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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, Plaintiff, v. ROCHE MOLECULAR SYSTEMS, ET AL., Defendants.	Case No. C 05 04158 MHP **STANFORD'S REPLY TO ROCHE'S RESPONSIVE CLAIM CONSTRUCTION BRIEF**
ROCHE MOLECULAR SYSTEMS, ET AL., Counterclaimants, v. THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY; THOMAS MERIGAN; AND MARK HOLODNIY, Counterclaim Defendants.	Date: October 3, 2007 Courtroom: 15, 18th Floor Hon. Marilyn Hall Patel

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TABLE OF CITATION CONVENTIONS

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'730 Patent	U.S. Patent No. 5,968,730, entitled "Polymerase Chain Reaction Assays for Monitoring Antiviral Therapy and Making Therapeutic Decisions in the Treatment of Acquired Immunodeficiency Syndrome," issued on October 19, 1999 (Docket No. 179, Ex. 1)
'705 Patent	U.S. Patent No. 6,503,705, entitled "Polymerase Chain Reaction Assays for Monitoring Antiviral Therapy and Making Therapeutic Decisions in the Treatment of Acquired Immunodeficiency Syndrome," issued on January 7, 2003 (Docket No. 179, Ex. 2)
'041 Patent	U.S. Patent No. 7,129,041, entitled "Polymerase Chain Reaction Assays for Monitoring Antiviral Therapy and Making Therapeutic Decisions in the Treatment of Acquired Immunodeficiency Syndrome," issued on October 31, 2006 (Docket No. 179, Ex. 3)
Bartlett Decl.	Declaration of John G. Bartlett, M.D., in Support of Roche's Responsive Claim Construction Brief (Docket No. 188)
Lifson Decl.	Declaration of Jeffrey D. Lifson, M.D., in Support of Roche's Responsive Claim Construction Brief (Docket No. 187)
Opening Br.	Stanford's Opening Claim Construction Brief (Docket No. 177)
Rhyu Decl.	Declaration of Michelle S. Rhyu Supporting Stanford's Opening Claim Construction Brief (Docket No. 179)
Rhyu Supp. Decl.	Supplemental Declaration of Michelle S. Rhyu in Support of Stanford's Reply to Roche's Responsive Claim Construction Brief (filed concurrently herewith)
Roche Br.	Roche's Responsive Claim Construction Brief (Docket No. 190)
Volberding Decl.	Declaration of Dr. Paul Volberding Supporting Stanford's Opening Claim Construction Brief (Docket No. 178)

I. INTRODUCTION

Roche has agreed to Stanford's definition of the "statistically significant" terms, leaving only four terms to be considered: "therapeutically effective"/"ineffective," "an antiretroviral agent," "measuring the HIV RNA copy number," and "presence"/"absence of detectable HIV-encoding nucleic acid." Stanford's constructions embrace the plain and customary meanings of these ordinary terms, and Roche has identified no evidence in the intrinsic record suggesting that the patentees intended to limit the scope of their inventions. Conversely, Roche repeatedly seeks to import limitations through conclusory expert testimony, effectively rewriting the claims to require particular assays, particular drugs, and actions by particular individuals. Roche's proposals flout accepted principles of claim construction.

Due to the infirmity of its claim construction arguments, Roche focuses on irrelevancies, waiting until page 19 of its 24-page brief even to begin the Argument section. Prior to addressing the claim terms, Roche seeks to distract the Court from the straightforward claim construction issues at hand by mischaracterizing the claimed inventions and intrinsic record, misstating the prior art knowledge in the field of anti-HIV clinical research, and misrepresenting Stanford's actions during claim construction discovery. These distractions should be ignored. A clear focus on the analysis of the disputed claim terms and systematic application of basic claim construction principles compels adoption of Stanford's constructions.

II. ARGUMENT

A. "therapeutically effective" and "therapeutically ineffective"

1. If the terms are construed, Stanford's definitions should be adopted.

No construction of these terms is necessary. Stanford's unrefuted arguments regarding plain meaning (Opening Br. at 7:20-9:1) confirm that the terms "therapeutically effective" and "therapeutically ineffective" do not require separate construction by the Court.

Should the Court nonetheless conclude that construction of these claim terms is necessary, the Court should adopt Stanford's proposed constructions. Dr. Bartlett's testimony comports with Dr. Volberding's testimony that persons of ordinary skill would understand these terms to refer generally to providing or failing to provide therapeutic benefits. (Volberding

Decl. ¶ 7; Rhyu Supp. Decl., Ex. 27 at 46:23-25, 47:21-25; Bartlett Decl. ¶ 37.) Indeed, Dr. Bartlett elaborated with a slate of objective therapeutic benefits that would have been understood by treating physicians, such as an increase in CD4 count. (Rhyu Supp. Decl., Ex. 27 at 47:1-25.)

Further, two aspects of Roche's original construction are no longer in real dispute. First, without explicitly admitting to changing its proposed construction, Roche no longer asserts that the term "therapeutically ineffective" is limited to ineffectiveness arising "as a result of drug resistance." (*Compare* Roche Br. at 19:19-20, *with* Docket No. 172, Ex. B at 4.)

Second, Roche has provided no cases or factual support for the treatment modification limitations in its proposed claim constructions, which would prevent treatment from being modified for "effective" agents and require treatment to be modified for "ineffective" agents. (Roche Br. at 20:1-6.) Roche's only cited extrinsic evidence consists of a single paragraph of Dr. Bartlett's declaration that does not relate to treatment modification. (*See id.* at 20:1-6 (citing Bartlett Decl. ¶ 36).) Moreover, during deposition, Dr. Bartlett agreed that Roche's constructions regarding treatment modification are incorrect:

> Q Is it your opinion that it is okay to change the therapy even though it is effective in stopping the virus?
>
> A Yes.
>
> . . . .
>
> Q . . . On the flip side of that, is it your opinion that antiretroviral treatment must be modified if viral load testing suggests that it is ineffective?
>
> . . . .
>
> A The answer is no.

(Rhyu Supp. Decl., Ex. 27 at 49:10-13, 49:24-50:4 (objections omitted).) Roche also ignores Stanford's legal arguments and factual support opposing importation of this limitation. (Opening Br. at 10:25-12:20.) Roche's proposed limitation regarding modification of treatment must therefore be rejected.

Roche's proposal to import a subjective intent limitation is likewise unsupported by the law and facts. Roche simply ignores the Federal Circuit's refusal to import a subjective intent limitation in assigning meaning to a claim. *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239

F.3d 1343, 1353-54 (Fed. Cir. 2001). (*See* Opening Br. at 9:2-20.) Arguing only that "it is Stanford that wrote the claims" (Roche Br. at 20:24-27), Roche fails to identify any basis in the claim language, patents, or prosecution history for importing a physician's intent when interpreting the claims. *Seachange Int'l, Inc. v. C-Cor Inc.*, 413 F.3d 1361, 1375-76 (Fed. Cir. 2005). Indeed, even Roche's expert testified that "therapeutic effectiveness" is defined by accepted objective criteria that were known in 1992 to physicians who treat HIV patients, not by the subjective, preconceived intent of individual treating physicians. (Rhyu Supp. Decl., Ex. 27 at 41:23-43:21, 46:4-22.)

Roche's attempt to distinguish *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293 (Fed. Cir. 2006) is unavailing and does not justify a subjective intent limitation. Roche's assertion that *Amgen* is distinguishable because the patent in that case lists specific therapeutic effects actually contradicts the holding of *Amgen.* In *Amgen*, the court rejected a construction that limited the "therapeutic effect" to a single effect, increasing hematocrit. *Id.* at 1302-03. The court concluded that the claimed "therapeutic effects" were ***not*** limited to the effects recited in the specification and file history but encompassed a composition with "a wide range of effects." *Id.* at 1303. Further, the discussion of "therapeutically effective amount" in *Amgen* focuses on the physical effects elicited by the therapeutic agent, not any physician's subjective intent in administering the amount. Accordingly, *Amgen* supports Stanford's position regarding the definition of "therapeutically effective."[1] Indeed, Roche has failed to identify a single case in which a limitation based on the state of mind of a physician was imported into therapy related claims. Roche's proposed subjective intent limitation is thus also unsupported and improper.

Accordingly, if the Court elects to construe these terms, "therapeutically effective" should be construed to mean "providing therapeutic benefits" and "therapeutically ineffective" should be construed to mean "not providing therapeutic benefits."

[1] Roche's assertion that the patents do not provide measures of therapeutic effectiveness is incorrect. The patents identify multiple measures, including decreases in viral load, increases in CD4 count, avoidance of drug resistance and compromised immune systems, and promoting survival. (*See, e.g.*, '730 patent at 2:14-52, 2:64-3:6, 7:50-8:14, 12:57-13:32.)

2. Roche's attempted distractions should be ignored.

Roche improperly attempts to inject infringement issues into claim construction. As this Court recently recognized, "'A claim is construed in the light of the claim language, the other claims, the prior art, the prosecution history, and the specification, ***not in light of the accused device***.'"[2] The case *Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 442 F.3d 1322, 1326-27 (Fed. Cir. 2006) does not override this long-standing doctrine, but instead merely suggests that the accused activity may help identify disputed claim limitations, not *define* them.[3]

Further, Stanford's refusal to waste the Court's time by responding to each of the erroneous factual assertions in Roche's brief should not be construed as any admission that those allegations are undisputed. Stanford objects to Roche's inclusion of those factual assertions as irrelevant to claim construction and incorrect. For example, Roche's statements at 6 n.4 and 14 n.5 are incorrect. Stanford submitted thorough infringement contentions on February 28, 2006, and twice supplemented these contentions. Stanford's contentions identify support for infringement of each element of each asserted claim, provide pinpoint citations to documents, and identify Roche's TaqMan kits, which use real time PCR. (Rhyu Supp. Decl., Exs. 30-31, 33.)

The Court should also reject Roche's attempt to use its improper deposition tactics to strike Dr. Volberding's testimony and obtain a claim construction that its own expert would not even support. Dr. Volberding was testifying only as an expert and answered all questions related to his opinions. Only where Roche went well beyond the reasonable limit of questions was Dr. Volberding was instructed not to answer. *See Lapenna v. Upjohn Co.*, 110 F.R.D. 15, 19 (E.D. Pa. 1986). The inappropriate questions related to Dr. Volberding's present-day use of viral load testing kits, not to the relevant 1992 timeframe (as Roche concedes). (Roche Br. at

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[2] *Apple Computer v. Burst.com, Inc.*, No. 06-00019 MHP, 2007 WL 1342504, at *16 (N.D. Cal. May 8, 2007) (quoting *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1118 (Fed. Cir. 1985) (en banc) (emphasis added)); *see also NeoMagic Corp. v. Trident Microsystems, Inc.*, 287 F.3d 1062, 1074 (Fed. Cir. 2002) ("It is well settled that claims may not be construed by reference to the accused device.").

[3] *See also Exigent Tech., Inc. v. Atrana Solutions, Inc.*, 442 F.3d 1301, 1309 n.10 (Fed. Cir. 2006) (holding that it is appropriate to consider the accused device only "when determining what aspect of the claim should be construed").

6:11-22 (citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313) (Fed. Cir. 2005) (en banc)).) Dr. Volberding answered an array of similar questions, and was instructed not to answer only when the questions were *exclusively* aimed at Dr. Volberding's present-day use. (*See* Rhyu Supp. Decl., Ex. 26 at 75:15-77:4, 81:13-88:13.) Confirming the irrelevance of the information sought, Roche has not demonstrated any prejudice, nor has Roche submitted any testimony for claim construction regarding the role of the manufacturer or laboratory, nor has it cited any cases supporting the relief it requests.

Roche's reference to Stanford's cancellation of Dr. Kramer's deposition is also a red herring, as Stanford complied with the Court's order and elected not to submit a declaration from Dr. Kramer in opening or reply. Roche was informed of the cancellation repeatedly and long before the deposition. (Rhyu Supp. Decl., Ex. 32; *see also* Docket No. 184, Exs. B, D.) The knowing decision by Roche's counsel to spend thousands of dollars traveling to Boston for a non-existent deposition was a stunt performed solely to mention it in Roche's brief and should be given no weight by the Court.[4]

B. "an antiretroviral agent"[5]

Roche does not dispute Stanford's construction to the extent it refers to "at least one" substance or Stanford's argument that the claims cover combination therapy involving multiple antiretroviral agents. Roche further concedes that the ordinary and customary meaning of "antiretroviral agent" does not include a time limitation and has provided no opposition to

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[4] Moreover, Roche's submission of a declaration by Dr. Lifson regarding the "presence" and "absence" terms violates Patent Local Rule 4-3(d) and this Court's Scheduling Order (Docket No. 161). Roche's 4-3(d) disclosure contained no disclosure of the substance of any testimony by Dr. Lifson regarding these terms, as Dr. Lifson confirmed in deposition. (Docket No. 172, Ex. G, at 3-4; Rhyu Supp. Decl., Ex. 28 at 88:14-89:4.) Nonetheless, Roche has attempted to add expert testimony on those terms. (*See* Lifson Decl.,¶¶ 45-46.) As this Court was aware in ruling on Roche's recent Emergency Motion, Stanford would be prejudiced if the Lifson testimony were allowed, because Stanford relied on the narrow scope of Roche's 4-3(d) disclosure in determining not to provide testimony from its expert, Dr. Fred Kramer. (*E.g.,* Docket No. 185 at 1:1-12.) Thus, the Court should disregard Roche's reliance on Dr. Lifson's testimony with regard to the "presence" and "absence" claim terms.

[5] Claims 14 and 19 of the '730 patent use the term "anti-HIV agent," which should be construed consistently with "an antiretroviral agent" as "at least one substance having or capable of having an effect against HIV."

Stanford's argument and evidence that the ordinary meaning of the words "antiretroviral agent" refers to a "substance having or capable of having an effect against a retrovirus." Indeed, Roche concedes that "in general, antiretroviral agents are drugs that are effective in reducing or stopping replication of retroviruses." (Roche Br. at 22:3-4; Rhyu Supp. Decl., Ex. 27 at 25:1-26:5, 27:9-28:4.) The remaining dispute, then, concerns whether to reject Roche's additional limitation that "antiretroviral agents" include only those agents that were "available to doctors for the treatment of AIDS/HIV infected patients in 1992."

Roche does not challenge the general rule articulated in *SuperGuide Corp. v. DirecTV Enterprises, Inc.*, 358 F.3d 870, 878 (Fed. Cir. 2004) that claim terms may encompass after-arising technologies.[6] (*See* Opening Br. at 14:20-15:14.) This holding of *SuperGuide* cannot be ignored. *Woods v. Interstate Realty Co.*, 337 U.S. 535, 537 (1940) ("[W]here a decision rests on two or more grounds, none can be relegated to the category of obiter dictum."). Accordingly, *SuperGuide* does not permit imposition of any temporal limitation or limitation to any particular category of antiretroviral agents.

Further, Roche mischaracterizes *SuperGuide*. Contrary to Roche's suggestion that digital television signals "were known and enabled . . . at the time of filing [in 1985]" (Roche Br. at 21:20-22), there is no recognition in the *SuperGuide* opinion that such signals were among "regularly received television signals" in 1985. Instead, the court recognized that "[b]y 1985, work on developing a standard for the transmission of digital video data for ***telephony*** had begun, and ***by 1988*** . . . there was sufficient interest by those in the video industry to establish a Motion Picture Experts Group ***to create*** a digital video standard for television broadcasts." *SuperGuide*, 358 F.3d at 879 (emphasis added). Far from finding the technology to be "known and enabled," the court relied on a defendant's acknowledgement that "[c]onceptual work for digital television signals had begun" by the time the patent was filed. *Id.* at 880 n.6. The court further relied on the conclusion that the patentees were "at least aware that digital television

[6] Roche also fails to distinguish Stanford's citation to *Marsh-McBirney, Inc. v. Montedoro-Whitney Corp.*, 882 F.2d 498, 504 (Fed. Cir. 1989), which contains the same holding as *SuperGuide*.

signals could be broadcast in the future." *Id.*

Accordingly, even under Roche's myopic reading of *SuperGuide*, the facts of this case warrant application of the general rule that after-arising technologies should be included. Like the early stage digital television signals in *SuperGuide*, the facts in this case show that numerous publications prior to 1992 identified targets of antiretroviral therapy and, correspondingly, possible antiretroviral agents.[7] In particular, at least two non-nucleoside antiretroviral agents (sponsored by Abbott and F. Hoffman-La Roche AG) were in clinical trials. (Volberding Decl. ¶¶ 15-16; Rhyu Supp. Decl., Ex. 26 at 48:14-21, 54:11-18, 137:2-9, 138:6-15.) It was also recognized that "[c]ertain combinations of anti-HIV agents may have synergistic activity when used together." (*See* Rhyu Decl., Ex. 7 at 872.) Thus, adopting Roche's construction would require the Court improperly to accept Roche's assertion that the term "antiretroviral agents" does not apply to drugs in early development in the face of contradictory publications. (*See* Rhyu Decl., Ex. 4 at 1541 ("We have thus far focused on the use of dideoxynucleosides as antiretroviral agents against HIV; however, a number of nucleosides that do not have an oxacyclopentane . . . sugar moiety [*i.e.*, non-dideoxynucleosides] have also been shown to be active against HIV in vitro.").) *See Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1585 (Fed. Cir. 1996). Further, although Roche has specifically argued about HAART therapy and protease inhibitors, Dr. Bartlett admitted in deposition that HAART therapy uses dideoxynucleosides in combination with other agents and that publications relating to protease inhibitors date back to the 1980s, with publications directed specifically to HIV protease existing prior to May 1992. (Rhyu Supp. Decl., Ex. 27 at 37:10-38:2, 38:11-13.) In short, the conceptual work for identifying antiretroviral agents other than those that had been FDA-approved had certainly begun as of 1992, and those of skill were aware that inhibitors of various aspects of the HIV life cycle could be proven clinically to have antiretroviral activity.

Roche's remaining argument for importing a temporal restriction rests on its

[7] *See* Rhyu Supp. Decl., Ex. 27 at 28:5-24 (conceding that persons of skill in 1992 knew the steps of the HIV replication cycle and that inhibiting any of the steps could inhibit replication of HIV).

mischaracterization of a sentence in the patent specification. The sentence plainly states: "Antiretroviral agent, as used herein, ***includes*** any known antiretroviral agent ***including***, ***but not limited to***, dideoxynucleosides."[8] ('730 patent at 8:39-41 (emphasis added).) Roche provides no response to Stanford's argument, supported by *Amgen*, 457 F.3d at 1302, that the use of "includes" and "including" is a non-limiting description of antiretroviral agent.[9] (*See* Opening Br. at 16:3-11.) *See also Semiconductor Energy Lab. Co. v. Chi Mei Optoelectronics Corp.*, No. 04-04675 MHP, 2006 U.S. Dist. LEXIS 13243, at *39-41 (N.D. Cal. Mar. 27, 2006) (Patel, J.) (term "generally" not limiting). Roche simply ignores these terms, misplacing its emphasis on the phrase "known antiretroviral agent."

Roche's reliance on *Kopykake Enterprises, Inc. v. Lucks Co.*, 264 F.3d 1377 (Fed. Cir. 2001) is inappropriate. The patentee in *Kopykake* conceded that the ordinary meaning of the claim term "screen printing" was limited to "printing by silk screening," but argued that the specification broadened the definition to include "conventional screen printing," "any other conventional printing process," and "any other conventional means and methods of applying [images]." 264 F.3d at 1380. Due to the limited scope of the claim term, the issue in *Kopykake* concerned whether the accused ink jet printing method was "conventional." Here, because the ordinary meaning of the term "antiretroviral agent" is not limited to any specific agent, and the written description does not provide a limiting definition, *Kopykake* is inapposite. Further, to override the specification and limit antiretroviral agents to the nucleosides that Dr. Bartlett claims were available in 1992 would also violate the rule that extrinsic evidence may not be used to contradict an unambiguous interpretation of the intrinsic evidence.[10] *See Pitney Bowes,*

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[8] Dr. Bartlett also testified that "known," the word used in the specification, is much different from "available," the word used in Roche's definition. Even according to Dr. Bartlett, a "known" antiretroviral agent includes a medication at any part of drug development, including analysis of compounds in a test tube. (Rhyu Supp. Decl., Ex. 27 at 35:18-36:16.)

[9] Even Roche's experts testified that they understand the term "including" to be non-exclusive. (Rhyu Supp. Decl., Ex. 28 at 76:17-77:23; Rhyu Supp. Decl., Ex. 27 at 7:25-8:24.)

[10] Dr. Bartlett's testimony regarding what was known in 1992 is contradicted by the publications cited in Stanford's Opening Brief and Dr. Volberding's declaration, which demonstrate public knowledge of various non-nucleoside antiretroviral agents. *See In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995) ("The person of ordinary skill in the art is a hypothetical person who is presumed to know the relevant prior art."). Further, Dr. Bartlett's testimony should be rejected

Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1308 (Fed. Cir. 1999). Accordingly, "an antiretroviral agent" refers to "at least one substance having or capable of having an effect against a retrovirus, such as HIV."

C. "measuring the HIV RNA copy number"

The plain meaning of "measuring the HIV RNA copy number" is sufficiently clear, making construction unnecessary. Roche's attempt to narrow the plain meaning to the techniques available in 1992, and to the assay described in the 1991 JID article, is improper under the law and facts of this case.

Roche's argument once again ignores the rules of claim construction, making no attempt to respond to the doctrine articulated in *SuperGuide* that claim terms may encompass later-developed technology. (*See* Opening Br. at 17:5-16; *supra*, Section II.B.) Roche further fails to address any of the claim construction cases that reject adding limitations that differ from the ordinary and customary meaning of the disputed term. (*See, e.g.*, Opening Br. at 17-18.) Even if the specification discloses only one way to measure HIV copy number, the Federal Circuit has repeatedly recognized that examples in the specification are not limiting.[11]

Neither the ordinary meaning of the "measuring" step nor the intrinsic evidence justify importing a temporal limitation. Indeed, Roche agrees that one of ordinary skill would interpret the "measuring" steps at issue "to be directed to using PCR to quantify the HIV RNA copy number." (Roche Br. at 22:25-27.) There is no intrinsic time limitation to this customary understanding. (Rhyu Supp. Decl., Ex. 28 at 40:21-41:15, 42:16-19.) Similarly, nothing in the ordinary meaning of "measuring the HIV RNA copy number" limits the measurement method to

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as conclusory and unreliable. *See Phillips*, 415 F.3d at 1318 ("[C]onclusory, unsupported assertions by experts as to the definition of a claim term are not useful to a court."). His declaration testimony is also internally inconsistent with his own deposition testimony. (*Compare* Rhyu Supp. Decl., Ex. 27 at 37:10-38:2, 38:11-13, *with* Bartlett Decl. ¶ 41.)

[11] *Phillips*, 415 F.3d at 1323 ("[W]e have expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment."); *In re Omeprazole Patent Litig.*, 483 F.3d 1364, 1372 (Fed. Cir. 2007); *Great Plains Lab., Inc. v. Metamatrix Clinical Lab.*, No. 04-2125-JTM, 2006 WL 2663680, at *9-10 (D. Kan. Sept. 15, 2006) (refusing to limit claims to analysis by gas chromatography where claim used term "analyzing").

"end-point PCR." Moreover, Roche does not contest Stanford's demonstration that the patentees never disclaimed the plain meaning. (*See id.* at 45:19-46:5.) Indeed, the specification is explicit that the measuring examples presented are "a preferred, non-limiting embodiment of the invention." ('730 patent at 4:64.) Further, as Dr. Lifson admitted during his deposition, the term "end-point PCR" was known to those of skill in the art in 1992. (Rhyu Supp. Decl., Ex. 28 at 50:19-51:8.) Had the patentees intended to limit the claim term to end-point PCR, they could have done so explicitly. *See SuperGuide*, 358 F.3d at 880 (rejecting restriction of term to analog television technology where patentees did not use the term "analog").

Having no basis in the intrinsic record for adding its proposed limitations, Roche improperly tries to use the issue of enablement to import the unwarranted limitation. (Roche Br. at 23:1-7 (citing *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1196 (Fed. Cir. 1999).) This approach fails for at least three reasons.

First, it is improper to consider invalidity issues when construing the "measuring" claim term, because the meaning of the term is unambiguous. The Federal Circuit has clearly limited the maxim that claims should be construed to preserve their validity "to cases in which 'the court concludes, after applying all the available tools of claim construction, that the claim is still ambiguous.'" *Phillips*, 415 F.3d at 1327-28 (citation omitted). *See also Apple Computer*, 2007 WL 1342504, at *12; *Regents of the Univ. of Cal. v. Dako N. Am., Inc.*, No. 05-03955 MHP, 2006 WL 1867618, at *6 (N.D. Cal. July 5, 2006) (Patel, J.). Because the claim construction analysis provided above shows that the meaning of the "measuring" step is unambiguous, the term may not properly be limited further. (Roche Br. at 22:25-27.) Indeed, Roche's gambit is not to preserve validity, but to avoid its heavy burden of proving invalidity by clear and convincing evidence by improperly interjecting enablement into the claim construction analysis.

Second, even if enablement considerations were appropriate here (they are not), the patents' disclosure enables the "measuring" term. Enablement does not require disclosing every possible embodiment of an invention, but instead "[t]he enablement requirement is met if the description enables any mode of making and using the claimed invention." *Engel Indus., Inc. v. Lockformer Co.*, 946 F.2d 1528, 1533 (Fed. Cir. 1991); *Johns Hopkins Univ. v. CellPro, Inc.*,

152 F.3d 1342, 1361 (Fed. Cir. 1998). Roche's cited case, *National Recovery*, is not to the contrary. *See, e.g.*, *Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052, 1071 (Fed. Cir. 2005) (distinguishing *Nat'l Recovery* as a case where the patentee failed to disclose *any* enabling embodiments). As the *Invitrogen Corp.* court made clear:

> Enablement does not require the inventor to foresee every means of implementing an invention at pains of losing his patent franchise. Were it otherwise, claimed inventions would not include improved modes of practicing those inventions. Such narrow patent rights would rapidly become worthless as new modes of practicing the invention developed, and the inventor would lose the benefit of the patent bargain.

429 F.3d at 1071. *See also SRI Int'l*, 775 F.2d at 1121. Further, "[t]he specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334-39 (Fed. Cir. 2003). Roche's brief fails to address any of these critical elements of the enablement standard.

Finally, even if the law did not preclude considering enablement here, Roche's argument should be rejected because it is premised on an array of factual misstatements.[12] For example, Roche's suggestion that the patents disclose no more than the assay taught in the JID article is simply wrong. Roche and Dr. Lifson ignore the numerous aspects of the assay described in the written description, including Example 6, that were not described in the JID article. (*See* Opening Br. at 18:9-17.) For example, during deposition, Dr. Lifson conceded that the patent, but not the JID paper, discloses a method that can detect 40 copies of HIV RNA. (*See* Rhyu Supp. Decl., Ex. 28 at 93:13-94:18.)

Roche and Dr. Lifson also assert incorrectly that the "measuring" limitation cannot include "real time PCR" because "all of the claims refer to 30 cycles of PCR." (Roche Br. at 23:11-12; Lifson Decl. ¶ 44.) But claims 1, 2, 3, 4, and 8 of the '041 patent are not limited to any particular number of cycles of PCR, yet still use the term "PCR."[13] Dr. Lifson also

[12] *See, e.g.*, *Pfizer, Inc. v. Teva Pharms., USA, Inc.*, 429 F.3d 1364 (Fed. Cir. 2005) (rejecting accused infringer's attempt to limit claims on enablement grounds as factually unsupported).

[13] Dr. Lifson's declaration includes many conclusory statements and statements based on

conceded that real time PCR is a type of PCR, uses the same three-step process as end-point PCR, and is a way to "measure" HIV RNA.[14] Further, even assuming *arguendo* that "about 30 cycles" or "PCR" were limited to end-point PCR, that would provide no reason to impose such a limitation into the separate claim limitation "measuring the HIV RNA copy number."

As to Dr. Lifson's example of the use of "internal controls," he admitted in deposition that "[t]here were certainly publications of procedures employing internal controls prior to May of 1992" and that the cRNA standard disclosed in the JID article technically could have been used as an internal control. (Rhyu Supp. Decl., Ex. 28 at 77:24-80:24.) In the first stage of this case, former Cetus employee Alice Wang confirmed that the cRNA standard used in the JID article could have been used as an internal standard. (Rhyu Supp. Decl., Ex. 29 at 116:2-117:22.) Accordingly, Roche's misstatements and unreliable assumptions contradict Roche's nonenablement argument and provide a third basis for rejecting it.

In sum, the plain meaning of the "measuring" term requires no construction. If the Court opts to construe this term, Stanford's construction should be adopted.

D. "presence of detectable HIV-encoding nucleic acid" and "absence of detectable HIV-encoding nucleic acid"

Roche does not appear to dispute that the plain meaning of these terms is sufficient to direct a jury in determining whether detectable HIV-encoding nucleic acid is present or absent. However, Roche proposes additional limitations to that construction that would (1) deem the result "qualitative" and (2) require a specific copy number for the detection limit. Roche provides no basis in the intrinsic or extrinsic evidence for importing such limitations.

Roche points to no language in the patent or prosecution history that would limit the claims to "qualitative" determinations. (Roche Br. at 23:22-24:17.) Roche instead relies on a misstatement of *Honeywell Int'l, Inc. v. ITT Indus., Inc.*, 452 F.3d 1312, 1319 (Fed. Cir. 2006)

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incorrect premises that contradict available publications. Such unsupported statements as in paragraphs 40 and 42-46 of his declaration are not useful and should be disregarded. *Phillips*, 415 F.3d at 1318.

[14] Rhyu Supp. Decl., Ex. 28 at 35:20-37:7, 49:15-50:4, 54:19-55:4, 63:9-64:11; Lifson Decl. ¶ 44 ("In real time PCR, ***measurements*** are performed by non-invasive ***measurement*** methods . . . .") (emphasis added).

arguing that a patentee's "reliance on his own statements to the PTO is entitled to virtually no weight in the claim construction process." (Roche Br. at 24:7-13.) Roche's argument is irrelevant because it ignores Stanford's numerous citations to supporting evidence in the written description. (Opening Br. at 20:7-14.) Further, the portion of *Honeywell* relied on by Roche states only that evidence of intent "to cover more than what his specification discloses" in the prosecution history cannot override a patentee's clear disclaimer of scope by defining his invention in the written description. *Honeywell, Int'l*, 452 F.3d at 1318-19. Indeed, Roche's misstatement of the law contradicts numerous cases in which statements from the prosecution history favoring the patent-holder's position were relied on by the court.[15] Accordingly, the patentees' characterization of the invention as a quantitative assay in both the written description and the prosecution history is highly relevant and must be considered in construing the claims. *Phillips*, 415 F.3d at 1317 ("[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention.").

Further, Roche's "qualitative" limitation is contradicted by its own expert. Dr. Lifson testified that the term, "detectably present or absent" means "that the test target sequence can be reliably ***quantified*** in the sample, test sample using a particular assay."[16] (Rhyu Supp. Decl., Ex. 28 at 87:9-11) (emphasis added).) Indeed, Dr. Lifson's definition of the term "detectably present or absent" closely parallels Stanford's definitions of the relevant terms.[17] (*See* Rhyu Supp. Decl., Ex. 28 at 88:4-8 (agreeing that "detectably present or absent" "refers to HIV copy numbers being above or below the threshold sensitivity of that particular assay"). Lacking any support in the record, Roche's proposed "qualitative" limitation must be rejected.

Roche's proposal to import a limitation requiring "40 copies of HIV RNA per 200

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[15] *Honeywell Int'l, Inc. v. Universal Avionics Sys. Corp.*, 493 F.3d 1358, 1361-64 (Fed. Cir. 2007); *Ventana Med. Sys., Inc. v. Biogenix Labs., Inc.*, 473 F.3d 1173, 1182-83 (Fed. Cir. 2006).

[16] *Nystrom v. Trex Co.*, 424 F.3d 1136 (Fed. Cir. 2005) is inapposite because it holds only that there is a presumption that different terms should have different constructions and Stanford's constructions for the "measuring" step and the "presence"/"absence" steps are different.

[17] Dr. Lifson's testimony as to the presence/absence limitations is limited to paragraph 45 of his declaration. This testimony should be rejected because it is conclusory and vague. *Phillips*, 415 F.3d at 1318. Further, as detailed above, this and other testimony by Dr. Lifson was not presented in Roche's 4-3(d) disclosure and, therefore, was waived.

microliters of sample" is also unfounded because it is premised on misunderstandings of established claim construction doctrine. Roche argues that "because presence/absence is not defined, Stanford should be limited to the detection levels it described as providing the results it relied upon: 40 copies per 200 ul of sample." (Roche Br. at 24:14-16.) However, the accepted legal standard demands exactly the opposite analysis. That is, the ordinary and customary meaning of a claim term may be narrowed only if the terms are expressly defined in that way. *E.g.*, *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1323 (Fed. Cir. 2003) ("We indulge a 'heavy presumption' that claim terms carry their full ordinary and customary meaning unless the patentee unequivocally imparted a novel meaning to those terms or expressly relinquished claim scope during prosecution.") (citations omitted). Likewise, importing limitations from the specification into the claims is proper only if the patentee clearly disavows some portion of the full scope of the claim. *E.g.*, *Conoco, Inc. v. Energy & Envt'l Int'l, L.C.*, 460 F.3d 1349, 1357-58 (Fed. Cir. 2006) ("[A]n inventor may use the specification to intentionally disclaim or disavow the broad scope of a claim. . . . However, this intention must be clear . . . and cannot draw limitations into the claim from a preferred embodiment.") (citations omitted). Because nothing in the intrinsic record indicates the patentees intended to limit the "presence" and "absence" terms to a specific copy number, the ordinary meaning should be adopted.

Moreover, as discussed *supra* in Section II.C, Roche's reliance on enablement arguments is misplaced. Upon applying "all the available tools of claim construction," it is unambiguous that the construction of the "absence" and "presence" terms is not limited to a specific detection limit of 40 copies of HIV RNA per 200 µl. *See Phillips*, 415 F.3d at 1327-28. Further, Roche has failed to show that nonenablement of the claim terms would even be an issue here. Because enablement does not require disclosing every possible embodiment of an invention, the quantitation assays disclosed in the patents are sufficient to enable the claim. If the Court opts to construe these terms, it should adopt Stanford's constructions.

III. LEVEL OF ORDINARY SKILL

The dispute as to the level of ordinary skill is not necessary to resolve for any of the claim construction issues. If the Court addresses the issue, Stanford's definition should be

adopted. The parties agree that a person of ordinary skill may come from two disciplines: physicians treating HIV patients, and MD or PhD researchers who have experience in molecular methods. The parties' definitions diverge in two significant ways. First, Stanford limits the physicians to those working on clinical HIV research involving antiretroviral agents, not just any "treating physician." Second, as to experience, Stanford requires that the experience relate to clinical HIV research involving antiretroviral agents, while Roche requires "at least two years of relevant laboratory bench experience conducting PCR assays." (*See* Opening Br. at 7:5-9; Roche Br. at 19:4-16.) Only Stanford's definition properly recognizes that the field of the patents is clinical HIV research.[18] (*See* Volberding Decl. ¶ 6.) Roche's definition, in contrast, defines individuals knowledgeable about portions of the invention without defining the general field of the invention.[19] Moreover, Roche's imposition of the requirement of "at least two years" lacks any basis (why not one or three years?) and would only add confusion (what constitutes "***relevant***" experience?). The experience relevant to the patents is indisputably clinical HIV research involving antiretroviral agents.

IV. CONCLUSION

For the foregoing reasons, Stanford respectfully requests that the Court adopt Stanford's proposed constructions and reject Roche's proposed constructions.

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[18] *Micro Motion, Inc. v. Exac Corp.*, 741 F. Supp. 1426, 1435 (N.D. Cal. 1990) ("The hypothetical person of ordinary skill in the art is one who is attempting to solve the problems the inventor addressed.") (internal quotations and citation omitted).

[19] *See, e.g.*, Rhyu Supp. Decl., Ex. 27 at 40:1-4 ("Q: . . . Did you come to an opinion as to what field of art was described in the patent? A: No.").