln. 14-37 (TRX 0001) (emphasis added). This "superior" "method of choice" "providing for ready insertion of the DNA" and "providing for ready construction of genes" specifically teaches to use Goldwasser protein as a source of amino acids and combine this with the prior art teachings of Alton, et al., (filed Apr. 15, 1983 and corresponding to PCT U.S.83/00605, published Nov. 24, 1983 as WO83/04053) to make an EPO clone. Dr. Lowe confirmed these prior art teachings throughout his testimony at trial. *See e.g.,* Lowe 205:17–207:12; *see also* Lowe 369:7-12; Lowe 188:11-23; Lowe 178:11-18, 257:12-14; Lowe 217:23–218:11; Lowe 228:19-22.

Similarly, the Background also describes that the prior art taught use of probes that could hybridize DNA clones from a mRNA or genomic library. The Background specifically states that these probes can be constructed from fragments of the protein.

> **Where substantial portions of the polypeptide's amino acid sequence are known, labelled, single-stranded DNA probe sequences duplicating a sequence putatively present in the "target" cDNA may be employed in DNA/DNA hybridization procedures carried out on cloned copies of the cDNA which have been denatured to single stranded form**. [See, generally, the disclosure and discussions of the art provided in U.S. Pat. No. 4,394,443 to Weissman, et al. and the recent demonstrations of the use of long oligonucleotide hybridization probes reported in Wallace, et al., Nuc.Acids Res., 6, pp. 3543-3557 (1979), and Reyes, et al., P.N.A.S. (U.S.A.), 79, pp. 3270-3274 (1982), and Jaye, et al., Nuc.Acids Res., 11, pp. 2325-2335 (1983). See also, U.S. Pat. No. 4,358,535 to Falkow, et al., relating to DNA/DNA hybridization procedures in effecting diagnosis; published European Patent Application Nos. 0070685 and 0070687 relating to light-emitting labels on single stranded polynucleotide probes; Davis, et al., "A Manual for Genetic Engineering, Advanced Bacterial Genetics," Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y. (1980) at pp. 55-58 and 174-176, relating to colony and plaque hybridization techniques; and, New England Nuclear (Boston, Mass.) brochures for "Gene Screen" Hybridization

> Transfer Membrane materials providing instruction manuals for the transfer and hybridization of DNA and RNA, Catalog No. NEF-972.]

'933 patent, Background, col. 3, ln. 51 – col. 4, ln. 9. (TRX 0001) (emphasis added). Applied here, the prior art in the Background would have also motivated the skilled worker to use Goldwasser's EPO protein fragments to construct hybridization probes to clone the EPO gene. Again, Dr. Lowe testified extensively on the record that these methods were available in the prior art. (*See e.g.*, Lowe 164:15-25, 167:16-168:12; Lowe 168:20-175:3, 238:15-239:4, 241:4-17, 256:20-257:5; TRX 2021; Lowe 247:20-24; TRX 2023; Lowe 241:15-242:6, 244:13-20; TRX 2022; Lowe 255:19–258:12; Lowe 256:3-19; Lowe 256:20–257:5).

D. Fristch's EPO Clone Is Prior Art

Even assuming that Amgen is correct that the prior art requires DNA sequences in order to render the asserted claims obvious (Amgen is wrong), Amgen's application for judgment as a matter of law would still fail because Roche presented prior art evidence of an EPO DNA clone as well as mammalian cells expressing the EPO gene at high levels.

The critical date of invention for prior art purposes is the filing date of the application until an earlier date is proved. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 449 (Fed. Cir. 1986). It is undisputed that the filing date of the Lin application is November 30, 1984, and Amgen has presented no evidence during Roche's case-in-chief suggesting that the critical date should be earlier.[3] (Lowe 260:1-18; TRX 7).

[3] In fact, Amgen would have been hard pressed to present such evidence during Roche's case since proof of invention dates normally requires inventor testimony corroborated with independent evidence. *See Chen v. Bouchard*, 347 F.3d 1299, 1309 (Fed.Cir.2003) ("[T]he purpose of corroboration... is to prevent fraud, by providing independent confirmation of the inventor's testimony."). The corroboration requirement is grounded on credibility, and Amgen presented neither inventor testimony nor corroborating objective evidence into the record. *See Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1171 (Fed Cir. 2006).

Roche presented unchallenged evidence that Dr. Edward Fritsch at Genetics Institute cloned an EPO cDNA, transfected it into COS and CHO cells, and expressed high levels of *in vitro* and *in vivo* biologically active human EPO.[4] All of this work was completed before November 30, 1984. Indeed, Amgen concedes that Dr. Fritsch cloned the EPO gene on July 1984, and that he expressed EPO in CHO cells in September 1984 – both before Amgen's filing date.[5] As Amgen has failed to introduce evidence of an earlier invention date for any of the claimed subject matter, Dr. Fritsch's invention stands as prior art for all of the asserted claims. Dr. Fritsch's invention, described in an article sent to the journal *Nature* in December 1984, and published in February 1985, was not abandoned, suppressed or concealed. Accordingly, there can be no dispute that Dr. Fritsch's invention stands as prior art under § 102(g)/103, and thus it renders each of the asserted claims invalid.

III. CONCLUSION

Based on the foregoing, Roche requests that the Court deny Amgen's Motion For Judgment as a Matter of Law, and in particular, those arguments advanced by Amgen's Counsel regarding Dr. Lowe's testimony.

DATED: September 25, 2007

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ROCHE DIAGNOSTICS GMBH, and
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[4] *See* TRX QEJ (G.I. EPO Quarterly Report 6/28/84 – 10/15/84); Fritsch 350:19–360:21; *see also* TRX PPK, OFD, OHV, QEI, OJC, QEJ, OIC.

[5] *See* D.I. 1031 at 2.

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