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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 OPENING 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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I. INTRODUCTION

The claims in this case are straightforward to construe. Indeed, many of the terms are already sufficiently clear for a jury, and require no further construction by the Court. Where the Court deems construction necessary, Stanford's proposed constructions are consistent with the ordinary and customary meaning of the disputed terms and are fully supported by the intrinsic record.

By contrast, Roche's proposed constructions are transparently driven by their theories of noninfringement and invalidity, rather than any rules of claim construction. For example, Roche attempts to import limitations that would require assessing a treating physician's intent. It seeks to limit the method for evaluating so that only antiretroviral agents known in 1992 can be evaluated. And Roche repeatedly seeks to restrict the claims to particular examples provided in the patent. Roche's constructions must be rejected, as they contradict long-established principles of claim construction. Roche's constructions ignore ordinary and customary meaning and add limitations having no relation to the language actually used in the claims. Roche's added limitations have no basis in the intrinsic record, or improperly import specific characteristics of sample embodiments disclosed in the written description. Many of Roche's proposed constructions would introduce ambiguity rather than clarify construction. In short, Roche ignores the rules of construction and contorts the claim language to conform to its arguments for noninfringement and invalidity.

Accordingly, the Court should adopt Stanford's proposed constructions.

II. FACTUAL BACKGROUND

A. Technology

The patents-at-issue relate to methods for evaluating the effectiveness of antiretroviral therapy against the Human Immunodeficiency Virus (HIV).[1] HIV is a retrovirus. Retroviruses have an RNA genome rather than the DNA genome typical of most viruses. HIV was known in the early 1990s to propagate by infecting T-cells in the human immune system and hijacking the

[1] Attached hereto as Exs. 1-3 to the Declaration of Michelle S. Rhyu in Support of Stanford's Opening Claim Construction Brief ("Rhyu Decl.").

T-cell's cellular machinery.[2] Upon infection, HIV binds specifically to a protein called "CD4," which is present on the surface of some T-cells. The virus inserts its contents, including the RNA that stores its genetic code, into the CD4 expressing cells. An enzyme called reverse transcriptase, which is also transferred from the virus to the T-cell, converts the HIV RNA to DNA, which is then integrated into the CD4 cell's genomic DNA. This integrated DNA form of the virus's genome is called "proviral DNA."[3] The proviral DNA reprograms the CD4 cells to produce HIV particles, ultimately killing the infected CD4 cell. At first, the effects of the virus are not severe, and early symptoms of the virus may go unnoticed for years. Over time however, HIV's cycle of infection and reproduction decimates the body's population of CD4 cells. Through this and other mechanisms of action, the body is no longer able to produce an effective immune response. Figure 1 shows the structure and life cycle of HIV.[4]

By the early 1990s, researchers had identified a number of strategies for treating HIV.[5] These strategies generally involved targeting molecules required for HIV infection and propagation with drugs that would inhibit their function. For example, scientists developed a class of drugs known as nucleoside analogues to act as reverse transcriptase inhibitors. Reverse transcriptase inhibitors interfere with the virus's ability to convert HIV RNA to DNA, which hinders the virus's ability to reprogram the CD4 cells. Other strategies for inhibiting HIV included blocking binding of HIV to CD4 (binding inhibitors), preventing integration of reverse transcribed HIV DNA into the CD4 cell genome (integrase inhibitors), and inhibiting the HIV protease enzyme (protease inhibitors).[6]

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[2] For general reviews of HIV biology, see Rhyu Decl., Ex. 4, Mitsuya et al., *Molecular Targets for AIDS Therapy*, 249 Science 1533, 1534 (1990); *id.*, Ex. 5, Greene, *AIDS and the Immune System*, 269 Scientific American 99, 99-103 (1993); *id.*, Ex. 6, Mellors, *Viral Load Tests Provide Valuable Answers*, 279 Scientific American 90, 90 (July 1998).

[3] *Id.*, Ex. 4, Mitsuya, *supra*, at 1536.

[4] Allison O'Brien, Dharmacon, Thermo Fisher Scientific, *Dharmacon SMARTpool siRNA - Identification of Genes Critical to HIV Replication*, http://www.dharmacon.com/m360/newsletter/archive/iss2_vol1/dhar_real_wrld.html (last visited August 10, 2007).

[5] *See, e.g.*, *id.*, Ex. 4, Mitsuya, *supra*; *id.*, Ex. 7, Yarchoan et al., *Anti-Retroviral Therapy of Human Immunodeficiency Virus Infection: Current Strategies and Challenges for the Future*, 78 Blood 859, 859 (1991).

[6] *See generally id.*, Ex. 4, Mitsuya, *supra*; *id.*, Ex. 7, Yarchoan, *supra*; *see also id.*, Ex. 9, European Patent Publication No. 0 402 646 A1 (filed May 17, 1990, published Dec. 19, 1990)

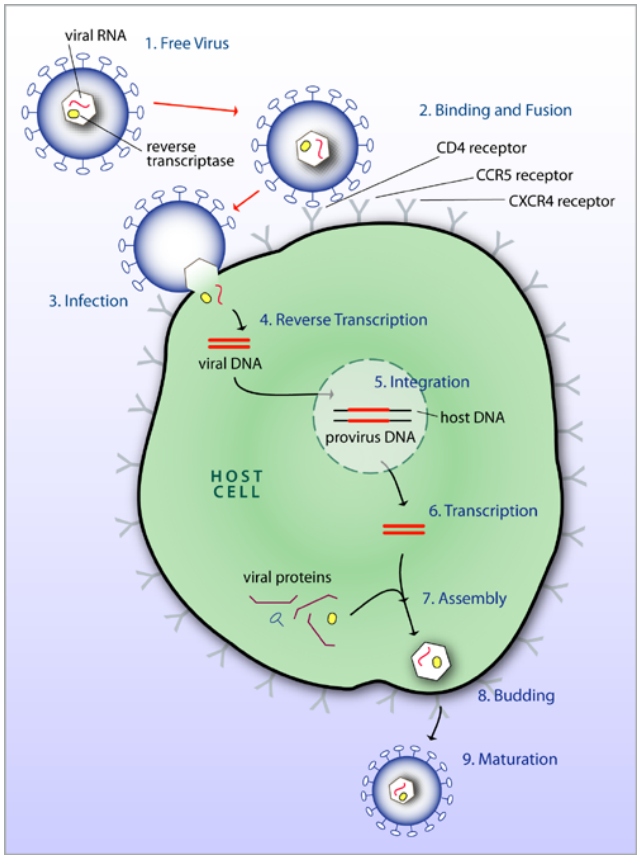

Figure 1. Structure and Life Cycle of HIV.

At that time, however, the field of HIV research and treatment lacked a fast, easy, and accurate means of assessing whether anti-HIV drugs were working. Various biological markers were investigated as potential means of monitoring HIV. For example, levels of viral proteins (such as the p24 protein that makes up the HIV capsule) had been monitored.[7] Some researchers looked at levels of molecules associated with immune system activation to gauge effectiveness of therapy. Investigators also attempted to evaluate effectiveness of treatment by monitoring patient samples for their ability to induce infection in other cells, a technique known as viral culturing. Despite initial optimism for each of these markers for monitoring HIV, none provided satisfactory methods for following the effectiveness of treatment.

(Abbott Laboratories); *id.*, Ex. 10, European Patent Publication No. 0 432 695 A2 (filed December 10, 1990, published June 19, 1991) (F. Hoffman-La Roche AG).

[7] For discussion of inadequacy of surrogate markers of HIV, see *id.*, Ex. 11, Mulder et al., *Rapid and Simple PCR Assay for Quantitation of Human Immunodeficiency Virus Type 1 RNA in Plasma: Application to Acute Retroviral Infection*, 32(2) J. Clin. Microbiology 292, 292 (1994).

In the context of a field needing better surrogate markers for monitoring the effectiveness of HIV therapy, Drs. Thomas Merigan, David Katzenstein, and Mark Holodniy invented the methods claimed in the patents-in-suit. The inventors did not purport to invent a polymerase chain reaction ("PCR") assay, as others had used PCR to detect HIV nucleic acids before them. For example, scientists had used PCR to screen blood products for HIV and to confirm a diagnosis of HIV infection.[8] They and others had also developed and published assays for measurement of HIV in plasma samples (so called "viral load") using PCR.[9] However, the usefulness of such methods for monitoring the effectiveness of therapy remained in question. In fact, one group using a PCR assay to measure viral load had reported finding no distinction between samples from treated and untreated patients.[10] Amid this uncertainty and the disappointing results observed using other surrogate markers, the question of whether changes in levels of HIV viral load correlated with the effectiveness of a given therapy was answered only when the named inventors conducted the experiments leading to the patents in suit. Indeed, following the work of these inventors, quantitative PCR testing HIV viral load became widely accepted for monitoring the effectiveness of HIV treatment. Today, viral load testing comprises the standard used by most clinical researchers and physicians in the United States.[11]

[8] *Id.*, Ex. 12, Schmeck, *New Test That Finds Hidden AIDS Virus Is a Sleuth With Value in Many Fields*, N.Y. Times at B7, B12 (June 21, 1988); *id.*, Ex. 13, Guatelli et al, *Nucleic Acid Amplification In Vitro: Detection of Sequences with Low Copy Numbers and Application to Diagnosis of Human Immunodeficiency Virus Type 1 Infection*, 2(2) Clin. Microbiol. Rev. 217, 225 (1989).

[9] *See id.*, Ex. 14, Holodniy et al., *Detection and Quantification of Human Immunodeficiency Virus RNA in Patient Serum by Use of the Polymerase Chain Reaction*, 163 J. Infectious Diseases 862 (1991); *id.*, Ex. 15, Ottmann et al., *The Polymerase Chain Reaction for the Detection of HIV-1 Genomic RNA in Plasma from Infected Individuals*, 31 J. Virol. Methods 273 (1991).

[10] *Id.*, Ex. 15, Ottmann, *supra*, at 273.

[11] *See id.*, Ex. 16, Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents, *Guidelines For The Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*, 5 (Oct. 10, 2006) ("viral load is critical for evaluating response to therapy").

B. The Patents-in-Suit

Three patents are at-issue in this litigation: U.S. Patent No. 5,968,730 ("'730 patent"), U.S. Patent No. 6,503,705 ("'705 patent"), and U.S. Patent No. 7,129,041 ("'041 patent"). The patents-in-suit share materially identical written descriptions.[12] Further, each of the patents-in-suit claims priority to U.S. Application Serial No. 07/883,327, which was filed May 14, 1992. (*See* '041 patent, title page.)

The '730 patent issued on October 19, 1999. Claims 1, 5-9, 13-14, 18-19, and 23 of the '730 patent are asserted in this litigation. Claim 9 is representative and recites:

> A method of evaluating the effectiveness of anti-HIV therapy of a patient comprising
>
> (i) collecting a plasma sample from an HIV-infected patient who is being treated with an antiretroviral agent;
>
> (ii) amplifying the HIV-encoding nucleic acid in the plasma sample using HIV primers in about 30 cycles of PCR; and
>
> (iii) measuring the HIV RNA copy number using the product of the PCR,
>
> in which an HIV RNA copy number greater than about 500 per 200 ul of plasma correlates positively with the conclusion that the antiretroviral agent is therapeutically ineffective.

('730 patent, claim 9.)

The '705 patent issued on January 7, 2003. Claims 1 and 5-10 of the '705 patent are asserted in this litigation. Claim 1 is representative and recites:

> A method of evaluating the effectiveness of anti-HIV therapy of an HIV-infected patient comprising:
>
> a) collecting statistically significant data useful for determining whether or not a decline in plasma HIV RNA copy numbers exists after initiating treatment of an HIV-infected patient with an antiretroviral agent by:
>
> (i) collecting more than one plasma sample from the HIV-infected patient at time intervals sufficient to ascertain the existence of a statistically significant decline in plasma HIV RNA copy numbers;
>
> (ii) amplifying the HIV-encoding nucleic acid in the plasma samples using HIV primers via PCR for about 30 cycles;

[12] Because the patents-in-suit share materially identical written descriptions, where possible, Stanford has cited only to the '730 written description in order to simplify the briefing.

> (iii) measuring HIV RNA copy numbers using the products of the PCR of step (ii);
>
> (iv) comparing the HIV RNA copy numbers in the plasma samples collected during the treatment; and
>
> b) evaluating whether a statistically significant decline in plasma HIV RNA copy numbers exists in evaluating the effectiveness of anti-HIV therapy of a patient.

('705 patent, claim 1.)

The '041 patent issued on October 31, 2006. Claims 1-4 and 8 of the '041 patent are asserted in this litigation. Claim 1 is the only independent claim from the '041 patent and recites:

> A method of evaluating the effectiveness of anti-HIV therapy of a patient comprising:
>
> correlating the presence or absence of detectable HIV-encoding nucleic acid in a plasma sample of an HIV infected patient with an absolute CD4 count, wherein the presence or absence of said detectable HIV-encoding nucleic acid is determined by
>
> (i) collecting a plasma samples from an HIV-infected patient who is being treated with an antiretroviral agent;
>
> (ii) amplifying HIV-encoding nucleic acid that may be present in the plasma sample using HIV primers via PCR and;
>
> (iii) testing for the presence of HIV-encoding nucleic acid sequence in the product of the PCR.

('041 patent, claim 1.) The text of each of the asserted claims with the disputed terms underlined is provided in the Appendix.

III. LEGAL BACKGROUND

Claim construction is a question of law for the Court. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 977-79 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). The "claims of a patent define the invention to which the patentee is entitled the right to exclude" and are generally given the "meaning that [they] would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc) (internal quotation omitted). The meaning of the claims is determined "in the context of the entire patent, including the specification." *Id.* at 1313. The Court may also consult the prosecution history and extrinsic evidence, although extrinsic evidence "is less significant than the intrinsic record in determining the legally operative

meaning of claim language." *Id.* at 1317 (internal quotation omitted); *see also Apple Computer v. Burst.com, Inc.*, No. 06-0019 MHP, 2007 WL 1342504, at *2-3 (N.D. Cal. May 8, 2007) (Patel, J.) (summarizing background claim construction principles); *Semiconductor Energy Lab. Co. v. Chi Mei Optoelectronics Corp.*, No 04-04675 MHP, 2006 U.S. Dist. LEXIS 13243, at *10-16 (N.D. Cal. Mar. 27, 2006) (Patel, J.) (same). A person of ordinary skill in the art is a Medical Doctor working on clinical HIV research involving antiretroviral agents or a Ph.D. researcher working on molecular methods relating to clinical HIV research involving antiretroviral agents. (*See* Declaration of Dr. Paul Volberding Supporting Stanford's Opening Claim Construction Brief ("Volberding Decl."), ¶ 6.)

IV. THE COURT SHOULD ADOPT STANFORD'S CONSTRUCTIONS OF THE DISPUTED TERMS

A. "therapeutically effective" and "therapeutically ineffective" ('730 patent, claims 1, 6, 9, 14, 19; '705 patent, claims 6-7, 9-10; '041 patent, claims 2-3)

Stanford's Construction	Roche's Construction
<u>therapeutically effective</u> No construction necessary. Alternatively, "providing therapeutic benefits"	<u>therapeutically effective</u> "elicits the medical effect intended by the treating physician such that the course of treatment is not modified"
<u>therapeutically ineffective</u> No construction necessary. Alternatively, "not providing therapeutic benefits"	<u>therapeutically ineffective</u> "fails to elicit the medical effect intended by the treating physician as a result of drug resistance such that the course of treatment is modified"

Like the terms identified in the Court's July 30, 2007 ruling, the terms "therapeutically effective" and "therapeutically ineffective" do not need a separate construction by the Court. (*See* Docket No. 173.)[13] Instead, the plain meaning of these terms is "sufficiently clear" to

[13] The Court identified the following terms raised in the parties' Joint Claim Construction and Prehearing Statement Under Patent Local Rule 4-3 (Docket No. 172) as not requiring construction at this time: "evaluating the effectiveness of anti-HIV therapy of a patient," "evaluating the effectiveness of anti-HIV therapy of an HIV-infected patient," "evaluating the effectiveness," "about 30 cycles," "SK38," "SK39," "conclusion," "The method of claim 7," and "correlating." (Docket No. 173; Rhyu Decl., Ex. 8 at 6:21-9:19.) Further, because there is no material distinction between the parties' constructions of "correlates positively," Stanford agrees that this term may be construed to mean "a particular result renders a particular

direct the jury's infringement fact-finding without further explication by the court. *See Semiconductor Energy Lab. Co.*, No. 04-4675 MHP, 2006 U.S. Dist. LEXIS 13243, at *16-18, *71-72; *Orion IP, LLC v. Staples, Inc.*, 406 F. Supp. 2d 717, 737-38 (E.D. Tex. 2005); *see also Phillips*, 415 F.3d at 1314 (noting that if terms use "commonly understood words," then "the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges").[14] Indeed, as this Court has previously noted, "[a]dding to or rephrasing the claim language often introduces more problems than it solves." *Semiconductor Energy Lab. Co.*, No. 04-4675 MHP, 2006 U.S. Dist. LEXIS 13243, at *17.

One district court has noted that there are generally three circumstances under which terms need to be construed: terms "that might be unfamiliar to the jury, confusing to the jury, or affected by the specification or the prosecution history." *Orion IP, LLC*, 406 F. Supp. 2d at 738. None of those circumstances exist here. The terms relating to therapeutic effectiveness use commonly known words in a way familiar to a lay juror, even when the terms are considered from the perspective of one of ordinary skill in the art. (Volberding Decl., ¶ 7; *see* Rhyu Decl., Ex. 17 at STAN 31816 (defining "therapeutic"); *id.*, Ex. 18 at STAN 31827 (same); *id.*, Ex. 18 at STAN 31821 (defining "effectiveness"); *id.*, Ex. 19 at STAN 31872 (defining "effective").) Further, nothing in the intrinsic record redefines the ordinary and customary meaning of these terms. Accordingly, no construction is necessary for these terms. *See, e.g.*, *United States Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997) (upholding district court's refusal to give separate instruction on "valve means" because claim construction "is not an obligatory exercise in redundancy"); *Level One Commc'ns, Inc. v. Seeq Tech., Inc.*, 987 F. Supp. 1191, 1203 (N.D. Cal. 1997) (Patel, J.) (applying plain language of claim term "sequencer," because "[a]bsent defendant's desire to incorporate the preferred embodiment into the claim, the court cannot see what about the term is ambiguous" and "the claim language is plain enough for

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conclusion more likely than other conclusions."

[14] *See also C.R. Bard, Inc. v. United States Surgical Corp.*, 388 F.3d 858, 863 (Fed. Cir. 2004) (noting that courts "regularly forgo detailed dictionary analyses if the term is as commonplace as 'conformable' or 'pliable'"); *W.E. Hall Co. v. Atlanta Corrugating, LLC*, 370 F.3d 1343, 1350 (Fed. Cir. 2004) (holding that the term "'[s]ingle piece' is sufficiently clear to make even resort to the dictionary unnecessary").

someone skilled in the art").

If the Court seeks to provide constructions for these terms, it should adopt Stanford's constructions and reject Roche's proposed constructions. Roche's proposed constructions do not address the ordinary and customary meaning of these terms, but instead interject three inappropriate limitations. First, Roche proposes that the terms are limited to whether the antiretroviral agent "elicits [or fails to elicit] the medical effect ***intended by the treating physician***." (Docket No. 172, Ex. B at 4 (emphasis added).) However, neither the patents nor the prosecution history cited by Roche mentions or refers to the physician's intent. (*Id.*; *see also* Volberding Decl., ¶ 9.) *Seachange Int'l, Inc. v. C-Cor Inc.*, 413 F.3d 1361, 1375-76 (Fed. Cir. 2005) (limitation with "no basis in the intrinsic record" may not be imported). Furthermore, subjective intent and state-of-mind limitations are inherently problematic and have been rejected by the Federal Circuit:

> Amazon's reading of the key passage from the file history ***injects subjective notions into the infringement analysis***. For example, if a would-be purchaser has made the decision to purchase an item before coming to BN's [Barnes and Noble's] menu page, and there the purchaser sees the item displayed, Amazon would have to concede that no single action taken after the item display would achieve placement of the order. Instead, the purchaser would need to take a first action to advance from the menu page to the product page, and then a second action to place the order. ***We are not prepared to assign a meaning to a patent claim that depends on the state of mind of the accused infringer***.

Amazon.com, Inc. v. Barnesandnoble.com, Inc., 239 F.3d 1343, 1353 (Fed. Cir. 2001) (emphasis added and omitted). This Court should reject them here as well.

Roche's argument thus hangs on a portion of a single dictionary definition. Roche's definition states that "effectiveness" is "[t]he ability to cause the expected or intended effect or result." (Docket No. 172, Ex. B at 4 (citing Rhyu Decl., Ex. 20, Taber's Cyclopedic Medical Dictionary 608 (17th ed. 1993).) Other dictionary definitions of "effectiveness," however, do not mention intent. (*E.g.*, Rhyu Decl., Ex. 18 at STAN 31821 (defining "effectiveness" as "the ability to produce a specific result or to exert a specific measurable influence"); *id.*, Ex. 19 at STAN 31872 (defining "effective" as "capable of bringing about an effect: productive of results").) Roche would have the Court improperly choose the only aspect of these definitions

that *varies* among the definitions. This is improper. *See, e.g.*, *Anderson v. Int'l Eng'g & Mfg., Inc.*, 160 F.3d 1345, 1348-49 (Fed. Cir. 1998) (noting conflicting dictionary definitions and stating that the conflicts "reinforce the observation that dictionary definitions of ordinary words are rarely dispositive of their meaning in a technological context"); *Hoechst Celanese Corp. v. BP Chems. Ltd.*, 78 F.3d 1575, 1580 (Fed. Cir. 1996) (rejecting reliance on dictionary definitions where definitions "do not distinguish in a dispositive manner between the contested technical meanings").

Furthermore, when Roche's dictionary definition is applied in context, as required under the law, it supports Stanford's construction. *See Linear Tech. Corp. v. Impala Linear Corp.*, 379 F.3d 1311, 1324 (Fed. Cir. 2004) (reversing claim construction that relied on definition of "simultaneous" while ignoring context of the remaining words in the term); *Phillips*, 415 F.3d at 1314 (collecting cases re context); *id.* at 1321 (rejecting over-reliance on dictionary definitions because they "focus[] the inquiry on the abstract meaning of words rather than on the meaning of claim terms within the context of the patent"). Here, the definition of "effectiveness" must be applied in the context of the claims, which refer to the effectiveness of antiretroviral agents and anti-HIV therapy. Thus, the context of the claims shows that the "intended effect" is to provide therapeutic benefits with regard to an HIV infection. (Volberding Decl., ¶ 9; *see* '730 patent at 2:14-52, 2:64-3:6, 7:50-8:14, 12:57-13:32 (describing therapeutic benefits).) Indeed, in cases in which the Federal Circuit has considered "effective" and "therapeutically effective" amount terms, it has construed them contextually by reference to the other words in the claims, not by applying dictionary definitions. *E.g.*, *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1303 (Fed. Cir. 2006) (holding that "[a] therapeutically effective amount is one that elicits any one or all of the effects often associated with in vivo biological activity of natural EPO"), *cert. denied*, 127 S. Ct. 2270 (2007).

Roche's second improper limitation seeks to require that a specific action be taken by a physician, such as choosing to modify or not modify treatment. (Docket No. 172, Ex. B at 4.) Such a requirement lacks any basis in the claim. *See, e.g.*, *Hoganas AB v. Dresser Indus., Inc.*, 9 F.3d 948, 950 (Fed. Cir. 1993) (holding that "extraneous limitations," *i.e.*, limitations that

have no textual basis, may not be imported and reversing district court's construction that imported an extraneous size limitation into the term "straw-shaped") (internal quotation omitted); *see also Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1248-49 (Fed. Cir. 1998) ("Without any claim term that is susceptible of clarification by the written description, there is no legitimate way to narrow the property right."). Here, the terms "therapeutically effective" and "therapeutically ineffective" are used in the patent to describe characteristics of antiretroviral agents or anti-HIV agents, not to refer to actions subsequent to assessing effectiveness, such as modifying treatment. (*See, e.g.*, '730 patent, claim 1 ("antiretroviral agent is therapeutically effective").)

Stated another way, Roche's construction should be rejected because it tries to replace an adjective with a verb. *E.g.*, *Network Appliance, Inc. v. Bluearc Corp.*, No. 03-5665 MHP, 2004 U.S. Dist. LEXIS 28344, at *68-69 (N.D. Cal. Nov. 30, 2004) (Patel, J.) (rejecting claim construction that would "replace the noun 'multi-tasking interface' with a verb"). The Federal Circuit has rejected such strained interpretations because they defy basic rules of grammar. *See Credle v. Bond*, 25 F.3d 1566, 1571-72 (Fed. Cir. 1994) (rejecting the appellant's attempt to construe an adjective ("description" of a bag) as a verb (importing a "method step") because that construction was "at war with its grammar and syntax and thus would force an unreasonable interpretation").

Roche's construction also violates the well-established rule that "[i]n examining the specification for proper context, . . . this court will not at any time import limitations from the specification into the claims." *Varco, L.P. v. Pason Sys. USA Corp.*, 436 F.3d 1368, 1373 (Fed. Cir. 2006) (internal quotation omitted). Here, the specification discusses altering treatment only as an example. Indeed, the quotation in Roche's claim chart occurs in a paragraph that begins "[i]n particular embodiments of the invention." ('730 patent at 2:40; Docket No. 172, Ex. B at 3 (quoting '730 patent at 2:45-49).) *Varco, L.P.*, 436 F.3d at 1375 (refusing to import limitation where specification used term "[i]n the preferred embodiment") (emphasis omitted). The arbitrariness of importing a limitation regarding modifying treatment is highlighted by the fact that Roche ignores other aspects of preferred embodiments. For example, the specification

describes "identif[ying], at an early stage, patients whose infection has become resistant to a particular antiretroviral drug regimen."[15] ('730 patent at abstract, 1:21-25; *see also id.* at 2:14-52, 2:64-3:6, 7:50-8:14.)

Roche's construction also conflicts with the understanding of persons of ordinary skill at the time of the invention. (*See* Volberding Decl., ¶¶ 10-12.) Such persons would not read the claim terms as preventing treatment from being modified if testing suggests the treatment is effective and vice-versa. It was well known that a treatment may properly be modified for a number of reasons, even if testing suggests that the treatment is effective. (*Id.*, ¶ 10.) For example, a particular patient may have unacceptably severe side effects from an otherwise effective antiretroviral agent or may be unwilling or unable to adhere to particular requirements for taking the agent. (*Id.*) Further, a change in other medications taken by a patient may be incompatible with an otherwise effective antiretroviral agent. (*Id.*) Likewise, it was well-known in the art at the time that a patient's failure to comply with, or to understand, the treatment regimen may yield tests suggesting the therapy is ineffective. (*Id.*, ¶ 11.) In such situations, a change in treatment is not necessarily required, but instead the treatment regimen may be further explained or the patient encouraged to comply with the regimen. (*Id.*) Accordingly, because the specification mentions altering treatment only as one example, it may not be imported as a limitation into the specification.[16] *In re Omeprazole Patent Litig.*, 483 F.3d 1364, 1372 (Fed. Cir. 2007) ("Absent some clear intent to the contrary, this court does not import examples from the specification into the claims.").

Finally, Roche attempts to import a "medical effect" limitation into the terms. Roche has not identified any intrinsic evidence or written extrinsic evidence in which the term

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[15] Indeed, Roche also tries to import this characteristic of drug resistance from an example in the specification, but only into the term "therapeutically ineffective." Persons of ordinary skill at the time of the invention, however, would not have understood therapeutic ineffectiveness to arise only due to drug resistance or therapeutic effectiveness to be due only to the absence of drug resistance. (Volberding Decl., ¶¶ 10, 12.)

[16] Roche's construction should also be rejected because it is vague. *See Nikon Corp. v. ASM Lithography B.V.*, 308 F. Supp. 2d 1039, 1072 (N.D. Cal. 2004) (Patel, J.) (rejecting proposed definition that would merely "substitute one imprecise verbal formula for another").

"medical effect" was used or explained. (*See* Docket No. 172, Ex. B at 4.) Thus, Roche has provided no basis to import the term "medical effect" and no suggestion as to what that term might mean in the context of these patents. *See Nikon Corp. v. ASM Lithography B.V.*, 308 F. Supp. 2d 1039, 1072 (N.D. Cal. 2004) (Patel, J.) (claim constructions that "contribute nothing but meaningless verbiage" should be avoided) (internal quotation omitted).

Accordingly, the Court should either adopt the plain meaning of these terms or adopt Stanford's constructions.

B. "an antiretroviral agent" ('730 patent, claims 1, 5-9, 13-14, 18-19, 23; '705 patent, claims 1, 5-10; '041 patent, claims 1-3, 8)[17]

Stanford's Construction	Roche's Construction
"at least one substance having or capable of having an effect against a retrovirus, such as HIV"[18]	"antiretroviral agents available to doctors for the treatment of AIDS/HIV infected patients in 1992"

The Court should adopt Stanford's construction for the term "an antiretroviral agent" to make clear for the jury that the word "an" has an established patent law meaning of "at least one." *E.g.*, *Free Motion Fitness, Inc. v. Cybex Int'l, Inc.*, 423 F.3d 1343, 1350 (Fed. Cir. 2005) ("'[A]' or 'an' in patent parlance carries the meaning of 'one or more' in open-ended claims containing the transitional word 'comprising.' This convention is overcome only when the claim is specific as to the number of elements or when the patentee evinces a clear intent to . . . limit the article.") (internal quotations and citations omitted; alterations in original). In this case, "an" means "at least one" because the transitional word "comprising" is used in each of the independent claims. Roche does not appear to dispute this point, using the plural "antiretroviral ***agents***" in its construction. (Docket No. 172, Ex. B at 2 (emphasis added).)

If this point is not explained, the jury may be confused about the applicability of the

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

[18] Stanford has eliminated the words "intended to have" from its construction of the claim term "an antiretroviral agent." This deletion does not change the substance of the construction disclosed by Stanford in the parties' joint statement (Docket No. 172).

patents-in-suit to combination therapy. (*See, e.g.*, '730 patent at 7:63-8:14, 9:46-48, 13:9-11 (referring to combination therapy).) Indeed, this very issue was addressed by the *Visible Genetics* court, which rejected the defendant's arguments that the claims of the related patents at-issue in that case were limited to monotherapy because the term "an" is singular. *Bd. of Trs. of the Leland Stanford Junior Univ. v. Visible Genetics, Inc.*, No. 01-3671 CRB, slip op. at 8 (N.D. Cal. Aug. 28, 1992) (Breyer, J.) (construing "an antiretroviral agent" as meaning "being treated with at least one agent having an effect against a retrovirus, such as HIV"), Rhyu Decl., Ex. 21.

Roche's attempt to restrict antiretroviral agents to those available in 1992 is improper and should be rejected. Indeed, rather than offering a meaning for the term, Roche simply repeats the term "antiretroviral agent" in its construction and then adds the time limitation. But there is nothing about the ordinary and customary meaning of "antiretroviral agent" that is limited to agents "available to doctors for the treatment of AIDS/HIV infected patients in 1992."[19] (Volberding Decl., ¶¶ 13-16.) Dictionary definitions from the time of the invention confirm a plain meaning that is not temporally limited. (*E.g.*, Rhyu Decl., Ex. 17 at STAN 31811 (defining "agent" as "something that produces or is capable of producing an effect"); *id.*, Ex. 17 at STAN 31814 (defining "retrovirus," in pertinent part, as "any of a group of RNA-containing viruses (as the Rous sarcoma virus and the HTLV causing AIDS)").)[20] Roche has not identified any written extrinsic evidence contradicting that general definition.[21]

The inappropriateness of imposing a temporal limitation here is confirmed by the Federal Circuit's decision in *SuperGuide Corp. v. DirecTV Enterprises*, 358 F.3d 870 (Fed. Cir.

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[19] Roche's construction is also unduly limited because the term "antiretroviral" refers to retroviruses generally, not only to HIV. (*E.g.*, Rhyu Decl., Ex. 22 at STAN 6372-73.)

[20] The meaning of the term "antiretroviral agent" remains the same today as on the priority date of the patents-in-suit. (*See, e.g.*, Rhyu Decl., Ex. 23 at STAN 34159-62 (defining "antiretroviral" as "acting, used, or effective against retroviruses;" defining "retrovirus" as "any of the family *Retroviridae* of single-stranded RNA viruses -- called also RNA tumor virus;" and "agent" as "something that produces or is capable of producing an effect").)

[21] The term "an antiretroviral agent" does not include any "implicitly time-dependent" language that might justify a temporal limitation, such as the term "traditionally" in the patent claims in *PC Connector Solutions LLC v. SmartDisk Corp.*, 406 F.3d 1359, 1362-63 (Fed. Cir. 2005).

2004). There, the district court limited the term "regularly received television signal" to analog signals based on its view of the state of the art at the time of the invention. *Id.* at 876. The Federal Circuit reversed, holding that the district court erred in "conclud[ing] that later or 'after-arising technologies' cannot fall within the literal scope of the claim at issue," because the claims "are not necessarily limited to that disclosed in the specification but rather are defined by the language of the claims themselves."[22] *Id.* at 878; *cf. SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1121 (Fed. Cir. 1985) (en banc) (en banc) ("The law does not require the impossible. Hence, it does not require that an applicant describe in his specification every conceivable and possible future embodiment of his invention."). Thus, the *SuperGuide* court held that "[t]he form of the television signal is irrelevant; it could be an analog signal, a digital signal, some combination of the two, *or another format*."[23] 358 F.3d at 881 (emphasis added). Correspondingly, in the current analysis, substances having or capable of having an effect against a retrovirus, such as HIV, are encompassed within the term "antiretroviral agent," irrespective of when they were developed.

Inexplicably, Roche relies on a single sentence from the specification, which actually contradicts its argument for a time limitation. (Docket No. 172, Ex. B at 2.) The sentence states that "[a]ntiretroviral agent, as used herein, ***includes*** any known antiretroviral agent including, but not limited to, dideoxynucleosides." ('730 patent at 8:39-41 (emphasis added).) The use of the term "includes" demonstrates that the specification is merely providing an example and is not limiting. Roche's construction would improperly read out the term "includes" from the

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[22] As an alternative ground for its decision, the *SuperGuide* court also held that "those skilled in the art knew both formats could be used for video" at the time of the invention. 358 F.3d at 880.

[23] Another case closely on point is *Marsh-McBirney, Inc. v. Montedoro-Whitney Corp.*, 882 F.2d 498 (Fed. Cir. 1989), *vacated on other grounds*, *Montedoro-Whitney Corp. v. Marsh-McBirney, Inc.*, 498 U.S. 1061 (1991), *opinion reinstated in pertinent part*, *Marsh-McBirney, Inc. v. Montedoro-Whitney Corp.*, 939 F.2d 969, 970 (Fed. Cir.). In that case, the patent was directed to a "probe" for monitoring the average velocity of sewage. *Marsh-McBirney, Inc.*, 882 F.2d at 504. The district court based a noninfringement finding on the fact that the accused device used a newly developed type of probe, a bi-directional acoustic probe. *Id.* The Federal Circuit reversed, holding that "[a]dvances subsequent to the patent may still infringe" and that "whether the velocity sensors are electromagnetic or acoustic, bi-directional or not, they are 'probes' encompassed by" the relevant claim term. *Id.*

specification and replace it with something that requires "only" the listed examples. In *Amgen, Inc.*, the Federal Circuit rejected such a result, reasoning:

> [T]he district court also determined that the specification indicates that the invention is limited to products that are "therapeutically effective" with respect to patients with anemia-like disorders, such as those listed at column 33, lines 22-28 of the '422 patent. For this determination, the court relied on a passage that recites several diseases that may be treated by the claimed invention. The passage begins, "Included within the class of humans treatable with products of the invention . . . ." ***However, this passage does not state that the claims encompass only products that treat such patients. Rather, by using the non-limiting word "included," it suggests some persons, but not all persons, who may benefit from the invention.***

See Amgen Inc., 457 F.3d at 1302 (reversing the district court's inclusion of a limitation to anemia-like diseases) (emphasis added; citations omitted; alteration in original).[24] This Court should reject Roche's argument as well.

Accordingly, Stanford's construction of "an antiretroviral agent" should be adopted. Alternatively, even if the Court were to impose a time limitation, there is no basis to limit antiretroviral agents to those that were "available to doctors for the treatment of AIDS/HIV infected patients in 1992" as proposed by Roche. Instead, the claims would need to include all potential types of antiretroviral agents appreciated by those of skill in the art at the time. (*See* Volberding Decl., ¶¶ 15-16.)

C. "measuring the HIV RNA copy number" ('730 patent, claims 9, 14, 19; '705 patent, claims 1, 8)

Stanford's Construction	Roche's Construction
No construction necessary. Alternatively, "estimating the number of copies of an HIV RNA sequence by evaluation"	"techniques available in May 1992 to quantify HIV RNA copy number using PCR, specifically the assay in the 1991 JID article as set forth in the specification"

As with many other claim terms, no construction is necessary for this term because the plain meaning suffices to guide the jury in its fact-finding.

[24] Moreover, Roche's construction improperly misinterprets this sentence from the specification, which says "known," not "known at the time of the invention."

If the Court construes this term, it should reject Roche's attempt to import two limitations, a time limitation to "techniques available in May 1992" and an assay limitation to the "assay in the 1991 JID article as set forth in the specification." (*See* Docket No. 172, Ex. B at 6.)

Roche's request for a time limitation to "techniques available in May 1992" should be rejected for the same reasons discussed in the previous section for the term "an antiretroviral agent." In short, Roche's construction should be rejected because nothing about the ordinary and customary meaning of the words in the claim term is limited to techniques available in 1992, *i.e.*, the words are not explicitly or implicitly "time-dependent." *Compare SuperGuide Corp.*, 358 F.3d at 878-81 (refusing to limit ordinary and customary meaning of "regularly received television signal" to signal format predominant at the time of the invention), *with PC Connector Solutions LLC*, 406 F.3d at 1362-63 (limiting computer ports to those in existence at the time of the invention because claim used the term "***traditionally*** connectible," which is "implicitly time-dependent") (emphasis added). (*E.g.*, *id.*, Ex. 24 at STAN 31859 (defining "measure" as "[t]o estimate by evaluation or comparison").)[25] Roche again cites no written extrinsic evidence to support its narrowing limitation.

Moreover, Roche's cited evidence from the specification refers solely to examples and, therefore, does not support importing into the claim language either a time limitation or a limitation to a particular assay described in the specification. *See DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (refusing to interject limitation different from how the disputed term "would ordinarily and customarily be understood"). Roche quotes one sentence of the specification, but omits the language from the beginning of the paragraph in which the sentence occurs, which states "[i]n a preferred, nonlimiting embodiment of the invention." ('730 patent at 4:63; Docket No. 172, Ex. B at 6 (quoting '730 patent at 5:32-36).) Roche also cites to other portions of the specification, but

[25] The definition of "measure" has not changed over time since the patent's priority date. (*See, e.g.*, Rhyu Decl., Ex. 23 at STAN 34163-64 (defining "measure" as "to ascertain the measurements of").) *C.R. Bard, Inc.*, 388 F.3d at 862-63; *W.E. Hall Co.*, 370 F.3d at 1350.

expressly admits that these are "quantification examples." (Docket No. 172, Ex. B at 6 (citing '730 patent at 4:1-5:55).) Examples from the specification do not limit the claims. *In re Omeprazole Patent Litig.*, 483 F.3d at 1372; *Great Plains Lab., Inc. v. Metametrix Clinical Lab.*, No. 04-2125-JTM, 2006 WL 2663680, at *9-10 (D. Kan. Sept. 15, 2006) (refusing to import requirement of using "Gas Chromatography-Mass Spectrometry" where claim used term "analyzing"); *cf. also Phillips*, 415 F.3d at 1323, 1324-27 ("[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.").

Finally, there is no basis for limiting the term to the assay described in the JID article Rhyu Decl., Ex. 14). As an initial matter, the assay actually disclosed as an example in the patents is different from the assay described in the JID article. (*Compare, e.g.*, '730 patent at 10:34-68, *with* Rhyu Decl., Ex. 14 at 863 (section titled "Enzyme-linked affinity assay").) The specification also refers to a variety of methods that were not used in the JID article. In particular, the JID article describes the use of a colorimetric measurement technique, while the specification explicitly recites a number of different techniques. (*See* '730 patent at 4:60-64 ("Probe may be detectably labeled by an enzyme, a radioisotope, a fluorescent compound, a chromogenic compound, or ***any other detectably labeled compound***.") (emphasis added).)

The Court need not construe the "measuring" term. If it does construe the term, it should adopt Stanford's construction.

D. "presence of detectable HIV-encoding nucleic acid" and "absence of detectable HIV-encoding nucleic acid" ('730 patent, claims 1, 6-8; '041 patent, claims 1-3)

Stanford's Construction	**Roche's Construction**
<u>presence of detectable HIV-encoding nucleic acid</u> No construction necessary. Alternatively, "the existence or occurrence of HIV-encoding nucleic acid above the lower level of sensitivity of the quantitative PCR assay"	<u>presence of detectable HIV-encoding nucleic acid</u> "qualitative result indicating greater than 40 copies of HIV RNA per ml"

Stanford's Construction	Roche's Construction
absence of detectable HIV-encoding nucleic acid No construction necessary. Alternatively, "the non-existence of HIV-encoding nucleic acid above the lower level of sensitivity of the quantitative PCR assay"	absence of detectable HIV-encoding nucleic acid "qualitative result indicating less than 40 copies of HIV RNA per ml"

No construction is necessary for these terms because the plain meaning is sufficient to guide the jury's fact-finding.

If the Court decides to construe the term, there are two disputes that should be resolved in Stanford's favor. First, the parties dispute the meaning of the term "detectable." This term properly refers to "the lower level of sensitivity" of whatever assay is actually used in practicing the claimed methods. (*See* '730 patent at 5:29-31 ("lower level of positivity"), 10:67-68 ("lower level of sensitivity"), 12:43-44 ("lower level of detection").) Roche, however, seeks to import a limitation that "detectable" refers exclusively to the specific detection limit of an example used in the specification, which Roche claims is "40 copies of HIV RNA per ml."[26] (Docket No. 172, Ex. B at 5.) The Court should reject Roche's proposed construction because the claims are not limited to the JID assay or any other assay example given in the specification for the reasons detailed in the immediately preceding section. *See, e.g.*, *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1370-71 (Fed. Cir. 2003) (refusing to limit term "improved competence" specifically to tenfold increases in performance).

In addition, Roche's attempt to interject a specific copy number limitation ignores the plain claim terms used by the patentee. The claims show that, when the patentee wanted to recite specific copy number limitations, it did so. (*E.g.*, '730 patent, claim 9.) Thus, it is improper to add such a limitation when one does not already exist in the claims. *See Dayco Prods., Inc. v. Total Containment, Inc.*, 258 F.3d 1317, 1328 (Fed. Cir. 2001) (refusing to read

[26] Under no circumstances is "40 copies of HIV RNA ***per mL***" supported by the specification. In support of its construction, Roche cites to a passage of the specification that identifies the detection limit in the specification example as "40 copies/***200 µl***" [microliter], not per ml [milliliter]. (Docket No. 172, Ex. B at 5 (citing '730 patent at 12:51) (emphasis added).)

in limitation requiring "plurality of recesses" where patentee explicitly included the term "plurality of . . . projections"); *see also Jack Guttman, Inc. v. Kopykake Enters.*, 302 F.3d 1352, 1358 (Fed. Cir. 2002) (construing claim term "non-tortuous" as allowing for curves based, in part, on other independent claims being expressly limited to a "substantially straight copy path").

Roche also seeks to import a requirement that the term refer to a "qualitative result." (Docket No. 172, Ex. B at 5.) The intrinsic record, however, flatly contradicts Roche's argument. The specification refers to the invention using the term "quantitative" throughout but nowhere even mention the term "qualitative." (*E.g.*, '730 patent at 4:53-57, 10:34-40, 12:58-60.) Indeed, the patents and prosecution histories explicitly distinguish an article by Ottmann as being non-quantitative. The specification states that "[a]lthough sensitivity is increased with increased cycle number, thus detecting signal in virtually all patients, the ability to show the ***quantitative changes demonstrated here*** with 30 cycles of amplification is lost." (*Id.* at 14:24-28 (emphasis added).) Similar statements are made in the prosecution histories. For example, in initially rejecting each of the claims of the '730 patent, the Patent Examiner relied on Ottmann as prior art. In distinguishing that article, the patentee argued:

> As discussed in the instant specification at page 28, Ottmann detected HIV RNA in plasma from 24 out of 25 patients who were receiving AZT. This contrast between Ottmann and the presently claimed invention is attributable to methodological differences. These differences, in part, prevented Ottmann from being able to show ***the quantitative results exhibited by the claimed invention*** . . . .

(Rhyu Decl., Ex. 25 at STAN 1435 (emphasis added).) Further:

> ***Using a non-quantitative PCR assay***, Ottmann found that HIV nucleic acid could be detected in serum or plasma regardless of antiretroviral treatment or disease status. . . . The results show that this method [Ottmann] is suitable for the detection of viral particles in plasma or serum from HIV-1-infected individuals irrespective of antiretroviral treatment.

(*Id.* at STAN 1458 (emphasis added).) Thus, the prosecution history makes clear that the results obtained in using the claimed method are quantitative, not qualitative. Indeed, the non-quantitative results from Ottmann taught away from the present invention because the Ottmann

test generated positive signals for patients undergoing treatment as well as those who had no treatment.

Roche has cited no relevant evidence to the contrary. Instead, Roche's identification of intrinsic evidence is limited to two inapposite portions of the specification that relate solely to the detection limit associated with an example described in the specification. (Docket No. 172, Ex. B at 5.) Further, as detailed above, it would be improper to limit the claims to these embodiments.

Accordingly, the Court should adopt the plain meaning of these terms or Stanford's constructions.

E. "collecting statistically significant data useful for determining whether a decline in HIV RNA copy numbers exists," "statistically significant data," and "statistically significant decline" ('705 patent, claims 1, 6-8)

Stanford's Construction	**Roche's Construction**
collecting statistically significant data useful for determining whether a decline in HIV RNA copy numbers exists "gathering data from the patient and/or other sources that is useful in assessing whether any decline in HIV RNA copy number was not the result of chance"[27]	collecting statistically significant data useful for determining whether a decline in HIV RNA copy numbers exists "collecting statistically significant data upon which a physician should rely in order to make a medical diagnosis about a patient"
statistically significant data No separate construction necessary. Alternatively, see *supra* "collecting statistically significant data useful for determining whether a decline in HIV RNA copy numbers exists"	statistically significant data "the probability that the relationship between data is not due to chance. The patent specification does not define any probability value for this data"
statistically significant decline "a decrease that is large enough, by itself or when compared to other data, that it was not likely the result of chance"	statistically significant decline "data upon which a physician should rely in order to make a medical diagnosis about decline of HIV. The patent specification does not define any probability value for this data"

[27] Stanford has added the word "not" into its construction of the claim term "collecting statistically significant data useful for determining whether a decline in HIV RNA copy numbers exists." This addition does not change the substance of the construction disclosed by Stanford in the parties' joint statement (Docket No. 172).

Stanford's proposed constructions for these terms should be adopted. Stanford's proposed constructions address two general issues. First, as the parties appear to agree, statistical significance refers to the likelihood that the result-in-question was or was not the result of chance. (*Compare* Stanford's construction of "collecting statistically significant data useful for determining whether a decline in HIV RNA copy numbers exists" as "gathering data from the patient and/or other sources that is useful in assessing whether any decline in HIV RNA copy number was ***not the result of chance***") (emphasis added), *with* Roche's construction of "statistically significant data" in part as "the probability that the relationship between data is ***not due to chance***") (emphasis added).) The agreement between the parties' constructions coheres with the ordinary and customary meaning of statistical significance. (*See* Rhyu Decl., Ex. 18 at STAN 31825 (defining "significant" as "in statistics, probably resulting from something other than chance"); *id.*, Ex. 17 at STAN 31815 (defining "significant" as "probably caused by something other than mere chance").)

Second, an issue raised by the claim terms is whether collecting information obtained from a patient and from other sources is within the literal scope of the claimed inventions. Stanford's constructions make clear that "collecting statistically significant data" includes "gathering data from the patient and/or other sources" and that a "statistically significant decline" refers to "a decrease that is large enough, by itself or when compared to other data." (Docket No. 172 at 3.) These constructions are consistent with the understanding of persons of ordinary skill. (*See* Volberding Decl., ¶ 17.) Roche's constructions do not contain any language disputing this point.

Accordingly, Stanford's proposed constructions for the three disputed terms relating to statistical significance should be adopted. Roche's proposed constructions, however, should be rejected because they conflict with the ordinary and customary meaning of the terms and improperly attempt to import limitations.

As to the term "collecting statistically significant data useful for determining whether a decline in HIV RNA copy numbers exists," Roche would have the Court improperly construe this term as meaning "collecting statistically significant data upon which a physician should rely

in order to make a medical diagnosis about a patient." (Docket No. 172, Ex. B at 7.) Roche's construction improperly reads in "physician" and "medical diagnosis" limitations. *See, e.g.*, *Renishaw PLC*, 158 F.3d at 1248-49; *Hoganas AB*, 9 F.3d at 950. Further, Roche's construction inappropriately reads out the portion of the claims that recite a decline in HIV RNA copy number. *See Aero Prods. Int'l, Inc. v. Intex Recreation Corp.*, 466 F.3d 1000, 1013 (Fed. Cir. 2006) (refusing to read out claim term "substantially" or render it illusory). Roche's construction also improperly changes the plain meaning of the claim term "useful" to mean "should," *i.e.*, required. *Hoganas AB*, 9 F.3d at 950. Finally, Roche's construction obfuscates rather than clarifies the meaning of the claim. It is unclear what Roche's limitation regarding "data upon which a physician should rely" means or how a jury could determine that fact. *See Nikon Corp.*, 308 F. Supp. 2d at 1072. Accordingly, Roche's construction should be rejected and Stanford's adopted.

As described above, Stanford seeks to define "statistically significant data" to be consistent with the construction of the term as used in the phrase "collecting statistically significant data useful for determining whether a decline in HIV RNA copy number exists." Specifically, such data demonstrate whether a particular observation is or is not the result of chance. In contrast, Roche's construction does not address the meaning of the term. For example, Roche apparently defines "statistically significant data" as "the probability that the relationship between data is not due to chance." But Roche provides no support for the suggestion that the data itself is a probability. That phrasing simply does not fit the claim language. *See Schoenhaus v. Genesco, Inc.*, 440 F.3d 1354, 1357 (Fed. Cir. 2006) (inserting competing constructions into claim language and holding that a construction which "renders claim 2 nonsensical . . . cannot be correct"); *Apple Computer*, No. 06-0019 MHP, 2007 WL 1342504, at *10 (rejecting proposed construction that would render claims nonsensical).

Roche's construction is further improper because it adds an irrelevant statement regarding the patent specification, interjecting that "[t]he patent specification does not define any probability value for this data." Such fact-findings are inappropriate as claim construction definitions. *See id.* at *11-12; *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1355 (Fed.

Cir. 1998) (refusing to find infringement-related facts on claim construction even where claims "us[e] terminology that is not as precise or specific as it might be"). To the extent Roche is seeking to make clear that the claims are not limited to a specific statistical "p-value," such as 1%, 5%, or 10%, this only confirms the unnecessary complexity injected by Roche's definition. This point is unnecessary because there is no limitation under Stanford's construction to a specific p-value. Thus, the second part of Roche's construction should be rejected because it is either improper or unnecessary.

Finally, Roche's construction of "statistically significant decline" compounds its errors by combining its improper constructions for the other two terms addressed in this section. Roche's construction of "statistically significant decline" has two parts. Roche takes the first part of its construction of "statistically significant decline" from its construction of "collecting statistically significant data useful for determining whether a decline in HIV RNA copy numbers exists." This construction is inappropriate, because nothing in the term "statistically significant decline" allows for the importation of the limitations "physician," "should rely," "medical diagnosis," or "decline of HIV." *Hoganas AB*, 9 F.3d at 950. Indeed, these extra limitations make little sense when inserted into the claims they are intended to clarify. For example, if the first part of Roche's construction is inserted into claim 1 of the '705 patent, it would read "evaluating whether ~~a statistically significant decline~~ data upon which a physician should rely in order to make a medical decision about decline of HIV in plasma HIV RNA copy numbers exists in evaluating the effectiveness of anti-HIV therapy of a patient." *See Schoenhaus*, 440 F.3d at 1357. This does not result in a further explanation of a claim, but instead improperly changes the meaning of the claim into something that can hardly be understood. Roche takes the second part of its construction of "statistically significant decline" verbatim from the second part of its construction of "statistically significant data." That language should be rejected for the same reasons as described above, *i.e.*, it is either improper or unnecessary.

V. 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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