Genentech, Inc. et al v. Sanofi-Aventis Deutschland GMBH et al Doc. 604

United States District Court
For the Northern District of California

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5 IN THE UNITED STATES DISTRICT COURT
6 FOR THE NORTHERN DISTRICT OF CALIFORNIA
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8 SANOFI-AVENTIS DEUTSCHLAND GMBH,
9 Plaintiff,
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11 v.
12 GENENTECH, INC. and BIOGEN IDEC INC.,
13 Defendants.
14
15 ______________________________________/

No. C 08-4909 SI; C 09-4919 SI

ORDER GRANTING SANOFI'S MOTION TO AMEND INFRINGEMENT CONTENTIONS; DENYING GENENTECH'S MOTION TO STRIKE; GRANTING IN PART GENENTECH'S MOTION FOR SUMMARY JUDGMENT OF NON-INFRINGEMENT; GRANTING IN PART SANOFI'S RULE 56(f) MOTION; AND GRANTING IN PART AND DENYING IN PART SUMMARY JUDGMENT MOTIONS RE: INVALIDITY AND INEQUITABLE CONDUCT

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18 Now before the Court are numerous motions in this case. For the reasons set forth below, the
19 Court GRANTS Sanofi's motion to amend infringement contentions, DENIES Genentech's motion to
20 strike, GRANTS IN PART Genentech's motion for summary judgment of non-infringement, GRANTS
21 IN PART Sanofi's motion for a Rule 56(f) continuance, and GRANS IN PART AND DENIES IN
22 PART the parties' motions for summary judgment regarding invalidity and inequitable conduct.
23
24 **BACKGROUND**
25 On April 1, 2010, plaintiff Sanofi-Aventis Deutschland GMBH ("Sanofi") filed an amended
26 complaint against defendants Genentech, Inc. ("Genentech") and Biogen IDEC, Inc. ("Biogen"). Sanofi
27 alleges that Genentech and Biogen have infringed U.S. Patent No. 5,849,522 (the "'522 patent"), entitled
28 "Enhancer for Eukaryotic Expression Systems," and U.S. Patent No. 6,218,140 (the "'140 patent"),

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which is also entitled "Enhancer for Eukaryotic Expression Systems."[1] The patents-in-suit relate to using certain DNA sequences known as enhancers that were identified in human cytomegalovirus ("HCMV"). Sanofi alleges that Biogen and Genentech have infringed the '522 and '140 patents by using the patented enhancers in the manufacture and sale of two pharmaceuticals, Rituxan® and Avastin®.

Deoxyribonucleic acid (DNA) contains the genetic code for all living organisms. To turn this code into proteins that can actually be used by a given organism, the completion of a multi-step process is required. Within an individual cell, the DNA is first "transcribed" into ribonucleic acid (RNA). Transcription is performed by a molecule called RNA Polymerase, which "reads" the DNA and helps to produce a complementary RNA strand. Once the complementary RNA strand has been produced, it is "translated" by cellular structures called ribosomes. Ribosomes decode the RNA into amino acids, which are the building blocks of proteins.

An enhancer is a segment of DNA that, along with associated proteins, can serve to increase the transcription of RNA from DNA. Enhancers are thought to act in concert with RNA Polymerase and other molecules called transcription factors to facilitate transcription. Some of the strongest known enhancers have been derived from viruses, which attack other organisms by taking over the cellular machinery and using it to produce proteins that the virus needs in order to reproduce. Although enhancers are often found immediately upstream[2] of the affected gene, they can also be effective despite being located thousands of base-pairs[3] away. Developments in biotechnology in the last thirty years

[1] Defendants' expert Dr. Levine explains the distinction between prokaryotic and eukaryotic organisms as follows: "Generally, prokaryotic organisms are simpler than eukaryotic organisms. Bacteria such as *E. coli* are examples of prokaryotic organisms. Eukaryotic organisms range from fairly simple – yeast, for example – to very complex, such as humans. Typically, the DNA of an organism is organized into one or more chromosomes. Prokaryotes typically have a single chromosome, while eukaryotes typically have multiple chromosomes. A distinguishing feature of eukaryotic organisms is that they have a discrete nucleus containing their chromosomes." Levine Decl. ¶ 13.

[2] The terms "upstream" and "downstream" are a means of describing directionality on a strand of DNA. When looking at a diagram of a DNA sequence, "upstream" is equivalent to the "5' direction" or "left," and "downstream" is equivalent to the "3' direction" or "right."

[3] The term "base-pair" is a reference to the structure of DNA. DNA is a double-stranded molecule; the two strands come together through the binding of two complementary base pairs. A DNA molecule may consist of thousands of base-pairs, connected into a long strand. Base-pairs are the

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have led to the use of enhancers in the production of pharmaceutical products. If an enhancer can be artificially introduced into a cell that produces a drug, that cell will be able to produce the drug at a much higher rate than would normally be possible. The level of efficiency created by genetic enhancers is, in part, what makes large scale pharmaceutical production possible.

Sanofi's predecessor, Behringwerke AG, filed the original U.S. application for the '522 and '140 patents on August 23, 1985.[4] The two patents share the same six inventors and the same single-page specification. The patents were prosecuted for more than a decade, with the '522 patent issuing in 1998 and the '140 patent issuing in 2001.

On August 6, 1992, Sanofi and Genentech entered into a license agreement which gave Genentech a nonexclusive license to a patent portfolio including the '522 and '140 patents.[5] In exchange for the license, Genentech was obligated to pay an annual fee to use the patents for research purposes, as well as royalties on all commercial products that utilized the patents. Genentech made the annual fee payments until 2008, but never paid Sanofi royalties. On June 30, 2008, Sanofi sent Genentech a request for information about whether any of Genentech's commercial products utilized the patents, and also to request that Genentech pay royalties due for such products. Genentech provided notice to Sanofi that the License Agreement was terminated, effective on October 27, 2008.

On October 27, 2008, Sanofi filed a complaint in the U.S. District Court for the Eastern District of Texas against defendants Biogen and Genentech alleging infringement of the HCMV enhancer patents. The same day, Genentech and Biogen filed a complaint in the Northern District of California requesting declaratory judgment of invalidity and non-infringement of the HCMV enhancer patents. Those two actions have been consolidated and are now before this Court.

The accused products are Rituxan® and Avastin®. Rituxan® is an antibody used in the treatment of non-Hodgkins lymphoma, chronic lymphocytic leukemia, and rheumatoid arthritis.

default measure of distance on a DNA strand, which scientists can use to specify the location of a genetic element.

[4] The patents originated from a German Patent Application No. DE 34 31 140.8, which was filed with the German Patent Office on August 24, 1984.

[5] The license agreement was for the prospective use of the patents when the patents issued.

Avastin® is an antibody used in the treatment of lung, colorectal, kidney and brain cancer. Both antibodies are produced by Chinese hamster ovary ("CHO") cell lines.

LEGAL STANDARD

Summary adjudication is proper when "the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). In a motion for summary judgment, "[if] the moving party for summary judgment meets its initial burden of identifying for the court those portions of the materials on file that it believes demonstrate the absence of any genuine issues of material fact, the burden of production then shifts so that the non- moving party must set forth, by affidavit or as otherwise provided in Rule 56, specific facts showing that there is a genuine issue for trial." *See T.W. Elec. Service, Inc., v. Pac. Elec. Contractors Ass'n*, 809 F.2d 626, 630 (9th Cir. 1987) (citing *Celotex Corp. v. Catrett*, 477 U.S. 317 (1986)). In judging evidence at the summary judgment stage, the Court does not make credibility determinations or weigh conflicting evidence, and draws all inferences in the light most favorable to the non-moving party. *See T.W. Electric*, 809 F.2d at 630-31 (citing *Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574 (1986)); *Ting v. United States*, 927 F.2d 1504, 1509 (9th Cir. 1991). The evidence presented by the parties must be admissible. *See* Fed. R. Civ. P. 56(c)(4). Conclusory, speculative testimony in affidavits and moving papers is insufficient to raise genuine issues of fact and defeat summary judgment. *See Thornhill Publ'g Co., Inc. v. GTE Corp.*, 594 F.2d 730, 738 (9th Cir. 1979). Because a patent is presumed valid, invalidity must be established by clear and convincing evidence. *See Takeda Chem. Indus., Ltd. v. Alphapharm Pty.*, Ltd., 492 F.3d 1350, 1355 (Fed. Cir. 2007); *Oakley, Inc. v. Sunglass Hut Int'l*, 316 F.3d 1331, 1339 (Fed. Cir. 2003).

DISCUSSION

I. Sanofi's motion to amend infringement contentions and Genentech's motion to strike

Sanofi has moved to amend its infringement contentions with regard to Rituxan® in a variety

of ways.[6] Biogen has filed a statement of non-opposition to the motion, but Genentech objects to the motion to amend. Sanofi's opposition to Genentech's motion for summary judgment of non-infringement asserts arguments based on the proposed amended infringement contentions. In response, Genentech has filed a motion to strike those portions of Sanofi's summary judgment opposition, as well as the portions of the declaration of Sanofi's expert Dr. Randolph Wall, that assert arguments based on the proposed amended infringement contentions.

Sanofi and Genentech hotly dispute whether Sanofi has been diligent in seeking to amend, as well as whether Genentech will be prejudiced by the amendment. The proposed amendments consist of the following:

For the '522 patent, Sanofi adds contentions that:

- Genentech "inserts" DNA into cells by growing the cells that produce Rituxan®
- Genentech uses an "isolated DNA enhancer" because the promoter DNA in the cells used to manufacture Rituxan® has been modified and/or is synthetic and therefore is not the native HCMV promoter
- Genentech practices a method of using the claimed enhancer that does not expose the cell to any downstream HCMV because the "HCMV material" that is allegedly taken from downstream of the +1 site of the IE gene in Rituxan® is not HCMV material because it is synthetic

For the '140 patent, Sanofi adds contentions that:

- Genentech's integrated plasmids perform the same function as the claimed plasmids, and do so in the same way and with the same result, thereby infringing claims 42 and 45 under the doctrine of equivalents

In addition, although Sanofi has not sought to amend its infringement contentions for Avastin® at this time, according to Genentech, Sanofi's summary judgment asserts a new infringement theory

[6] Sanofi has not sought to update its infringement contentions with regard to the other accused product, Avastin®, due to the ongoing discovery disputes between the parties over the testing of Avastin® host cells. However, several of the "new" arguments asserted by Sanofi in opposition to Genentech's motion for summary judgment with respect to Avastin® are similar or identical to those asserted with respect to Rituxan®, and thus Genentech has moved to strike these arguments as well.

for Avastin®, namely that the Avastin® cell line has not been exposed to "material from outside of the upstream region of the IE gene of HCMV" because HCMV DNA in the Avastin® plasmid has been altered.

The Court has reviewed the parties' voluminous filings on the motion to amend infringement contentions and the motion to strike, and concludes that Sanofi should be permitted to amend because there has been no undue delay and Genentech will not be prejudiced by the amendments. Accordingly, the Court GRANTS Sanofi's motion to amend and DENIES Genentech's motion to strike. Genentech has responded to the "new" arguments in its summary judgment reply, and in some cases anticipated those arguments and addressed them in its opening papers. The Court has considered Sanofi's amended infringement theories on the merits, and concludes that Genentech's motion for summary judgment of non-infringement should largely be granted. As set forth below, the Court concludes that Rituxan® and Avastin® do not infringe claims 1 and 2 of the '522 patent because (1) Rituxan® and Avastin® do not practice the step of "inserting" into a mammalian cell an isolated DNA enhancer; (2) in both Rituxan® and Avastin® HCMV DNA "that is upstream of the transcription start site" is not "the only HCMV material to which the mammalian cell is exposed"; and (3) Rituxan® cells do not meet the claim requirement of using an "isolated DNA enhancer" because the Rituxan® cell lines include a promoter.[7]

With respect to the '140 patent, the Court concludes that Rituxan® and Avastin® do not infringe claims 42-45, either literally or pursuant to the doctrine of equivalents, because the cells used to manufacture both products do not include a "recombinant DNA plasmid" as required by claims 42 and 45, and the cells are not "transformed with a recombinant DNA plasmid" as required by claims 43 and 44.

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[7] In light of the ongoing testing of Avastin® host cells, the Court GRANTS Sanofi's Rule 56(f) motion with regard to whether Avastin® uses an "isolated DNA enhancer."

II. **Genentech's motion for summary judgment of non-infringement**

A. '522 Patent[8]

Claim 1 of the '522 patent reads as follows,

> 1. The method to increase expression of a gene in a mammalian cell comprising inserting into a mammalian cell an isolated DNA enhancer consisting of DNA from the upstream region of the major immediate early (IE) gene of the human cytomegalovirus (HCMV) and a heterologous gene that is to be expressed, wherein the DNA from the upstream region of the IE gene of HCMV is the only HCMV material to which the mammalian cell is exposed.

1. "inserting into a mammalian cell an isolated DNA enhancer": Rituxan® and Avastin®

a. Literal infringement

Genentech contends that neither Rituxan® nor Avastin® infringes because the foreign DNA used to create those cell lines was "inserted" years before the issuance of the '522 patent. During the claim construction phase of this case, the parties stipulated that "inserting" means "putting or introducing into." Thus, claim 1 requires that an infringer put or introduce the claimed "isolated DNA enhancer" into a mammalian cell. It is undisputed that IDEC Pharmaceuticals inserted foreign DNA into a CHO cell in 1991 to create the Rituxan® cell line, and that Genentech inserted the foreign DNA into a CHO cell in January 1996 to create the Avastin® cell line. Sanofi agrees that because these events occurred prior to the issuance of the '522 patent on December 15, 1998, they cannot be infringing acts. *See Monsanto Co. v. Syngenta Seeds, Inc.*, 503 F.3d 1352, 1359-60 (Fed. Cir. 2007).

Instead, Sanofi argues that Genentech "inserts" enhancer DNA through mitosis. Sanofi contends that Genentech's growth and replication of enhancer-containing Rituxan® host cells causes the claimed enhancer to be "put[] or introduce[d] into" successive generations of cells through the process of mitosis. Sanofi argues that Genentech actively promotes cell growth, DNA replication, and cell division by maintaining its Rituxan® host cells under appropriate growth conditions, in a medium that includes a chemical to ensure that the enhancer is introduced into each daughter cell and is not lost during cell

[8] Sanofi alleges infringement of claims 1 and 2 of the '522 patent. Claim 2 is dependent on claim 1. Because the Court concludes that Rituxan® and Avastin® do not infringe claim 1, the Court does not reach the additional infringement arguments regarding dependent claim 2.

division. Sanofi relies on the Biologic License Application ("BLA") that Genentech[9] filed with the FDA stating that Rituxan® is produced by inserting the HCMV enhancer into each of the cells used to manufacture Rituxan®:

> IDEC-C2B8 [Rituxan®] is produced by Chinese hamster ovary (CHO) cells into which the DNA coding for the chimeric immunoglobin chains [on a plasmid that includes the HCMV enhancer] has been inserted.

Krummen Decl. Ex. B. Sanofi argues that there is nothing in the patent specification or prosecution history requiring that "insertion" be limited, as Genentech contends, to the introduction of enhancer DNA into a host cell only by means of transfection.

The Court concludes that Genentech does not practice the step of "inserting" and thus does not literally infringe Claims 1 and 2 of the '522 patent. The parties agreed that "inserting" should be construed to have its ordinary and plain meaning of "putting or introducing into a mammalian cell." In cell division, nothing is "put or introduced" into a mammalian cell as is required by the claim construction. Instead, the DNA is divided and replicated within a single cell. Sanofi's infringement argument that mitosis constitutes "inserting" ignores that the claims specify that what is being inserted is an "isolated DNA enhancer," which the Court construed as being "separated by human intervention from the promoter DNA in its original source." For DNA to be separated by human intervention, it must actually be manipulated by a human being, not merely replicated within a hamster cell by the cell's own natural processes. The Court finds it significant that the specification of the '522 patent repeatedly describes the introduction of foreign DNA into mammalian cells through transfection, while nowhere in the '522 patent is there any discussion of cell division. *See* '522 patent at 1:20, 1:42, 2:20, 2:51-54. (describing "co-transfection" of monkey cells, "co-transfection with the 'enhancer trap,'" and referring to "transfected" cell).

In addition, the Court finds that Sanofi's reliance on the BLA is misplaced because Sanofi has omitted language on the same page that explains what is meant by the quoted statement: "The expression vector was inserted into the CHO cells, DG44, using electroporation." Krummen Ex. B at GNE-SA 274. Dr. Levine explains that electroporation is a method by which cells are subjected to an

[9] The BLA was originally filed by Biogen-IDEC, but by virtue of Genentech's agreements with Biogen-IDEC, the BLA now governs Genentech's production of Rituxan®.

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electric current, permitting foreign DNA to enter the cells. Levine Decl. ¶ 9. Thus, the BLA's use of the word "inserted" is referring to the technique used in the initial creation of the cells in 1991, not cell division.

b. Doctrine of equivalents

Alternatively, Sanofi contends that Genentech's host cells infringe the '522 patent under the doctrine of equivalents. Sanofi argues that mitosis of Genentech's host cells performs the exact same function – inserting the Rituxan® plasmid into daughter cells – as transfection, in an insubstantially different way, which achieves the same result.

Under the doctrine of equivalents, "a product or process that does not literally infringe upon the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused product or process and the claimed elements of the patented invention." *Warner-Jenkinson Co. v. Hilton Davis Chemical Co.*, 520 U.S. 17, 21 (1997); *see also Cybor Corp. v. FAS Tech., Inc.*, 138 F.3d 1448, 1459 (Fed. Cir. 1998) ("An accused device that does not literally infringe a claim may still infringe under the doctrine of equivalents if each limitation of the claim is met in the accused device either literally or equivalently."). The accused device may infringe under the doctrine of equivalents where the "'equivalent' [element of the device] differs from the claimed limitation only insubstantially." *Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.*, 149 F.3d 1309, 1315 (Fed. Cir. 1998).

The Court finds that the doctrine of equivalents is inapplicable to the "inserting" step. Sanofi's theory of infringement would greatly increase the scope of the claims. As Genentech notes, under the literal meaning of the claims, Genentech would be free to use cells and the progeny of cells that had been transfected prior to the issuance of the patents. However, once the patent issued, Genentech would infringe under the doctrine of equivalents by using the progeny of those same cells. The Supreme Court has cautioned that "[i]t is important to ensure that the application of the doctrine, even as to an individual element, is not allowed such broad play as to effectively eliminate that element in its entirety." *Warner-Jenkinson Co.*, 520 U.S. at 29.

The Court also finds that "inserting by mitosis" differs substantially from inserting by

transfection. In mitosis, nothing is put into or introduced into a cell; instead, the cell's chromosomes are naturally duplicated, resulting in two daughter cells that have the same DNA as the parent cell. In transfection, a human causes foreign DNA to pass through the cell membrane, and the result is a modified cell containing foreign DNA. As Dr. Levine explains,

> [T]ransfection serves to alter a cell by the introduction of foreign DNA, whereas mitosis and cell division serve to faithfully duplicate a cell and its genome.
>
> Transfection and cell division also work in very different ways. In transfection, a scientist takes steps to ensure that foreign DNA crosses the cell membrane and is placed inside the cell. In mitosis and cell division, the entire genome – all of a cell's genetic material – is replicated, without the introduction of any foreign DNA from outside a cell.
>
> The results of transfection and cell division are not the same. The result of a scientist transfecting a cell with foreign DNA is the creation of a modified cell containing foreign DNA. Mitosis results in the creation of two identical daughter cells from the division of a single parent cell.

Levine Decl. ¶¶ 12-14.

2. "isolated DNA enhancer"

The Court defined "isolated DNA enhancer" as "a DNA sequence, separated by human intervention from the promoter DNA in its original source, that (1) strongly stimulates transcription of a linked gene, (2) functions independent of orientation, and (3) functions even if located long distances upstream or downstream relative to the initiation site of the linked gene."

a. Rituxan®

Genentech contends that Rituxan® cannot infringe the '522 patent because it is made using a combined "promoter/enhancer," not an "isolated DNA enhancer" as required by Claim 1. Genentech argues that the Rituxan® cell line includes the HCMV promoter. The Rituxan® cell line includes one HCMV fragment that consists of a "567 base pair DNA molecule isolated from the IE promoter/regulatory region of HCMV" and the other "CMV promoter/enhancer" consists of a "334 base pair DNA molecule isolated from the IE promoter/regulatory region of HCMV." Amended Compl. ¶¶ 27-28 (allegations regarding Rituxan® based on the Anderson patent).

Genentech argues that because the Rituxan® fragments contain HCMV promoter DNA, they

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were not "separated by human intervention from the promoter DNA in its original source" and are not "isolated DNA enhancers." Genentech cites the claim construction order, in which the Court noted that Figure 1a illustrates the location "of the native HCMV promoters, denoted by 'C' and 'T.'" The "C" in Figure 1a represents a short DNA sequence – "CAAAT" – and the "T" represents a short sequence – "TATAA." These sequences span positions -62 to -23. Genentech asserts that the two promoter/enhancer fragments found in the Rituxan® cell line include both of these promoter sequences, as well as the sequences in between. In addition, Genentech contends that there is no infringement because the Court's definition of "isolated DNA enhancer" requires that the DNA molecule must "function[] independent of orientation" and "function[] even if located long distances upstream or downstream relative to the initiation site of the linked gene." Docket No. 383 at 7. Genentech cites Sanofi's Responses to Second Set of Interrogatories, in which Sanofi conceded that neither of the HCMV fragments in the Rituxan® cell line is "capable of (a) strongly activating transcription of a linked gene, (b) functioning independent of orientation, and (c) functioning even if located long distances upstream or downstream relative to the initiation site of the linked gene." Gross Decl. Ex. 6 at 7.

In response, Sanofi contends that Genentech uses an "isolated DNA enhancer" because although the two copies of the HCMV enhancer present in Rituxan® are physically linked to promoters, neither promoter is the native HCMV IE promoter. Sanofi argues that the evidence shows that the promoters used to drive expression of the Rituxan® genes were intentionally altered and/or synthetic, and thus they are not the native HCMV promoter. In addition, Sanofi argues that Genentech uses an "isolated DNA enhancer" because the HCMV enhancers in Rituxan® enhance expression of genes from other non-HCMV promoters.

The central problem with both of Sanofi's contentions is that regardless of whether the Rituxan® fragments can be viewed as containing non-native HCMV promoters – a point that Genentech disputes – the fragments nevertheless contain promoters. The Court construed "isolated DNA enhancer" as "a DNA sequence, separated by human intervention from the promoter DNA in its original source, *that (1) strongly stimulates transcription of a linked gene, (2) functions independent of orientation, and (3) functions even if located long distances upstream or downstream relative to the initiation site of the*

linked gene." (emphasis added). It is undisputed that promoters, from whatever source and whether altered or synthetic, are not capable of functioning independent of orientation, nor are they capable of functioning even if located long distances upstream or downstream relative to the initiation site of the linked gene. Indeed, Sanofi has admitted that the two Rituxan® fragments described *supra* (the 567 base pair fragment extending from position 361 to position 927 of Figure 3a of the Anderson patent and the 334 base pair fragment depicted from position 2018 to position 2351 in Figure 3B of the Anderson patent) do not have these capabilities. *See* Gross Decl. Ex. 6 at 7 (Sanofi's Responses to Second Set of Interrogatories). As such, Sanofi has failed to raise any issue of fact to defeat summary judgment. The Court finds that the undisputed evidence shows that the Rituxan® cells do not meet the claim requirement of using an "isolated DNA enhancer" because the Rituxan® cell lines include a promoter.

b. Avastin®

Genentech contends that the cell line used to manufacture Avastin® does not include an enhancer from HCMV and therefore does not meet the limitation of the '522 patent because it does not include an "isolated DNA enhancer consisting of DNA from the upstream region of the major immediate early (IE gene of the human cytomegalovirus (HCMV)." Genentech relies on its own evidence regarding the Avastin® cell line, and criticizes the absence – at the time of the briefing on this motion – of any testing showing that Avastin® contains the HCMV enhancer. However, after the briefing was complete Judge Zimmerman granted Sanofi's motion to compel the production of Avastin® host cells for testing. Accordingly, to the extent Genentech's motion for summary judgment of non-infringement makes factual arguments that will be addressed by the testing that is currently underway, the Court GRANTS Sanofi's motion for a Rule 56(f) continuance. However, as discussed in this order, to the extent that Genentech seeks summary judgment of non-infringement on grounds that are independent of the testing, the Court will resolve those arguments and finds that a continuance is not warranted.

3. " only HCMV material to which the mammalian cell is exposed."

Claim 1 specifies that the enhancer consists of "DNA from the upstream region" of the HCMV IE gene, and that the DNA from this region "is the only HCMV material to which the mammalian cell

is exposed." The Court construed "DNA from the upstream region of the major immediate early (IE) gene of human cytomegalovirus (HCMV)" to mean "DNA from the region that is upstream of the transcription start site of the major IE gene of HCMV." Docket No. 383 at 10. Thus, claim 1 requires that HCMV DNA "that is upstream of the transcription start site" be "the only HCMV material to which the mammalian cell is exposed."

a. Rituxan®

Genentech contends that Rituxan® does not infringe because it incorporates DNA that is downstream of the transcription start site, namely the sequence found in HCMV from -7 to +23 of the immediate early region of HCMV. In response, Sanofi argues that "the purported HCMV downstream DNA that Genentech relies on is part of a much larger fragment of DNA that was chemically synthesized by a machine, not taken from any natural viral source. [A person of ordinary skill in the art ("POSA")] would understand that this chemically synthesized fragment of DNA is not 'HCMV material,' even if it contains a small DNA region having the same sequence as HCMV DNA. To constitute 'HCMV material,' the downstream DNA must be from the HCMV genome." Opp'n at 12:25-13:5. For support, Sanofi cites Dr. Wall's declaration, which states,

> I understand that Genentech argues that the Rituxan® expression plasmid contains 22 base pairs of HCMV DNA from downstream of the +1 site of the HCMV IE gene.
>
> That alleged HCMV DNA is not viral DNA, but rather it was synthesized on a machine and is part of a much larger 120 base pair synthetic fragment. Scientists, including Dr. Reff, one of the inventors of the '137 patent, would not regard the 120bp DNA fragment synthesized for insertion into the Rituxan® expression plasmid as viral material. Dr. Reff testified that he synthesized the fragment of DNA shown on BIOG-SA0001799 using a "machine," and used it to reintroduce DNA sequences "similar to the sequence in HCMV" that had been deleted during the construction of the plasmid leading to the Rituxan® construct.

R. Wall Decl. ¶¶ 54-55.

Genentech responds that synthetic HCMV DNA is "HCMV material." Genentech cites Dr. Levine's declaration, which states,

> When scientists worked with DNA in the 1980s they rarely used only the minute amounts of DNA present in the original biological source from which it was extracted. Indeed, the field of molecular biology flourished as a result of scientists' ability to "clone" DNA in their laboratories. In other words, DNA cloning is an integral method

for the production of the large quantities of specific DNAs needed to perform most molecular manipulations, such as restriction mapping and the creation of recombinant DNAs.

. . .

To create a recombinant DNA plasmid containing viral regulatory DNAs, scientists typically do not take DNA directly from the virus and combine it with a gene of interest. Rather, scientists first clone the viral DNA fragment by putting it into a plasmid and inserting that plasmid into bacterial cells, which in turn, copy the plasmids. This cloned viral DNA then can be "cut and pasted" together with a gene of interest, to create the desired recombinant DNA plasmids. Scientists since the early 1980s have long relied on such molecular cloning techniques. Cloned DNA copies have the same nucleotide sequence as the source DNA.

Similarly, DNA molecules also can be made by machines ("oligonucleotide synthesizers") to create sequences that are identical to those found in nature. In it possible to create a viral DNA sequence of even several hundred base pairs with such machines, rather than extracting the DNA from a virus itself or cloning it in bacteria. The source of the DNA (e.g., a viral particle, a bacterial cell, or a laboratory machine) does not affect the function of the DNA sequence. Such "synthetic" DNA is identical in sequence to the corresponding native DNA and is therefore recognized and used by cells in exactly the same way. A cell does not discriminate between DNA that is synthesized in a laboratory and DNA that is synthesized in a living cell.

Cloning plasmids requires the use of bacteria such as *E. coli*, which are living cells that have the biological machinery to replicate these circular, extrachromosomal pieces of DNA. The plasmid Anti-CD20 in TCAE8 is one such example. I have reviewed a lab notebook that showed that in creating the Rituxan® antibody, scientists grew this plasmid, then called "B1 in TCAE8," by replicating it in *E. coli*.

Levine Decl. ¶¶ 21, 23-25.

Genentech also argues that Sanofi's contention that synthetic DNA sequences that are identical to sequences found in HCMV are not "HCMV material" would lead to absurd results. Genentech notes that before any man-made vector including viral DNA is transfected into a cell, that vector is first "cloned" in bacteria, so it originated from bacteria, not from a virus such as HCMV. Genentech also argues that under Sanofi's theory, none of the DNA in the cells used by Genentech constitutes "HCMV material," and therefore under Sanofi's own arguments, the manufacture of Rituxan® does not infringe the '522 patent.

The Court concludes that Rituxan® does not infringe because it incorporates DNA that is downstream of the transcription start site, and thus HCMV DNA "that is upstream of the transcription start site" is not "the only HCMV material to which the mammalian cell is exposed." As an initial matter, there is nothing in the claim language, specification, or this Court's claim construction that requires that the "HCMV material" be natural DNA as opposed to synthetic DNA. In addition, Dr.

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Wall's declaration does not establish that a POSA would not consider synthetic HCMV DNA to be "HCMV material." Dr. Wall asserts that scientists would not consider synthetic HCMV DNA to be viral material, but the only support provided for that assertion is the statement from Dr. Reff's deposition in which he states that he synthesized the fragment of DNA using a "machine," and used it to reintroduce DNA sequences "similar to the sequence in HCMV." Neither of these statements by Dr. Reff establishes that Dr. Reff or other scientists would not consider the synthetic HCMV DNA to be "HCMV material." In contrast, Dr. Levine's declaration provides a factual basis from which to conclude that the synthetic HCMV DNA fragment in Rituxan® is "HCMV material."

Further, although Sanofi cites Dr. Reff's statement that he introduced DNA sequences "similar to the sequence in HCMV" to suggest that the sequence in Rituxan® differs from the viral HCMV sequence, it is undisputed – and Sanofi has alleged – that the Rituxan® cell line contains a DNA fragment that is identical to a fragment of the HCMV sequence covered by the '522 patent. *Compare* Gross SJ Decl. Ex. 1 (the '522 patent), Fig. 1b at nucleotide position -7 to +23, *with* Gross SJ Decl. Ex. 3 (the Anderson patent), Feb. 3A at nucleotide position 934 to 964 (showing identical DNA sequence); Amended Compl. ¶ 23 (alleging that the Anderson patent shows "the complete DNA sequence of the recombinant DNA plasmid used to transform the Rituxan® Host Cells.").

Finally, the Court agrees with Genentech that if the Court were to accept Sanofi's position that synthetic HCMV DNA is not "HCMV material," then Rituxan® does not infringe because Rituxan® does not, under Sanofi's construction, contain "HCMV material."

b. Avastin®

Similar to the arguments with regard to Rituxan®, Genentech contends that regardless of the Avastin® test results, Avastin® does not infringe because it is undisputed that Avastin® contains two introns from the HCMV IE gene. Introns are transcribed and are therefore downstream of the transcription start site. *See* Claim Construction Levine Decl. ¶ 30 (Docket No. 307) (explaining structure of HCMV genomic DNA in the IE region, including intron, along with diagram showing that intron is downstream of transcription start site). Thus, Genentech argues that Avastin® does not infringe because HCMV DNA "that is upstream of the transcription start site" is not "the only HCMV

material to which the mammalian cell is exposed."

Sanofi argues that the introns are not from the HCMV IE gene, but instead "are each defined by a splice donor site derived from the cytomegalovirus immediate early gene and a splice acceptor site derived from an IgG heavy chain variable region (VH) gene," and that "the intron upstream of the heavy chain contains the cDNA of murine [mouse] dihydrofolate reductase [DHFR]." Opp'n at 21:20-23 (quoting the 2003 BLA submitted in connection with Avastin®, found at Krummen Decl. Ex. D at GTNE0000016). Sanofi continues, "A 'splice donor' is simply a DNA sequence that is several nucleotides long, that together with a 'splice acceptor' defines the boundaries of an intron to be removed from a messenger RNA. . . . the splice donor site in the Avastin® expression plasmid was 'modified in order to impair splicing.' Thus, like the non-native HCMV promoter in the Rituxan® expression plasmid, the splice donor sequence found in the Avastin® expression plasmid is not 'HCMV material' at all – either from downstream of +1, or from anywhere else in the HCMV genome." Opp'n at 22:1-7.

Although Sanofi asserts that the HCMV DNA found in the Avastin® cell line is not "HCMV material," Sanofi has not submitted any evidence raising a triable issue of fact on this point. The undisputed evidence in the record shows that the HCMV DNA in Avastin® comes from downstream of the transcription start site. *Compare* Stake Reply Decl. Ex. 6 at BIOG-SA0004195 (native HCMV sequence) *with* Krummen Decl. Ex. D at GNE 26 (Avastin® sequence); *see also* Levine Decl. ¶ 26 (evaluating the approximately 45-base pair sequence from Avastin® BLA and concluding that "[t]his DNA corresponds to the HCMV DNA from positions +76 to +120 downstream of the +1 transcription start site, as seen in Figure 1b of the '522 patent. This DNA sequence is definitely located downstream of the transcription start site (+1) and not from the upstream region of the HCMV IE gene."). Accordingly, the Court concludes that Avastin® does not infringe because it incorporates DNA that is downstream of the transcription start site, and thus HCMV DNA "that is upstream of the transcription start site" is not "the only HCMV material to which the mammalian cell is exposed."

B. '140 Patent, Claims 42-45

Claims 42-45 of the '140 patent read as follows:

42. A recombinant DNA plasmid comprising a DNA molecule isolated from the

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immediate early (IE) promoter/regulatory region of human cytomegalovirus (HCMV) and a heterologous gene positioned downstream and operatively linked to said molecule, wherein the DNA molecule enhances the transcription of DNA in an animal or mammalian host cell expression system.

43. A eukaryotic host cell transformed with a recombinant DNA plasmid comprising a DNA molecule isolated from the immediate early (IE) promoter/regulatory region of human cytomegalovirus (HCMV) and a heterologous gene positioned downstream and operatively linked to said DNA molecule, wherein the DNA molecule enhances the transcription of DNA in an animal or mammalian host cell expression system.

44. The transformed eukaryotic host cell of claim 43 wherein said host cell is a mammalian host cell.

45. A recombinant DNA plasmid comprising a DNA molecule isolated from the PstI m fragment of the immediate early (IE) region of human cytomegalovirus (HCMV) and a heterologous gene positioned downstream and operatively linked to said DNA molecule, wherein said DNA molecule enhances expression of said heterologous gene.

The Court construed "recombinant DNA plasmid" as "circular, extrachromosomal molecule comprising DNA from two or more sources." Claims 42 and 45 require a "recombinant DNA plasmid," and claims 43 and 44 require a "host cell transformed with a recombinant DNA plasmid." The parties have agreed that "transformed" means "altered to include foreign DNA." Docket No. 237 at 3. Genentech contends that Rituxan® and Avastin® do not infringe claims 42-45 because the foreign DNA used to produce Rituxan® and Avastin® is linear and stably integrated into chromosomes and is therefore not extrachromosomal or circular.

1. Claims 42 and 45: doctrine of equivalents

Sanofi argues that the cells used to manufacture Rituxan® and Avastin® infringe claims 42 and 45 under the doctrine of equivalents. Sanofi asserts that any differences between Genentech's integrated plasmids and the claimed plasmids are insubstantial because the linear and circular plasmids are literally the same DNA molecule. *See* R. Wall Decl. ¶¶ 64-67. Sanofi also argues that the fact that one is extrachromosomal and one is chromosomal is likewise an insubstantial difference because both provide the necessary DNA in the correct arrangement. *Id.* Thus, argues Sanofi, Genentech's integrated plasmids perform the same function, in the same way, and with the same result, as would "circular, extrachromosomal" plasmids.

Genentech argues that Sanofi is attempting to recapture through the doctrine of equivalents the

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argument that the Court rejected during claim construction, i.e., that when DNA is integrated into a host cell's chromosome it is still a plasmid. The claim construction order, quoting the Hauschka Declaration (at Docket No. 305 ¶ 12), noted,

> Once the foreign DNA has been integrated into chromosomal DNA, however, it was no longer a 'recombinant DNA plasmid.' Once might use the term 'plasmid DNA' to indicate that the DNA in question originated from a plasmid, but that term does not mean that the DNA, once incorporated, is still a plasmid. When incorporated into a eukaryotic chromosome, the plasmid DNA would lose essential characteristics of a plasmid, including its extra-chromosomal existence and ability to replicate extra-chromosomally and independently of the cell life cycle.

Docket No. 383 at 14. Genentech notes that it is undisputed that after foreign DNA is integrated into a cell's chromosome, it is no longer circular or extrachromosomal. Genentech argues that Sanofi's contention – that DNA that is linear is equivalent to DNA that is circular, and that DNA that is integrated into the chromosome is equivalent to extrachromosomal DNA – would vitiate the requirement that a "recombinant DNA plasmid" is a "circular, extrachromosomal molecule."

Genentech also argues that Sanofi's assertion that integrated DNA "serves the exactly same function, in the same way, to achieve the same result as the plasmids claimed in the patent in suit" is factually incorrect. Genentech notes that Sanofi admits that stably integrated DNA permits "long-term stable expression" of the DNA, making stable integration necessary for commercial manufacture of a protein. *See* R. Wall Claim Construction Decl. ¶ 29 (Docket No. 276). In contrast, eukaryotic cells that have been transiently transfected with plasmids lose the ability to produce protein over time. Dr. Levine explains,

> When foreign DNA is inserted into a eukaryotic cell through transfection, the cell is often "transiently" transformed[10] by the foreign DNA. This means that the cell contains foreign DNA, such as a recombinant DNA plasmid, but it is not stably integrated into the cell's genome. When the foreign DNA is not integrated, it is typically degraded by cellular processes or diluted as the cell divides. Thus, transiently transfected eukaryotic cells eventually lost their ability to produce proteins encoded by the foreign DNA.

Levine Decl. ¶ 15. Genentech also asserts that another undisputed difference between integrated DNA and DNA plasmids is due to the fact that gene expression is affected by the surrounding DNA sequences found at the location at which introduced DNA is integrated; surrounding DNA sequences cannot affect the expression of a plasmid that is not integrated into a chromosome. *See* R.S. Barnett *et al.*, "Antibody

[10] The Court addresses the parties' dispute regarding "transformed" *infra*.

Production in Chinese Hamster Ovary Cells Using an Impaired Selectable Marker," in Henry Y. Wang & Tadayuki Imanaka, Eds. Antibody Expression and Engineering American Chemical Society (1995) at 27, 39 (Docket No. 452-14).

The Court concludes that the cells used to manufacture Rituxan® and Avastin® do not infringe claims 42 and 45 under the doctrine of equivalents. To find infringement by equivalents, the Court would be required to vitiate the requirement that a "recombinant DNA plasmid" is a "circular, extrachromosomal molecule." A claim should not be interpreted to vitiate a claim element. *Warner-Jenkinson*, 520 U.S. at 29. "Claim vitiation applies when there is a 'clear, substantial difference or a difference in kind' between the claim limitation and the accused product." *Trading Techs. Int'l, Inc. v. eSpeed, Inc.*, 595 F.3d 1340, 1355 (Fed. Cir. 2010) (quoting *Freedman Seating Co. v. Am. Seating Co.*, 420 F.3d 1350, 1360 (Fed. Cir. 2005)). A linear, chromosomal molecule is different in kind from a circular, extrachromosomal molecule. Further, it is undisputed that a linear, chromosomal molecule, which can become stably integrated DNA, performs a different function (long-term stable expression), whereas circular, extrachromosomal molecules cannot be stably integrated and over time degrade and lose their ability to produce proteins encoded by the foreign DNA. Neither Rituxan® nor Avastin® contains a "recombinant DNA plasmid" as required by claims 42 and 45, and thus the Court finds that there is no infringement. *See Decisioning.com, Inc. v. Federated Dep't Stores, Inc.*, 527 F.3d 1300, 1315 (Fed. Cir. 2008) ("[O]ur construction of 'remote interface' encompasses only publicly-accessible computer equipment that is located remotely from the data processing system and that facilitates the exchange of information between the applicant and the transaction processor. Thus, Appellees' systems that are accessed solely via consumer-owned personal computers do not literally infringe the '007 patent. Further, Decisioning is precluded from asserting that those systems infringe under the doctrine of equivalents, as doing so would vitiate an element of the claims-i.e., 'remote interface' as construed.").

2. Claims 43 and 44: literal infringement and doctrine of equivalents

Claims 43 and 44 are directed to cells that have been "transformed" with a "plasmid." During claim construction, the parties agreed that "transformed" means "altered to include foreign DNA."

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There is no dispute that the cells used to manufacture Rituxan® and Avastin® do not include circular, extrachromosomal molecules ("recombinant DNA plasmids"). Accordingly, there is no infringement.

Sanofi contends that Rituxan® and Avastin® infringe because "transformation includes the steps of linearizing the plasmid (i.e., making a cut in the circular plasmid), and putting that DNA into a mammalian cell, where it is then imported into the nucleus and integrated into the host cell genome." Opp'n at 14. Sanofi argues that the process of transformation entails the stable integration of the plasmid into the host cell genome, and that it is scientifically incorrect to say that a mammalian cell has been "transformed" but does not have the plasmid integrated into its DNA. As Genentech notes, to a large degree Sanofi's arguments are a belated attempt to revise the Court's construction of "recombinant DNA plasmid" as "a circular, extrachromosomal molecule," as well as an attempt to revise the agreed-upon construction of "transformed" as now requiring stable integration of foreign DNA into the host cell's genome. The Court rejects Sanofi's attempts to revise claim construction in order to avoid summary judgment of non-infringement. A cell that has been transiently transfected has been "altered to include" the plasmid and therefore meets the parties' agreed-upon construction of "transformed": "altered to include foreign DNA."

Moreover, Sanofi's contention that "transformation" can, as a matter of science, only occur when the plasmid DNA is integrated stably into the host cell, would read out the '140 patent's only embodiment, in which cells were transiently transfected with a plasmid. *See* '140 patent, 2:51-54 ("The enhancer action on β-globin transcription was determined by S1 nuclease analysis of cytoplasmic RNA after transient expression in HeLa cells."). An interpretation that would exclude the only embodiment in the specification "is rarely, if ever, correct and would require highly persuasive evidentiary support . . . ." *Vitronics v. Conceptronic Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996).

Finally, for the reasons stated *supra* with regard to claims 42 and 45, the Court concludes that there is no infringement under the doctrine of equivalents.

III. Biogen's motion for summary judgment of invalidity

Biogen moves for summary judgment of invalidity for lack of written description. Biogen contends that the claims in suit are invalid because the claimed genus of DNA sequences is far broader

than anything the applicants actually invented or described. Biogen argues that the patents' disclosure demonstrates that the applicants discovered two HCMV DNA fragments, "C2" and "C4," that boosted transcription of RNA. Biogen contends that while the applicants obtained numerous claims expressly limited to C2 and C4, the claims at issue here are much broader and cover enormous numbers of nucleic acids of unknown length and sequence within large regions of HCMV DNA. Biogen argues that the patents' specification provides no guidance to determine whether any specific sequence is covered other than by trial-and-error experimentation.

The written description requirement is contained in 35 U.S.C. § 112, which states: "[t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use [the invention]." The requirement serves "to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him." *In re Alton*, 76 F.3d 1168, 1172 (Fed. Cir. 1996) (internal quotation and citation omitted). Whether the specification for a challenged claim meets this requirement is a question of fact to be assessed on a case-by-case basis. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1561, 1563 (Fed. Cir. 1991); *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997).

In order to satisfy the written description requirement, the patent specification must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."); *see also Eli Lilly*, 119 F.3d at 1566; *Vas-Cath*, 935 F.2d at 1563. "One shows that one is 'in possession' of the invention by describing the invention, with all its claimed limitations . . . . by such descriptive means as words, structures, figures, diagrams, formulas, etc." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997) (emphasis omitted); *see also Application of Wertheim*, 541 F.2d 257, 262 (C.C.P.A. 1976) ("The primary consideration is factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure."). Expert testimony eliciting industry standards can work to "expand the breadth of the specification." *In re Alton*, 76 F.3d at 1176.

"[I]nvalidating a claim requires a showing by clear and convincing evidence that the written description requirement has not been satisfied." *Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052, 1072 (Fed. Cir. 2005).

A. '522 patent

Claim 1 of the '522 patent covers:

> 1. The method to increase expression of a gene in a mammalian cell comprising inserting into a mammalian cell an isolated DNA enhancer consisting of DNA from the upstream region of the major immediate early (IE) gene of human cytomegalovirus (HCMV) and a heterologous gene that is to be expressed, wherein the DNA from the upstream region of the IE gene of HCMV is the only HCMV material to which the mammalian cell is exposed.

Biogen contends that the DNA recited in claim 1 is not limited to C2 and C4, the two specific enhancer fragments disclosed in the specification, but rather that the claim covers the use of all DNA sequences of any length and any position that are derived from the "upstream region" and function as an "isolated DNA enhancer." The Court defined the "upstream region" as the "region that is upstream of the transcription start site of the major IE gene of HCMV." Thus, one end of the "upstream region" is at +1 (the transcription start site of the major IE gene), while the other end is not defined in the claim and potentially encompasses the entire linear HCMV genome from +1 up to its 5' terminus.

Biogen raises the same overbreadth arguments with respect to claim 2. Claim 2 is as follows:

> 2. The method as claimed in claim 1, wherein the DNA enhancer consists of the DNA from the PstI restriction enzyme site upstream of the transcription start site to position -118 of the PstI-m fragment, or an enhancer-active part thereof.

The parties agree that the recited region in Claim 2 spans from -1138 to -118 with respect to the transcription start site of the major IE gene. Biogen argues that the claim is invalid because the claimed enhancer may be either the entire fragment, having over a thousand base pairs, or a sub-fragment of any length.

Biogen argues that the claims are invalid for lack of written description because a claim reciting a "genus" of DNA sequences – such as "an isolated DNA enhancer consisting of DNA from the upstream region" – is adequately described only if a "representative number" of sequences are disclosed or if the specification describes "structural features common to the members of the genus, which

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features constitute a substantial portion of the genus." *Eli Lilly*, 119 F.3d at 1569. Biogen argues that C2 and C4 are not "representative" of all enhancer fragments within an enormous region of DNA. Biogen also contends that the specification does not disclose any molecular structure corresponding to the functional limitation that the DNA be an "isolated DNA enhancer." Biogen argues that although the disclosure provides the sequences of C2 and C4, there is no explanation as to why these fragments have enhancer activity, and no disclosure identifying other fragments elsewhere in the upstream region that might function as enhancers. Biogen argues that the specification does not disclose any way to identify an "isolated DNA enhancer" other than brute-force experimentation to test whether a particular sequence acts as an enhancer. Biogen argues that the disclosure of the enhancer trap method for finding enhancers is not sufficient to save the claim because "[a]n adequate written description of a DNA requires more than . . . a potential method for isolating it; what is required is a description of the DNA itself." *Fiers v. Revel*, 984 F.2d 1164, 1170 (Fed. Cir. 1993).

In opposition, Sanofi contends that Biogen has not met its burden to show by clear and convincing evidence that the claims are invalid. Sanofi has submitted the expert declaration of Professor Deborah Spector, who states that a POSA in 1984[11] would have understood, based on the disclosure of the HCMV IE enhancer, including its location within the HCMV genome, its structure, function and methods by which it is obtained and used, that the claims are directed to a particular, well-defined enhancer. Sanofi argues that at the very least, based on the Spector declaration, and Biogen's failure to submit any expert evidence regarding what a POSA would have understood about the claims, that Sanofi has presented a genuine material factual dispute that precludes summary judgment.

In her declaration, Dr. Spector states,

> The specification[12] states that the "enhancer is located in the Hind III E fragment (Greenaway et al., loc. cit.), which includes the Pst I m fragment (about 2.1 kb)." As I explained above, the restriction map of the HCMV genome had been published by 1984 and the locations and sizes of the Hind III E and Pst I m fragments were known. At this time, the Hind III E fragment was also considered to correspond to the IE gene region

[11] Written description is determined as of the filing date of the patent. *Ariad*, 598 F.3d at 1355. Here, the patents originated from German Patent Application No. DE 34 31 140.8, which was filed with the German Patent Office on August 24, 1984.

[12] The '522 and '140 patents share the same specification.

of HCMV, and it was known that the 2.1 kb Pst I (or the Pst I m) fragment included elements of the major IE gene promoter. A POSA would therefore understand the patents to teach that the enhancer was located in the approximately 2.1 kb Pst I m fragment.

The patents further describe the precise locations of two enhancer active fragments, called C2 and C4. C2 is located at positions -118 to -458 and C4 is located at positions -263 to -524 with respect to the transcription start site. The transcription start site, designated at +1, was known in 1984. It is also shown in Figures 1a and 1b of the patents. With this knowledge of the nucleotide positions of the C2 and C4 enhancer active fragments, a POSA could have identified and isolated those fragments from the HCMV genome.

The specification also describes that the inventors discovered the HCMV enhancer in the Pst I m fragment using the "enhancer trap" method that had been developed in the Schaffner laboratory. Specifically, the inventors sonicated (that is, broke into fragments using sound energy) the approximately 2.1 kb Pst I m fragment, to create smaller DNA fragments of approximately 300 base pairs (bp) each. Using the enhancer trap, they identified the two fragments of the HCMV enhancer, which they called C2 and C4. The success of this experiment confirms to the POSA that the enhancer was located in the Pst I m fragment and provides another method by which it could be obtained.
. . .

Because a POSA would understand from the specification that C2 and C4 have enhancer activity, a POSA would understand that the repeat sequences they contain are associated with that activity discovered by the inventors. The patents disclose the nucleotide sequences for the C2 and C4 enhancer active fragments and the repeat sequences of the enhancer are shown in both the Figures in the patents. In Figure 1a, the repeats are depicted by the arrows drawn above the HCMV DNA and in Figure 1b, the repeats are underlined in the sequence data.

A POSA would also understand from the specification that both the C2 and C4 fragments have enhancer activity and can be used separately or together as one enhancer, which is the way they exist in the virus. Additionally, a POSA is told in the specification that the enhancer can be used with or without the HCMV promoter.
The specification then explains that "[d]eletion mutants, for example obtained by Aha II and religation of the various combinations, are also enhancer active." From this, a POSA would know that some alterations or deletions can be made to the enhancer sequence without eliminating all enhancer activity. However, because only the C2 and C4 fragments were shown in the specification to have enhancer activity, a POSA would recognize that an HCMV DNA sequence that contains no overlap with either of the C2 or C4 fragments would not have any enhancer activity.

Spector Decl. ¶¶ 30-32, 34-36.

The Court concludes that although Biogen has raised serious questions about the validity of the claims at issue, Biogen has not shown invalidity by clear and convincing evidence and thus summary judgment is inappropriate. Biogen argues that the Spector declaration does not raise a triable issue of fact because the claims cover functionally-defined genus claims, which under Federal Circuit case law are adequately described only by "a recitation of a representative number" of DNA sequences or a

“recitation of structural features common to the members of the genus.” *Eli Lilly*, 119 F.3d at 1569. However, Sanofi asserts that the patents do not claim a genus, but instead claim an enhancer from a well-defined region of HCMV. Sanofi cites Dr. Spector’s declaration, in which she states,

> I have read the argument in Biogen’s brief that attempts to show that the claims encompass a vast genus of small sequences taken from anywhere between the major IE gene +1 site to the terminus of the HCMV genome, a region that is approximately 17,000 bp in length. I disagree with Biogen’s assertions that a POSA would understand the claims in this way. The claims are directed to the enhancer that is located in a well-defined region of the HCMV genome and which, on the basis of the specification discussed above, would be easily identified by a POSA. This enhancer was discovered by the inventors using a method designed to identify any enhancer located in the DNA region analyzed. Because the enhancer trap identified two overlapping enhancer-active fragments, a POSA would not expect any other enhancer to be located in the HCMV IE gene region and, in fact, no other enhancer has since been identified in this region.

Spector Decl. ¶ 38. Biogen responds that the claim language is not limited to any particular enhancer, and that the claim language does not contain any of the limitations that Dr. Spector asserts that a POSA would understand based on the specification. Biogen’s arguments may be well-founded. However, on summary judgment, Biogen must prove invalidity by clear and convincing evidence, and the Court is required to view the evidence and disputed factual issues in Sanofi’s favor. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 962 (Fed. Cir. 2002). Accordingly, the Court DENIES Biogen’s motion.

B. ‘140 patent

The ‘140 patent has 45 claims. Claims 1-41 are drawn to C2 or C4; sequences that are 80% homologous to C2 or C4; and uses of those sequences in plasmids, host cells, and methods. Sanofi has not asserted these claims, and instead has asserted Claims 42-45. Claims 42-44 recite “a DNA molecule” isolated from the “promoter/regulatory region” and are as follows:

> 42. A recombinant DNA plasmid comprising a DNA molecule isolated from the immediate early (IE) promoter/regulatory region of human cytomegalovirus (HCMV) and a heterologous gene positioned downstream and operatively linked to said molecule, wherein the DNA molecule enhances the transcription of DNA in an animal or mammalian host cell expression system.
>
> 43. A eukaryotic host cell transformed with a recombinant DNA plasmid comprising a DNA molecule isolated from the immediate early (IE) promoter/regulatory region of human cytomegalovirus (HCMV) and a heterologous gene positioned downstream and operatively linked to said DNA molecule, wherein the DNA molecule enhances the transcription of DNA in an animal or mammalian host cell expression system.
>
> 44. The transformed eukaryotic host cell of claim 43 wherein said host cell is a

mammalian host cell.

The Court has defined the "promoter/regulatory region" recited in these claims as "the approximately 524-base-pair region of DNA that is immediately upstream of the transcription start site of the major early gene of HCMV." Thus, each of these claims requires a DNA molecule that is isolated from the "promoter/regulatory region" that "enhances the transcription of DNA."

Biogen contends that the "promoter/regulatory region" claims (claims 42-44) do not satisfy the written description requirement for all of the same reasons that Biogen contends that the claims of the '522 patent are invalid: the specification does not describe any structures within the "promoter/regulatory region" that perform the function of "enhanc[ing] the transcription of DNA" other than C2 and C 4 and thus require trial-and-error experimentation to determine whether any particular DNA molecule meets that functional limitation; the specification does not recite a "representative number" of the thousands of possible sequences in the "promoter/regulatory region"; and the specification does not disclose structural features common to the members of the genus. Biogen asserts that claim 45,[13] which does not recite the "promoter/regulatory region," and instead recites the larger "Pst I m fragment," suffers from these same problems.

Sanofi responds with the same arguments asserted above with respect to the '522 patent: namely, Dr. Spector's statements that a POSA would have understood, based on the specification (which is the same for both patents) that these patents adequately describe the claimed HCMV IE enhancer. In addition, Dr. Spector states that a POSA would understand the term "promoter/regulatory region" to mean the "portion upstream from the coding region of the gene that includes the promoter and other regulatory elements that control transcription of a gene, as this was terminology that was well known in the art at the time the patent was filed." Spector Decl. ¶ 41.

Biogen argues that Sanofi's assertion that both patents are directed to an enhancer "squarely

[13] Claim 45 covers:

> 45. A recombinant DNA plasmid comprising a DNA molecule isolated from the PstI m fragment of the immediate early (IE) region of a human cytomegalovirus (HCMV) and a heterologous gene positioned downstream and operatively linked to said DNA molecule, wherein said DNA molecule enhances expression of said heterologous gene.

Instead of reciting the "promoter/regulatory region," this claim uses the much larger Pst I m fragment.

contradicts the Court's claim construction ruling, which rejected Sanofi's argument that the 'DNA molecule' of the '140 patent's claims should be construed to be an enhancer." Reply at 5:9-10. The Court's claim construction order held,

> Claims 42, 43 and 45 claim plasmids comprising a DNA molecule, "wherein the DNA molecule enhances the transcription of DNA" (claims 42 and 43) or "wherein said DNA molecule enhances expression . . . ." (Claim 45). Sanofi contends that the term in claims 42 and 43 means "the DNA molecule acts as an enhancer, capable of: (1) strongly activating transcription of a linked gene, (2) functioning independent of orientation, and (3) functioning even if located long distances upstream or downstream relative to the initiation site of the linked gene, to increase the rate of transcription of the heterologous gene above a basal level for that gene." Sanofi's proposed definition for term in claim 45 contains the same language, with the addition of the clause "which results in an increase in the amount of protein coded by that heterologous gene to be produced." At the claim construction hearing, Sanofi clarified its position that the "DNA molecule" in this term should be construed to be an "enhancer."
>
> > In contrast, defendants contend that "wherein the DNA molecule enhances the transcription of DNA" in claims 42 and 43 means "wherein the DNA molecule causes more production of RNA from DNA." For claim 45, defendants propose the same language, with the addition of "and more production of protein, from the heterologous gene."
>
> The Court adopts defendants' constructions. Defendants' constructions define transcription and expression, and the parties are in basic agreement on how to define these processes. The Court agrees with defendants that there is no need to define "DNA molecule." In the three claims, "the DNA molecule" (claims 42 and 43) and "said DNA molecule" (claim 45) refer back to antecedents in the claim. The antecedent in claims 42 and 43 is "a DNA molecule isolated from the immediately early (IE) promoter/regulatory region" of HCMV. '140 patent, col. 5, lines 1-3 and 9-11. In claim 45, the antecedent is "a DNA molecule isolated from the PstI m fragment of the immediate early (IE) region of human cytomegalovirus (HCMV)." *Id.*, col. 6, lines 5-7. There is nothing in the antecedent language that limits the "DNA molecule" only to an "enhancer." Instead, the "DNA molecule" in claims 42 and 43 is isolated from the "promoter/regulatory region," which could include all or part of the promoter. The "DNA molecule" in claim 45 is isolated from the "PstI m fragment," which is approximately 2,000 base-pairs and includes DNA sequences other than just an enhancer.
>
> The prosecution history also does not support Sanofi's construction of the "DNA molecule" as limited to an enhancer. The parties agree that the claims of the '140 patent were copied from the Stinski Patent. As discussed *supra*, the applicants distinguished claim 1 of the '522 patent, which uses the language "isolated DNA enhancer," from the Stinski patent by arguing that their "enhancer" was different from the "promoter" portion of Stinski's "promoter-regulatory region." Gross Decl. Ex. 24 at 9. In addition, during the prosecution of the '140 patent, the applicants told the Patent Office that the claimed "DNA molecule" was broader than just an enhancer. On May 10, 1999, the applicants filed an appeal brief after failing to overcome an anticipating prior art reference, the Stinski patent.
>
> > The fact that Stinski may have identified a sequence that includes the enhancer does not establish that Stinski explicitly or necessarily disclosed each and every element of claim 56 [claim 42 in the '140 patent]. Claim 56 requires more elements than the DNA molecule

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> isolated from the IE promoter/regulatory region of HCMV and is not even limited to such a molecule that is an enhancer.
>
> Supp. Gross Decl. Ex. A at 12. Sanofi's proposed construction of "DNA molecule" as consisting solely of the enhancer is inconsistent with these statements in the prosecution history, and thus cannot be adopted. *See Chimie v. PPG Industries, Inc.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005).
>
> There are several other problems with Sanofi's proposed constructions. Sanofi is attempting to incorporate its construction of the noun phrase "isolated DNA *enhancer*" from the '522 patent into the verb phrase "wherein the DNA molecule *enhances* . . . ." Sanofi's construction "is at war with its grammar and syntax and thus would force an unreasonable interpretation." *Credle v. Bond*, 25 F.3d 1566, 1571-72 (Fed. Cir. 1994). In addition, Sanofi's construction includes the phrase "increases the rate of transcription." However, neither the claims nor the specification mentions the "rate" of transcription. The specification refers only to increases in the amount of RNA and protein made by a cell.

Docket No. 383 at 17-18.

To the extent that Biogen argues that the "DNA molecule" in claims 42, 43 and 45 of the '140 patent need not include an "enhancer," the Court disagrees. At claim construction, Sanofi argued that the "DNA molecule" should be construed as limited solely to an "enhancer." The Court did not adopt Sanofi's construction because the Court concluded that "DNA molecule" is broader than simply an enhancer, and thus could include other components of a gene. However, the Court agrees with Sanofi that the "DNA molecule" in claims 42, 43 and 45 of the '140 patent must include an "enhancer" because "DNA molecule" must be understood "not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). Here, the '140 patent explicitly states that "[t]he invention is directed to an enhancer for eukaryotic expression systems," '140 Patent 1:12-15, and the specification repeatedly refers to the "enhancer."[14]

For the reasons stated above with regard to the '522 patent, the Court finds that Biogen has not proved invalidity by clear and convincing, uncontradicted evidence, because Dr. Spector's declaration raises issues of fact as to what a POSA would have understood based on the specification. Summary judgment of invalidity must be denied.

[14] The parties' pretrial submissions shall propose new constructions of "DNA molecule" that make clear that the "DNA molecule" includes an enhancer.

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IV. Sanofi's motion for summary judgment of no inequitable conduct

A. Legal standard

"Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the [PTO], which includes a duty to disclose to the [PTO] all information known to that individual to be material to patentability . . . ." 37 C.F.R. § 1.56(a). A breach of the duty of candor may lead to a finding of inequitable conduct rendering the entire patent unenforceable. *See Honeywell Int'l Inc. v. Universal Avionics Sys. Corp.,* 488 F.3d 982, 999-1000 (Fed. Cir. 2007). "To hold a patent unenforceable due to inequitable conduct, there must be clear and convincing evidence that the applicant (1) made an affirmative misrepresentation of material fact, failed to disclose material information, or submitted false material information, and (2) intended to deceive the [PTO]. . . ." *Cargill, Inc. v. Canbra Foods, Ltd.,* 476 F.3d 1359, 1363 (Fed. Cir. 2007). Both the materiality and intent elements are fact-driven, *McKesson Info. Solutions, Inc. v. Bridge Med., Inc.*, 487 F.3d 897, 902 (Fed. Cir. 2007), and it is the accused infringer that bears the burden of proving a threshold level of these elements, *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.,* 537 F.3d 1357, 1365 (Fed. Cir. 2008). A greater showing of materiality allows a lesser showing of intent, and vice versa. *McKesson,* 487 F.3d at 913.

"Although the premises of inequitable conduct require findings based on all the evidence, a procedure that may preclude summary determination, a motion for summary judgment may be granted when, drawing all reasonable factual inferences in favor of the non-movant, the evidence is such that the non-movant can not prevail." *Astrazeneca Pharms. LP v. Teva Pharms. USA, Inc.,* 583 F.3d 766, 770 (Fed. Cir. 2009) (quoting *ATD Corp. v. Lydall, Inc.,* 159 F.3d 534, 547 (Fed. Cir. 1998)). In order to survive summary judgment, the party asserting the inequitable conduct defense must "introduce evidence from which a trier of fact could find materiality and intent by clear and convincing evidence." *Abbott Labs. v. TorPharm, Inc.*, 300 F.3d 1367, 1379 (Fed. Cir. 2002).

B. Discussion

Defendants allege that the named inventors and their attorneys committed inequitable conduct by doing the following: (1) failing to disclose to the Patent Office the fact that Mark F. Stinski had

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previously developed the same invention before they filed their German application in August 1984; (2) engaging in forum-shopping within the Patent Office by, after the examiner rejected all claims of the '658 application as obvious over the Stinski patent and while the appeal of those rejections was pending, re-filing those identical claims and failing to disclose to the new examiner (Examiner Degen) the fact that the claims had already been rejected; (3) making misrepresentations to the examiner about the potency of the C2 enhancer while withholding their own contrary scientific data; and (4) deceptively convincing the Patent Office that they were entitled to the filing date of the earlier German patent application by relying on an abstract that never in fact appeared in the original German application.

Sanofi seeks summary judgment of no inequitable conduct on these claims, contending that defendants do not have clear and convincing evidence of materiality or intent. The Court finds that with the exception of the claim regarding the German patent abstract, defendants have raised triable issues as to both materiality and intent, and therefore that summary judgment is inappropriate. With regard to the first claim – the patentees' failure to disclose the Stinski abstract and presentation to the Patent Office – the Court finds that there are triable issues because while the Stinski patent was disclosed to the Patent Office, the Stinski patent did not disclose that the Stinski group performed experiments before May 1, 1984 (the deadline for the submission of abstracts). Stake Decl. Ex. 2. The timing of the Stinski group's inventive activity is relevant to whether Sanofi can establish a priority date of August 24, 1984 for the patents-in-suit.

With regard to the failure to disclose to Examiner Degen the rejections of identical claims in the co-pending '658 application, Sanofi argues that there is no inequitable conduct because the face of the '143 patent states that it is a continuation of the '658 patent; originally the same examiner (Examiner Carter) examined both the '658 and the '143 patents; the applicants disclosed the '658 patent on an Information Disclosure Statement; and Examiner Degen's notes shows that she "reviewed parents" while examining the '143 application. Stake Decl. Ex. 8 at GNE_SA 42310. However, the Federal Circuit has held that simply disclosing the existence of a parent application does not suffice to disclose all adverse decisions issued during prosecution of that patent. *See McKesson*, 487 F.3d at 924; *Li Second Family Ltd. Partnership v. Toshiba Corp.*, 231 F.3d 1373, 1379-81 (Fed. Cir. 2000). Further, while Sanofi argues that there is no evidence of intent to deceive the PTO because originally Examiner

Carter was responsible for examining both the '658 and '143 applications, a jury could find that the applicants intended to deceive the PTO by failing to disclose the rejections once Degen became the examiner.

On the third claim of inequitable conduct, defendants allege that the applicants knew that only the C4 enhancer, and not the C2 enhancer, was stronger than the SV40 enhancer, but that the applicants misrepresented that both enhancers were superior to SV40 in order to overcome obviousness rejections. Sanofi cites portions of the record in which the applicants stated that the "HCMV enhancer" was superior to the SV40 enhancer, and Sanofi argues that the applicants were referring to both the C4 and C2 fragments acting together as "the enhancer," and thus that there was no misrepresentation. However, as defendants argue, the applicants also repeatedly stated that the "enhancers" were superior to SV40, and there is evidence showing that the examiner came to believe that the "C2 and C4 [sequences] . . . were shown to be stronger enhancers than the SV40 enhancer." Stake Decl. Ex. 8 at GNE_SA41487. Sanofi also argues that, contrary to defendants' allegations, it did not withhold contrary scientific evidence (showing that the C2 enhancer was not stronger than the SV40 enhancer) in the Boshart article because that article was cited in Dr. Fleckenstein's declaration to the PTO. However, the evidence is unclear as to whether the examiner actually considered the Boshart article, and thus summary judgment is not appropriate.

Finally, defendants allege that the applicants committed inequitable conduct by allegedly misleading the PTO as to whether the Abstract had been part of the original German priority application. On May 10, 1999, during the prosecution of the '213 application (one of the applications that led to the '140 patent), the applicants sought to antedate, or "swear behind" the Stinski '062 patent so that it would not be considered prior art by submitting a sworn translation of their German priority application. Stake Decl. Ex. 8 at GNE_SA 42875-82. The copy of the German application that was submitted for this purpose, which contained an abstract, was certified by the president of the German Patent Office as a true and accurate copy of the application as it existed in the German Patent Office. *Id.* at GNE_SA0042883, GNE_SA0042889. However, the version of the German application that was

originally filed with the PTO in 1985[15] did not contain an abstract.

Sanofi argues that there is no inequitable conduct because the abstract was merely cumulative of the specification of the German application, and because there is no evidence of deceptive intent. The abstract states,

> An enhancer, which is more active than that of SV40 and has a broad spectrum of cells, has been located in the upstream region of the major immediate early gene of human cytomegalovirus, and isolated from this region. This enhancer is therefore suitable for eukaryotic expression systems, where it can be incorporated upstream or downstream of the structural gene or the regulatory region.

Stake Decl. Ex. 8 at GNE_SA0042893. Sanofi argues that the German abstract is cumulative of the specification and claims of the original German application because, *inter alia*, the applicants' submission that accompanied the sworn translation of the German application, which listed "exemplary support" for each pending claim, did not rely on the German abstract as the sole basis of priority support for any of the claims. Autz Decl. Ex. 3 at GNE_SA0042876-18. Sanofi also notes that defendants have not adduced any evidence that the Examiner relied on the German abstract for any purpose.

With regard to intent, Sanofi argues that the applicants' counsel, Mr. Barker, testified that he relied on the certification from the President of the German patent office that he had received a "correct and accurate reproduction" of the original submission of the German application. Autz Decl. Ex. 29 (Barker Depo. at 64:16-65:5). In addition, there is no indication that the inventors or anyone else involved in the patent prosecution, aside from Mr. Barker, even knew that the German Priority Application was resubmitted in 1999.

The Court concludes that defendants have not raised a triable issue of fact as to whether the applicants engaged in inequitable conduct regarding the resubmission of the German application. The Court agrees with Sanofi that the abstract is not material because the applicants did not rely on the abstract as the sole basis of support for any of the claims. *See Star Scientific*, 537 F.3d at 1366. Defendants argue that the abstract is material because the abstract provided "new" information about the location of the enhancer, namely that the HCMV enhancer is located upstream from the major IE

[15] On August 23, 1983, the applicants filed the parent application of the patents-in-suit. Stake Decl. Ex. 8 at GNE_SA42322-34. Along with this application, the applicants submitted a "certified copy" of the German application; that copy did not contain the abstract.

gene, while the German application simply states that the enhancer is located at "-118 to -458 and '263 to '524" relative to the "published DNA sequence." Stake Decl. Ex. 8 at GNE_SA0042891 at 2:10-13. The Court finds it unnecessary to resolve the parties' disputes about whether the abstract contained more specific information about the location of the enhancer because, in any event, the abstract was not cited as the sole support for any claim. Further, there is no evidence that Mr. Barker or the inventors intended to deceive the PTO. *See Star Scientific*, 537 F.3d at 1366.

Accordingly, the Court GRANTS Sanofi's motion for summary judgment of no inequitable conduct with regard to defendants' claim that the applicants deceived the PTO about the German abstract, and DENIES the balance of Sanofi's motion.

V. Sanofi's motion for summary judgment of no invalidity under 35 U.S.C. § 102(g)

A. Legal standard

Title 35 U.S.C. § 102(g) provides that "[a] person shall be entitled to a patent unless . . . before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it." 35 U.S.C. § 102(g)(2). "Prior invention by another invalidates a claimed invention under section 102(g)(2) if the prior inventor either reduced the invention to practice first, or conceived of the invention first and subsequently reduced the invention to practice." *Rosco, Inc. v. Mirror Lite Co.*, 304 F.3d 1373, 1381 (Fed. Cir. 2002).

B. Discussion

Sanofi seeks summary judgment of no invalidity under 35 U.S.C. § 102(g) for both patents. However, in their opposition, defendants state that they do not claim that the '522 patent is invalid under 35 U.S.C. § 102(g), but rather that the prior inventions of the Stinski Group, the Upjohn Group, and the Merck Group, combined with the Weber reference, render the claims of the '522 patent obvious. Defendants have separately moved for summary judgment on this ground, and the Court addresses these arguments *infra*.

With respect to the '140 patent, Sanofi asserts that the inventors of the '140 patent were the first to conduct the experiments necessary to conceive and reduce to practice the HCMV enhancer, which

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they first disclosed in the German patent application dated August 24, 1984 and at the Ninth International Herpesvirus Workshop, which commenced the same day. Hersh Decl. Ex. 9, 14. Sanofi contends that Dr. Stinski, the Upjohn Group and the Merck Group only worked with large fragments of DNA, which they recognized only as promoters to initiate transcription of a gene, and that none of those groups ever performed the experiments necessary to reveal the presence of an enhancer. Sanofi argues that while Dr. Stinski, the Upjohn Group and the Merck Group each experimented with fragments of HCMV DNA, none of these groups tested whether the HCMV fragment functioned as an enhancer. Thus, Sanofi argues, there is no clear and convincing evidence that the alleged prior inventors possessed "the knowledge about the invention to show a conception." *Invitrogen*, 429 F.3d at 1064; *see also Heard v. Burton*, 333 F.2d 239, 243 (C.C.P.A. 1964) ("we consider it fatal to [Heard's] case that not until after the [critical date] did Heard recognize that his 'ammonia-aged' catalyst . . . 'contained any different form of alumina at all.'")

Defendants first respond that the "fundamental fallacy of Sanofi's motion is its argument that the prior inventors had to invent an 'isolated DNA enhancer' in order to anticipate the claims of the '140 patent." Defendants' Oppo. at 2:7-8. However, as discussed *supra*, the "DNA molecule" in claims 42, 43 and 45 of the '140 patent must include, but is not necessarily limited to, an "enhancer." Defendants also argue, more persuasively, that there are numerous issues of fact regarding whether the alleged prior inventors recognized that the DNA sequences they used included enhancers. Defendants have submitted evidence showing that the three groups of prior inventors were focused specifically on enhancing eukaryotic gene expression, and they have submitted evidence which, viewed in the light most favorable to defendants, shows that the three groups recognized that the DNA molecules they used contained enhancers. *See generally* evidence cited at Defs' Opp'n at 16-19.

Sanofi has not cited any authority for the proposition that conception requires that prior inventors conduct laboratory experiments showing all attributes of an invention. Instead, the cases cited by Sanofi addressed "unrecognized accidental duplication [where] the invention exists but remains unrecognized," and thus the need for "objective evidence to corroborate an inventor's testimony concerning his understanding of the invention." *Invitrogen*, 429 F.3d at 1064 (discussing *Heard*). Here, defendants have raised a triable issue of fact as to whether the alleged prior inventors invented the HCMV

enhancer, and whether they understood that they invented the HCMV enhancer.

VI. Defendants' motion for summary judgment of invalidity

Defendants seek summary judgment that (1) claims 42-45 of the '140 patent are invalid because the Stinski patent anticipates the claims; and (2) claims 1 and 2 of the '522 patent and claims 42-45 of the '140 patent are obvious over at least the Weber and Thomsen references.

A. Anticipation

1. German priority date

Defendants contend that claims 42-45 of the '140 patent are invalid because the Stinski patent anticipates the claims. The application for the Stinski patent was filed on January 30, 1985. Sanofi claims that it is entitled to an invention date of August 24, 1984, the filing date of the German Application. Defendants contend that the '140 patent is not entitled to the foreign priority date of the German application because the foreign filing does not meet the disclosure requirements provided in 35 U.S.C. § 112, including the written description requirement. "[C]laims set forth in a United States application are entitled to the benefit of a foreign priority date if the corresponding foreign application supports the claims in the manner required by section 112, ¶ 1." *In re Gosteli*, 872 F.2d at 1010.

Defendants argue that the German application does not meet the written description requirement because the German application does not disclose a DNA sequence, and instead the specification lists coordinates for the C2 and C4 enhancer fragments ("positions -118 to -458 and -263 to -524") from an unidentified "published DNA sequence." Wall Decl. Ex. 19 at SA-US0000760. Defendants argue that the failure to disclose sequence information renders claims to allegedly novel DNA sequences invalid. Defendants also argue, as Biogen did on its motion for summary judgment of invalidity for lack of written description, discussed *supra*, that the German application's disclosure does not support broad genus claims, and that the application does not disclose "either a representative number of species falling within the scope of the genus or structural features common to the members of the genus." *Eli Lilly*, 598 F.3d at 1350.

Sanofi has submitted the declaration of Dr. Spector in which she states, *inter alia*, that the

German application provided sufficient information for a POSA to recognize, obtain and use the HCMV enhancer. *See* Spector Decl. ¶¶ 44, 46-49, 52, 54. On this disputed record, the Court cannot grant summary judgment and conclude that German application is invalid for lack of written description. In light of the disputes of fact regarding whether Sanofi is entitled to the German priority date, the Court finds it unnecessary to address the parties' arguments about whether the Stinski patent anticipates the claims of the '140 patent.

2. Conception and reduction to practice

In its opposition to defendants' motion, Sanofi also asserts that regardless of whether it can claim priority from the German application, it is entitled to an earlier invention date than Stinski based on "conception of the '140 Patent claims in the United States by August 24, 1984, the date the Boshart Abstract was published," and diligent reduction to practice by filing a domestic patent application in 1985. Opp'n at 7-10.

However, defendants contend that this is a new and previously undisclosed theory of priority, and that Sanofi is barred from asserting it for the first time in opposition to summary judgment. Defendants state that the first interrogatory that Genentech served in this case – two years ago – required Sanofi to "[d]escribe in detail the conception and reduction to practice of the claims of the patents-in-suit," including the "dates of and locations" of these events. Gross Decl. Ex. 1 at 7. Sanofi responded twice, stating that all relevant events occurred in Europe, not the United States, and invoking Section 104 of the Patent Code to claim the benefit of the filing date of the German application. *Id.* Ex. 2 at 6-7; Olson Decl. Ex. 33 at 6-8. Sanofi stated,

> the six inventors named on the patents-in-suit jointly conceived of the subject matter of the claims between 1982 and 1984, in Erlangen, Germany and Zurich, Switzerland. Sanofi-Aventis Germany further states that, according to its current understanding, the six inventors named on the patents-in-suit reduced the subject matter of the claims to practice between 1982 and 1984, in Erlangen, Germany and Zurich, Switzerland[.]

Olson Decl. Ex. 33 at 7. According to defendants, Sanofi never supplemented its response to disclose a theory of conception in the United States in 1984, or diligence in reduction to practice by filing the domestic patent application in 1985. At the hearing on this matter, Sanofi did not dispute defendants' assertion that Sanofi did not previously disclose this theory in discovery, nor did Sanofi offer any

explanation of its failure to do so.

A party that fails to provide information in discovery "is not allowed to use that information . . . to supply evidence on a motion, at a hearing, or at a trial, unless the failure was substantially justified or is harmless." Fed. R. Civ. Proc. 37(c)(1); *see also Asyst Techs. v. Empak, Inc.*, No. 98-cv-20451, 2006 WL 870970, at *6 (N.D. Cal. Mar. 31, 2006) (rejecting on summary judgment a non-infringement theory not disclosed in interrogatory responses). Sanofi has not provided any justification for its failure to disclose this new theory of domestic conception and reduction to practice. The Court finds that Sanofi's failure to disclose this theory was not harmless, as defendants have not been able to investigate through discovery these allegations of domestic conception and diligence. For example, defendants state that when they deposed M. Paul Barker, the patent attorney responsible for the '522 and '140 patents, they focused on obviousness, not conception or diligence. Similarly, defendants did not question the inventors about "diligence" in the United States. Allowing Sanofi to assert this new theory at this late date would be prejudicial to defendants. Discovery has closed, this case has been pending since 2008, and there is a trial date set for June 13, 2011.

Accordingly, Sanofi is barred from asserting that it is entitled to an earlier invention date than Stinski based on conception of the '140 Patent claims in the United States by August 24, 1984, the date the Boshart Abstract was published, and diligent reduction to practice by filing a domestic patent application in 1985.

B. Obviousness

1. Legal standard

A granted patent is presumed valid, 35 U.S.C. § 282, and to invalidate the patents-in-suit, defendants must prove by clear and convincing evidence that "the subject matter as whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a); *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). Obviousness under 35 U.S.C. § 103 is a question of law, with underlying factual considerations regarding (1) the scope and content of the prior art, (2) the differences between the prior art and the claimed invention, (3) the level of ordinary skill in the art, and (4) any relevant secondary

considerations. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966). A claimed invention is invalid for obviousness "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103.

"Although it is well settled that the ultimate determination of obviousness is a question of law, it is also well understood that there are factual issues underlying the ultimate obviousness decision." *McGinley v. Franklin Sports, Inc*., 262 F.3d 1339, 1349 (Fed. Cir. 2001). Summary judgment may be appropriate if "the content of the prior art, the scope of the patent claim, and the level of ordinary skill in the art are not in material dispute, and the obviousness of the claim is apparent in light of these factors." *KSR*, 550 U.S. at 427 (citing *Graham*, 383 U.S. at 17). However, a factual dispute as to any one of these elements will defeat the motion. *See Helifix Ltd. v. Blok-Lok, Ltd.*, 208 F.3d 1339, 1346 (Fed. Cir. 2000).

2. Discussion

Defendants contend that claims 1 and 2 of the '522 patent and claims 42-45 of the '140 patent are obvious based on the Thomsen and Weber references. In February 1984, the Stinski group published the Thomsen reference, Darrell R. Thomsen *et al.*, "Promoter-regulatory region of the major immediate early gene of human cytomegalovirus," P.N.A.S. 81:659-663 (1984) (E. Wall Decl. Ex. 10). This paper disclosed the DNA sequence of the "promoter-regulatory region" of the major IE gene, which extended 489 base pairs upstream of the transcription start site of the gene. The disclosed DNA sequence includes the entire C2 enhancer and most of the C4 enhancer described in the disclosure of the patents-in-suit. In early 1984, the Schaffner laboratory published the Weber reference, Frank Weber, *et al.*, "An SV40 'Enhancer Trap' Incorporates Exogenous Enhancers or Generates Enhancers from its Own Sequences," *Cell*, Vol. 36, April 1984 (E. Wall Decl. Ex. 13). The Weber reference discloses an "enhancer trap" method of identifying viral DNA sequences that function as enhancers.

Defendants contend the claims at issue are obvious because a person of skill in the art in the early 1980s had every reason to combine the teachings of the Thomsen and Weber references.

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Defendants argue that those in the art were motivated to express therapeutically useful proteins in high quantities and numerous publications documented efforts to locate enhancers that could be used to increase expression of genes encoding these proteins. Defendants contend that to identify these enhancers, one of skill in the art would have turned to the Weber reference, which disclosed the "enhancer trap," a method of isolating enhancers. Then, defendants argue, a skilled artisan would have been led from the Weber reference, which disclosed that there was a strong and versatile enhancer in the IE region of HCMV, to the Thomsen reference, which disclosed the precise sequence of a region of DNA involved in the transcription of the major IE gene. Defendants argue it was "obvious to try" using the Thomsen reference sequence in the enhancer trap. *KSR*, 550 U.S. at 421.

Sanofi contends that summary judgment should be denied because there are disputes of fact as to the scope and content of the Weber and Thomsen references, as well as disputes regarding the motivation to combine the references. The Court agrees. Sanofi has submitted the declaration of its expert, Dr. Spector, in which she states, *inter alia*, that nothing in the prior art would have motivated or suggested to one of ordinary skill in the art that an enhancer was present in HCMV. Dr. Spector disputes Dr. Levine's description of the content of prior art, Spector Decl. ¶¶ 133-34, and states that during the relevant time period, the presence of a highly transcribed region (as disclosed in the Thomsen reference) would not predict to a person of ordinary skill that the region contained an enhancer. *Id.* ¶¶ 140-43. Dr. Spector's declaration raises a number of disputes regarding obviousness, and thus the Court cannot conclude that defendants have met their burden on summary judgment. *See generally id.* ¶¶ 122-66. Further, because the Weber and Thomsen references were considered by the PTO during prosecution, "part of [defendants'] burden is to show that the PTO was wrong in its decision to grant the patent. When new evidence touching validity of the patent not considered by the PTO is relied on, the tribunal considering it is not faced with having to disagree with the PTO or with deferring to its judgment or with taking its expertise into account. The evidence may, therefore, carry more weight and go further toward sustaining the attacker's unchanging burden." *American Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F.2d 1350, 1360 (Fed. Cir. 1984).

On this disputed record, defendants have not shown for purposes of summary judgment that the PTO was wrong in its decision to grant the patents because of obviousness. Accordingly, the Court

DENIES defendants' motion for summary judgment of invalidity.

CONCLUSION

For the reasons stated above, the Court hereby GRANTS Sanofi's motion to amend infringement contentions, DENIES Genentech's motion to strike, GRANTS IN PART Genentech's motion for summary judgment of non-infringement, DENIES Biogen IDEC's motion for summary judgment of invalidity for lack of written description, GRANTS IN PART Sanofi's motion for summary judgment of no inequitable conduct, DENIES Sanofi's motion for summary judgment of no invalidity, and DENIES defendants' motion for summary judgment of invalidity. (Docket Nos. 407, 412, 448, 501, 543, 551, 554, and 557).

IT IS SO ORDERED.

Dated: March 7, 2011

SUSAN ILLSTON
United States District Judge

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