IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

GENETICS INSTITUTE, LLC,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Civ. No. 08-290-SLR
	)	
NOVARTIS VACCINES AND DIAGNOSTICS, INC.,	)	
	)	
	)	
Defendant.	)	

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MEMORANDUM OPINION

Dated: February 24, 2010
Wilmington, Delaware

ROBINSON, District Judge

I. INTRODUCTION

This is an action to determine priority of invention brought under 35 U.S.C. § 291. Plaintiff Genetics Institute, LLC ("GI" or "plaintiff") filed its complaint on May 16, 2008. In its complaint, plaintiff stated that it owns U.S. Patent No. 4,868,112 ("the '112 patent"), entitled "Novel procoagulant proteins." Plaintiff seeks an adjudication of priority vis-a-vis two patents assigned to Novartis Vaccines and Diagnostics, Inc. ("defendant"): U.S. Patent Nos. 6,060,447 ("the '447 patent") and 6,228,620 ("the '620 patent").

II. BACKGROUND

A. Procedural History

From the start of this case, defendant has disputed plaintiff's claim of ownership of the '112 patent and, consequently, the court's jurisdiction in this 35 U.S.C. § 291 action. In lieu of an answer, defendant filed a motion to dismiss for lack of jurisdiction over the subject matter or, in the alternative, for transfer under 28 U.S.C. § 1404 to the Eastern District of Texas.[1] (D.I. 8) In response to defendant's motion, plaintiff adduced uncontraverted documentary evidence indicating that, despite a transfer of assets to Wyeth in 1996, plaintiff retained its rights in the '112 patent. The court denied defendant's motion without prejudice on February 18, 2009. (D.I. 26; D.I. 28 (amended)) The court allowed discovery to proceed in order to vet the issue. The court

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[1]Defendant sought transfer and possible consolidation with E.D. Tex. Civ. No. 08-067, an action brought by defendant against Wyeth. Plaintiff is a wholly-owned subsidiary of Wyeth but is not a party to that suit. Defendant did not name any specific prior art in its invalidity pleadings in that case.

The court notes that, on January 26, 2010, a merger was announced whereby Wyeth will become part of Pfizer Inc.

thereafter sought additional briefing by the parties regarding jurisdiction and transfer. (D.I. 41) On May 7, 2009, the court denied defendant's motion for reargument (D.I. 29), and set a schedule for jurisdictional discovery, claim construction briefing, and for defendant to renew its motion. (D.I. 53; D.I. 54)

On July 28, 2009, against a backdrop of disputes regarding the scope of permissible discovery, the court ordered that the parties produce documents for *in camera* review regarding jurisdiction. (D.I. 75) Following its review, and because of persisting ambiguities on the issue, the court ordered plaintiff to file a disclaimer by Wyeth or submit to unfettered jurisdictional discovery. (D.I. 80) Claim construction briefing commenced pursuant to the court's schedule, and plaintiff subsequently filed a disclaimer by Wyeth on August 19, 2009. (D.I. 99) Following an additional conference with the parties, the court halted jurisdictional discovery, set a discovery period on priority of invention, and set a briefing schedule for defendant to renew its motion to dismiss on the grounds of lack of standing and no interference-in-fact. (D.I. 110) Defendant filed its motion to dismiss on September 19, 2009. (D.I. 115) Oral argument on claim construction, jurisdiction and interference-in-fact was held on October 23, 2009. In view of the impending February 28, 2010 expiration of the '112 patent, a pretrial conference was held December 3, 2009, and a three-day bench trial on priority of invention commenced on December 14, 2009.

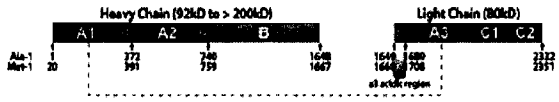
B. Scientific Background

The '112 patent describes procoagulant proteins that are similar to human Factor VIII. Factor VIII is an essential blood clotting factor also known as anti-hemophilic

factor ("AHF"). Defects in the gene encoding Factor VIII[2] result in hemophilia A, a genetic disorder associated with prolonged bleeding.

Factor VIII protein circulates in the blood in inactive form. Factor VIII is activated (to Factor VIII-A) in a reaction catalyzed by the enzyme thrombin.[3] Once activated, Factor VIII-A serves as a cofactor[4] for the enzyme Factor IX-A. The formation of a Factor VIII-A–Factor IX-A complex activates Factor X enzyme (to Factor X-A) which, in turn, activates more thrombin. The active enzyme thrombin converts fibrinogen to fibrin, which is then cross linked by Factor XIII to form a blood clot. Activated Factor VIII becomes inactivated in the process and cleared from the blood stream. The foregoing chain of reactions is generally referred to as the "blood clotting cascade." (D.I. 175 at 303:8-21)

The mature Factor VIII protein consists of 2,332 amino acids and is characterized by several "domains" – portions of the protein that fold into a three dimensional structure independent from the other portions of the protein. (*Id.* at 214:11-17) Starting from the N terminal of the molecule, the domains have been labeled the A1, A2, B, A3, C1 and C2 domains, as illustrated below. (*Id.*)



[2]The gene is located on the X chromosome.

[3]Also called activated Factor II (Factor II-A).

[4]Generally, a cofactor is a non-protein chemical compound, typically an enzyme, that is bound to a protein and is required for the protein's biological activity. *See* http://en.wikipedia.org/wiki/Cofactor_(biochemistry).

Each of the A1-A3 domains is bordered by an acidic region known as a1, a2, and a3. Amino acids 1 to 740 constitute the A1 and A2 domains.[5] This region has a molecular weight of 92 kilodaltons ("kD") and is often referred to as the "heavy chain." (*Id.* at 214:18-215:13) Amino acids 741 to 1648 constitute the B domain of Factor VIII. (*Id.*) The B domain is unnecessary for Factor VIII functional activity. (D.I. 175 at 214:18-215:3; *id.* at 312:3-22; D.I. 177 at 633:16-634:1) Amino acids 1649 to 2332 constitute the 80 kD "light chain," which includes what is referred to as the "a3 acidic region" (amino acids 1649-1689), the A3 domain, and the C1 and C2 domains. (D.I. 175 at 311:24-313:4) The a3 acidic region is cleaved when Factor VIII is activated by thrombin in the body.

The a3 acidic region of Factor VIII is critical with respect to Factor VIII's performance. This particular region of the Factor VIII protein binds to von Willebrand factor ("vWF"), a large blood protein that prevents the degradation of Factor VIII and thereby acts as a stabilizing carrier protein in the human bloodstream. (*Id.* at 380:3-23; D.I. 176 at 561:5-11; D.I. 177 at 628:19-629:3) If Factor VIII is not able to form a complex with vWF, the halflife of Factor VIII in plasma is reduced about five-fold. (D.I. 175 at 393:1-7; D.I. 177 at 629:10-20) Thus, the association of Factor VIII with vWF is critical to regulating coagulation activity in the blood. (D.I. 175 at 381:3-10) Conversely, a Factor VIII protein that cannot bind vWF may give rise to unwanted clots in areas such as heart vessels because unbound Factor VIII can bind blood platelets even when no injury has been detected. (D.I. 177 at 637: 22-25; *id.* at 638:12-23)

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[5]The court will refer to the amino acids of Factor VIII by reference to the Ala-1 numbering system, unless otherwise indicated.

Traditionally, treatment of hemophilia A involved administering partially purified Factor VIII derived from porcine or human plasma. (PTX-81 at 3; D.I. 175 at 301:24-302:3) In the 1980s, human plasma sources had become contaminated with viruses, such as HIV or hepatitis, making treatment of hemophilia with Factor VIII derived from plasma dangerous. (D.I. 175 at 302:10-15) Recombinant Factor VIII, made by DNA cloning, promised to be a safer and abundant new source of therapeutic material. (*Id.* at 302:16-21) The cloning of Factor VIII, however, turned out to be an enormous technical undertaking, because the protein was nearly an order of magnitude larger than any other protein that had been cloned at that time. (D.I. 174 at 126:23-127:14) The large size of the protein meant that the corresponding DNA sequence was also large, which complicated the cloning process. (*Id.*) Scientists raced to be the first to clone Factor VIII. After this had been achieved, the focus of Factor VIII work shifted to finding a smaller recombinant protein that mimicked the biological activity of Factor VIII in humans. The parties dispute who first discovered that the a3 acidic region (on the light chain) should be preserved.

C. Patents at Issue

The '112 patent claims priority to U.S. Patent Application No. 725,350 ("the '350 application"), filed April 12, 1985. U.S. Patent Application No. 07/010,085 ("the '085 application"), a continuation in part application, was filed April 11, 1986 and claims priority to the '350 application. The '085 application incorporates by reference the contents of the '350 application, which was subsequently abandoned. The '112 patent issued September 19, 1989. John J. Toole Jr. ("Toole") is the sole named inventor on the '112 patent, which is assigned to GI.

The '447 and '620 patents share a common history. Both can trace priority to U.S. Patent Application No. 06/822,989 ("the '989 application"), filed January 27, 1986. Several consecutive continuation in part applications followed. The '447 and '620 patents issued from separate continuation applications (and two divisionals) filed in the chain. Named inventors on the patents are: Barbara Chapman; Rae Lyn Burke; Mirella Ezban Rasmussen; and Jan Moller Mikkelson. The '447 and '620 patents are assigned to Chiron Corporation and Novo Nordisk A/S. The '112 patent appears on the face of both the '447 and '620 patents.

Plaintiff asserts that the following sets of claims interfere: (1) claim 1 of the '112 patent and claim 68 of the '620 patent; (2) claim 5 of the '112 patent and claim 74 of the '620 patent; (3) claim 9 of the '112 patent and claim 83 of the '620 patent; and (4) claims 9 and 10 of the '112 patent and claim 1 of the '447 patent.

The '112 patent and '620 patent each contain claims to recombinant human Factor VIII proteins, host cells containing (and capable of expressing) the recombinant DNA which upon expression results in the recombinant Factor VIII, and methods for producing recombinant Factor VIII by culturing these host cells. The claims differ in terms of how they define the Factor VIII proteins encoded by the nucleic acids.

The recombinant protein of the '112 patent contains the amino acid sequence for human Factor VIII except for a **deletion** (between 581 and 949 amino acids long) between amino acids 740 to 1690 in the Ala-1 numbering system.[6] This deletion range

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[6]'112 patent claim 1 reads as follows.

1. A recombinant DNA which upon expression results in a truncated Factor VIII protein which is an active procoagulant wherein the recombinant DNA encodes

encompasses the inactive B domain (amino acids 640 to 1648) and, additionally, a portion of the light chain, including the a3 acidic region (amino acids 1649 to 1689). Claim 10 of the '112 patent claims a recombinant Factor VIII protein having one of three specific deletions (amino acids 1000-1582, 778-1659, or 778-1694).[7]

The '620 patent defines the recombinant Factor VIII protein in terms of the **retained** portions. Claim 68 of the '620 patent provides a recombinant protein lacking all or part of the B domain, and having at least 90% sequence identity with the heavy and light chains (the A1 and A2 domains (amino acids 1 to 740) and the a3, C1 and C2 domains (amino acids 1649 to 2332)).[8] Optionally, up to 10 amino acids of the B

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for a protein having the amino acid sequence of a human Factor VIII:C except for having a deletion corresponding to at least 581 amino acids within the region between Arg-759 and Ser.-1709, wherein the amino acid numbering is with reference to Met-1 of the human Factor VIII:C leader sequence.

[7]'112 patent claim 10 reads as follows.

10. A truncated human Factor VIII:C protein which is an active procoagulant protein having a peptide sequence of human Factor VIII:C but lacking a peptide region selected from the group consisting of:
(a) the region between Pro-1000 and Asp-1582;
(b) the region between Thr-778 and Pro-1659; and,
(c) the region between Thr-778 and Glu-1694.

[8]'620 patent claim 68 reads as follows.

68. A nucleic acid composition for introducing nucleic acid into a eukaryotic host cell to obtain expression of a recombinant protein lacking all or a portion of the B domain of human Factor VIII, wherein said recombinant protein consists of: a first amino acid sequence which consists of an amino acid sequence having at least 90% sequence identity with the contiguous amino acid sequence of amino acids 1 to 740 of the native, mature A domain of human Factor VIII and optionally up to 10 amino acids of the human Factor VIII B domain sequence contiguous to amino acid 740 as encoded by the polynucleotide present in plasmid pSVF8-200 (ATCC No. 40190); and a second amino acid sequence which consists of an amino acid sequence having at least 90% sequence identity

domain can be retained, such that the retained portions are amino acids 1 to 750 and 1639 to 2332.

Claim 1, the only claim of the '447 at issue, is directed to a composition comprising Factor VIII proteins. That claim specifies that the Factor VIII proteins consist of two polypeptides: a first comprising an amino acid sequence of the A domain, and a second corresponding to the C domain. At least a 90% sequence identity with each region is required.[9]

D. The Priority Dispute

According to plaintiff, all of the claims of the '112, '620, and '447 patents are directed to embodiments of the same subject matter: truncated Factor VIII variants lacking all or part of the B domain of the protein while retaining procoagulant activity. Plaintiff asserts that Toole conceived these truncated Factor VIII variants by October

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with the contiguous amino acid sequence of amino acids 1649 to 2332 of the native, mature C domain of human Factor VIII and optionally up to 10 amino acids of the human Factor VIII B domain sequence contiguous to amino acid 1649 as encoded by the polynucleotide present in plasmid pSVF8-200 (ATCC No. 40190); wherein said nucleic acid encodes said first and second amino acid sequences, and further wherein said recombinant protein is capable of coagulation activity in a coagulation activity assay.

[9]'447 patent claim 1 reads as follows.

> 1. A composition comprising Factor VIII:C proteins, wherein the Factor VIII:C proteins consist essentially of a first polypeptide comprising an amino acid sequence of the A domain of human Factor VIII:C as encoded by the polynucleotide present in plasmid pSVF8-200 (ATCC No. 40190) or an amino acid sequence that differs therefrom in having not more than 10 number % amino acid substitutions, and a second polypeptide comprising an amino acid sequence of the C domain of human Factor VIII:C as encoded by the polynucleotide present in plasmid pSVF8-200 (ATCC No. 40190) or an amino acid sequence that differs therefrom in having not more than 10 number % amino acid substitutions.

15, 1984, completed actual reduction to practice by February 8, 1985, and completed constructive reduction to practice on the date of filing of the '350 application, April 12, 1985.

According to defendant, there is no interference-in-fact because its patents are directed to a variation that preserves the light chain and the a3 acidic region within it, while the '112 patent is directed toward the deletion of a key part of those functional domains. If an interference-in-fact is found, defendant argues that the common subject matter between the claims is the group of Factor VIII compounds with a deletion of at least the region between amino acids 750 and 1639 and at most the region between amino acids 740 and 1649, which deletion does not invade functional domains. Defendant argues that the foregoing is separately patentable from larger deletions that invade the functional domains of Factor VIII, as well as smaller deletions of as few as 581 amino acids. Defendant alleged at trial that it had a fully documented and corroborated conception of this subject matter on February 28, 1985, and diligently reduced it to practice by September 10, 1985.

Defendant seeks to exclude Toole's work and claims from the court's definition of the interfering subject matter, insofar as defendant's alleged conception date (February 28, 1985) is preceeded by Toole's proffered conception date (October 15, 1984). Plaintiff argues that there are no claims of the '620 and '447 patents that contain subject matter that is patentably distinct from the properly-defined count.

Defendant's characterization of the interfering subject matter would also exclude

Wyeth's commercial recombinant Factor VIII protein, "ReFacto®,"[10] which retains the a3 acidic region. The '112 patent was set to expire September 19, 2006, based on a seventeen-year statutory term. In 2000, counsel for plaintiff requested and obtained an extension of patent term under 35 U.S.C. § 156[11] based on the period of time ReFacto® was in the regulatory approval process. (D.I. 11, ex. 8) The United States Patent and Trademark Office ("PTO") granted an extension through February 28, 2010.[12] (D.I. 10, ex. 8) The claims cited by plaintiff as covering ReFacto® were claims 9 and 10 of the '112 patent. Defendant also seeks a determination that ReFacto® is outside of the (properly construed) scope of these claims and, therefore, the '112 patent has expired.

E. Summary of Issues Before the Court

Defendant has filed a renewed motion to dismiss this case based in part on plaintiff's alleged lack of standing. Defendant emphasizes that Wyeth plans to assert

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[10]"[A]n antihemophilic factor for use in therapy for factor VIII deficiency comprising a purified protein produced by recombinant DNA technology." (D.I. 11, ex. 8 at 2) Wyeth appears to have stopped offering ReFacto® as of May 2009. Its current product, "Xyntha®," is advertised to have "the same molecular structure as ReFacto® with improved purification technology." *See http://www.hemophiliavillage.com/refacto.html.*

[11]"The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent, which shall include any patent term adjustment granted under section 154(b), if – . . . (4) the product has been subject to a regulatory review period before its commercial marketing or use[.]" 35 U.S.C. § 156(a). Generally, "[t]he term of a patent eligible for extension under subsection (a) shall be extended by the time equal to the regulatory review period for the approved product which period occurs after the date the patent is issued[.]" 35 U.S.C. § 156(c).

[12]The '447 and '620 patents will not expire until 2017 and 2018, respectively.

the '112 patent as alleged prior art in the copending Texas litigation, and rehashes its arguments made prior to the disclaimer filed by Wyeth in this action.

The alternative ground for defendant's motion to dismiss is a lack of subject matter jurisdiction. A determination that the '112 patent was improperly granted a patent term extension (and, therefore, is expired) would defeat jurisdiction. Further, the *sine qua non* of an action under 35 U.S.C. § 291 is actual interference between patents. *See Albert v. Kevex Corp.*, 729 F.2d 757, 760-61 (Fed. Cir. 1984). Absent interference-in-fact, dismissal is appropriate.

If an interference-in-fact is found, the court must define the "count," or the common subject matter between the claims. *See Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1168 (Fed. Cir. 2006) (although Federal Circuit precedent has not addressed whether an official "count" is required, the district court must, at a minimum, be "clear about the identity of the interfering subject matter" in a § 291 action) (citing *Slip Track Sys., Inc. v. Metal-Lite, Inc.*, 304 F.3d 1256, 1264 (Fed. Cir. 2002)). Once the interfering subject matter has been defined, the court must award priority of invention. A finding of invalidity, if appropriate, may follow the priority determination.

III. STANDARDS

A. Interference-in-Fact

An interference-in-fact exists only if both plaintiff and defendant have at least one claim that is designated to correspond to a count and those claims define the "same patentable invention." 37 C.F.R. § 1.601(j). The phrase "same patentable invention" is defined as follows.

> Invention "A" is the same patentable invention as an invention "B" when invention "A" is the same as (35 U.S.C. [§]102) or is obvious (35 U.S.C. [§] 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A." Invention "A" is a separate patentable invention with respect to invention "B" when invention "A" is new (35 U.S.C. [§]102) and non-obvious (35 U.S.C. [§]103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A."

37 C.F.R. § 1.601(n). These inquiries are referred to as the "two way test" for interference-in-fact. *Eli Lilly & Co. v. Board of Regents of University of Washington*, 334 F.3d 1264, 1268 (Fed. Cir. 2003). "As written, section 1.601(n) incorporates the standards for both anticipation under § 102 and obviousness under § 103 in determining the existence of an interference, permitting either circumstance to satisfy that leg of the two-way test." *Medichem, S.A. v. Rolabo, S.L.*, 353 F.3d 928, 934 (Fed. Cir. 2003) (emphasis added). "Under the two-way test, an invention A is not the 'same invention' as invention B if A is neither anticipated by, nor obvious in view of, invention B – even though invention B is anticipated by, or obvious in view of, invention A." 3A-10 Chisum on Patents § 10.09.

B. Anticipation

The first step in both the anticipation and obviousness analyses is a proper construction of the claims. *Id.* (citing *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 970-71 (Fed. Cir. 1995)). The second step is a comparison of the properly construed claim to the prior art. *Id.* at 933 (citation omitted).

For anticipation to be found, "the four corners of a single, prior art document [must] describe every element of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue

experimentation." *Advanced Display Sys. Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000) (citations omitted). The Federal Circuit has stated that "[t]here must be no difference between the claimed invention and the referenced disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991). The elements of the prior art must be arranged or combined in the same manner as in the claim at issue, but the reference need not satisfy an *ipsissimis verbis* test. *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. Mar. 26, 2009) (citations omitted). "In determining whether a patented invention is [explicitly] anticipated, the claims are read in the context of the patent specification in which they arise and in which the invention is described." *Glaverbel Societe Anonyme v. Northlake Mktg. & Supply, Inc.*, 45 F.3d 1550, 1554 (Fed. Cir. 1995). The prosecution history and the prior art may be consulted "[i]f needed to impart clarity or avoid ambiguity" in ascertaining whether the invention is novel or was previously known in the art. *Id.* (internal citations omitted).

C. Obviousness

"A patent may not be obtained . . . 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." 35 U.S.C. § 103(a). Obviousness is a question of law, which depends on several underlying factual inquiries.

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is

> determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 405 (2007) (quoting *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966)). "Because patents are presumed to be valid, *see* 35 U.S.C. § 282, an alleged infringer seeking to invalidate a patent on obviousness grounds must establish its obviousness by facts supported by clear and convincing evidence." *Kao Corp. v. Unilever U.S., Inc.*, 441 F.3d 963, 968 (Fed. Cir. 2006) (citation omitted).

"[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. Likewise, a defendant asserting obviousness in view of a combination of references has the burden to show, by clear and convincing evidence, that a person of ordinary skill in the relevant field had a reason to combine the elements in the manner claimed. *Id.* The Supreme Court has emphasized the need for courts to value "common sense" over "rigid preventative rules" in determining whether a motivation to combine existed. *Id.* at 419-20. "[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *Id.* at 420.

In addition to showing that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed process, a defendant must also demonstrate, by clear and convincing evidence, that "such a person would have had a reasonable expectation of success in doing so."

PharmaStem Therapeutics, Inc. v. ViaCell, Inc., 491 F.3d 1342, 1360 (Fed. Cir. 2007).

IV. DISCUSSION

A. Plaintiff Has Standing

As discussed *supra*, defendant has had ample opportunity to demonstrate that the court lacks jurisdiction over plaintiff in this matter. The court carefully evaluated the evidence regarding ownership of the '112 patent and concluded, in February 2009, that plaintiff adduced uncontraverted documentary evidence indicating that it owned the '112 patent. (D.I. 28) Following additional discovery and briefing, the court denied defendant's motion for reargument. (D.I. 29) The court conducted an *in camera* review of documents on the issue; the additional evidence did not further clarify the issue. (D.I. 80[13])

On August 19, 2009, Wyeth filed a disclaimer providing that plaintiff has at all times owned the '112 patent and that Wyeth has never owned the '112 patent. (D.I. 99) The court is satisfied that the disclaimer by Wyeth sufficiently terminates the dispute as to ownership. Put another way, it is the court's opinion that plaintiff has satisfied its burden to demonstrate that it had enforceable rights in the '112 patent at the time the suit was filed. The issue is preserved for purposes of appeal.

B. Claims 1, 5 and 10 of the '112 Patent Have Not Expired

Also as discussed *supra*, plaintiff was awarded a patent term extension under 35 U.S.C. § 156 based on the period of time ReFacto® was in the regulatory approval process. According to defendant, any claims that do not cover ReFacto® are not

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[13]The court incorporates its prior opinions by reference. (D.I. 28; D.I. 80)

subject to patent term extension. (D.I. 116 at 38) Claims 1 and 5 were not cited by plaintiff to the PTO as covering ReFacto® in the first instance, and claim 10 does not encompass ReFacto® as construed by defendant.

Defendant has not cited any caselaw supporting its theory that patent term extension applies on a claim-by-claim basis. In contrast, the House Report discussing the Hatch-Waxman Act provides, under those "rights to be extended," that "all provisions of the patent law apply **to the patent** during the period of extension." H.R. Rep. 98-857(I), 1984 U.S.C.C.A.N. 2647 at *2672-73, 1984 WL 37416 at *39 (Leg. Hist. June 21, 1984). Absent any legal authority holding that Congress intended to extend the rights of only specific patent claims, the court dismisses defendant's interpretation of § 156.[14]

C. There is No Interference-in-Fact

1. '112 claim 9 and '620 claim 83 (method claims); '112 claim 5 and '620 claim 74 (host cell claims); and '112 claim 1 and '620 claim 68 (protein claims)

a. Claims contrasted

The '112 patent and '620 patent each contain claims to recombinant human

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[14]Defendant appears to recognize the weakness of its argument in this respect; less than four pages were devoted to its position between its opening and reply papers. Defendant, therefore, devoted little attention to the task of demonstrating the impropriety of the PTO's determination that a patent extension was warranted. *See Pfizer, Inc. v. Ranbzxy Labs., Ltd.*, 457 F.3d 1284, 1290 (Fed. Cir. 2006) (determination is given "great deference") (quoting *Glaxo Operations, UK Ltd. v. Quigg*, 894 F.2d 392, 399 (Fed. Cir. 1990). The court notes that, under its adopted claim construction, ReFacto® may not be encompassed by claim 10. It is less than clear whether ReFacto® is encompassed by claim 9. Insofar as defendant has not attempted to meet its high burden in this regard, the court does not render a determination regarding the propriety of the PTO's grant of patent term extension.

Factor VIII proteins, host cells containing (and capable of expressing) the recombinant DNA which, upon expression, results in the recombinant Factor VIII, and methods for producing recombinant Factor VIII by culturing these host cells. As the claims only differ in terms of how they define the Factor VIII proteins encoded by the nucleic acids, the court begins its analysis with a comparison of the claimed recombinant proteins.

The recombinant protein of the '112 patent contains the amino acid sequence for human Factor VIII except for a deletion (between 581 and 949 amino acids long) between amino acids 740 to 1690 in the Ala-1 numbering system. This clearly encompasses the inactive B domain (amino acids 640 to 1649) and, additionally, a portion of the light chain (including the a3 acidic region) which begins at amino acid 1649.

The '620 patent defines the recombinant Factor VIII protein in terms of the retained portions. Claim 68 of the '620 patent provides a recombinant protein lacking all or part of the B domain, and having at least 90% sequence identity with the contiguous portions of the heavy and light chains (the A1 and A2 domains (amino acids 1 to 740) and the a3, C1 and C2 domains (amino acids 1649 to 2332)). Optionally, up to 10 amino acids of the B domain can be retained, such that the retained portions are amino acids 1 to 750 and 1639 to 2332.

b. Anticipation

The parties frame the anticipation analysis as an inquiry into whether the '620 patent discloses a "species" within the "genus" provided by the '112 patent. As an initial matter, the court disagrees that this framework is the most appropriate. Plaintiff has arbitrarily defined two groups within the range of variants encompassed by its claims.

Plaintiff asserts that the '112 patent discloses "proteins having a complete C domain as well as proteins with deletions in the C domain," or a "genus of two." (D.I. 128 at 31, 36) Not surprisingly, the '620 patent discloses one of these two species of deletions – proteins having a complete C domain. Anticipation as a matter of law, however, cannot depend on a party's fortuitous grouping of variants encompassed within a claim. To do so would permit parties to alter the import of the prior art. *See Atofina v. Great Lakes Chemical Corp.*, 441 F.3d 991, 999 (Fed. Cir. 2006) ("[A] very small genus can be a disclosure of each species within the genus").

Even were the court to embark on this analysis, it is apparent that each patent discloses a genus including separately patentable species. Indeed, with claim 1 of the '112 patent encompassing about 68,000 variants,[15] the '620 patent cannot encompass a "species" subsumed by this sizable group because only certain variants are within the scope of claim 1 of the '112 patent. For example, a 909-amino acid deletion between amino acids 740 and 1649 (as per the '620 patent) is encompassed by a 949-amino acid deletion between amino acid 740 and 1689 (as per the '112 patent). The same 909-amino acid deletion is not entirely within a 581-amino acid deletion as provided by the '112 patent. Conversely, a 581-amino acid deletion in the B domain (as per the '112 patent) is encompassed by a 909-amino acid deletion in the B domain (as per the '620 patent). A 581+ amino acid deletion encroaching into the light chain (through amino acid 1689) is outside of the '620 patent.

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[15]Defendant calculates this number as follows: 949 total range - 581 amino acid minimum deletion length = 368; 949 - 582 amino acid deletion length = 367; etc. and 368 + 367 + 366 . . . 1 is 67,896. (D.I. 138 at 16, n. 4)

The facts at bar are better analyzed, in the court's opinion, as a comparison between ranges of deletions. In this sense, there is a lack of homology between the amino acid deletion ranges contemplated by each patent. While the '112 patent permits deletion of a portion of the C domain (amino acids 1649 to 1689), the '620 patent does not. The disclosure of a range "is only that of a range, not a specific [point] in that range[, i.e.,] the disclosure of a range is no more a disclosure of the end points of the range than it is each of the intermediate points." *Atofina,* 441 F.3d at 1000 (the disclosure of a temperature range of 150 C–350 C was not a specific disclosure of the range of 100 C–500 C).

The '112 patent permits (and claims) a deletion between amino acids 740 and 1689; there is variability both in the position and the length of the deletion (581 to 949 amino acids long). The '620 patent provides a longer deletion (between 889 and 909 amino acids) in a smaller range (amino acid 740 to 750 through amino acid 1639 to 1649) having a certain percentage (90-100%) of sequence identity to the heavy and light chains of human Factor VIII. The a3 acidic region of the C domain is, however, left intact in all permitted combinations in the '620 patent. Accordingly, the invention of the '112 patent (a deletion up to amino acid 1689) is not the invention of the '620 patent (a deletion terminating at amino acid 1649, thus preserving the entire a3 acidic region).[16]

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[16]The interference-in-fact analysis requires only a comparison of the parties' claims, not their specifications. *See In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). The specification, however, characterizes the invention and impacts claim interpretation. The court notes in this regard that the '112 patent does not disclose those variants claimed by the '620 patent with "sufficient specificity" such that the disclosure of the '112 patent anticipates the '620 patent claims. *See MPEP* § 2131.03(II) (discussing anticipation with respect to overlapping ranges); *Atofina*, 441 F.3d at 999-1000 (same). There is no disclosure of a deletion terminating at amino acid

The two way test is not satisfied with respect to the '112 and '620 patents on anticipation.[17]

c. Obviousness

Although the court takes up the issue on defendant's motion to dismiss, plaintiff bears the burden of establishing an interference-in-fact between the alleged interfering claims. *See Albert*, 729 F.2d at 761 ("When challenged, the pleader must establish that interference does in fact exist."). In this regard, plaintiff primarily devoted its efforts in its answering papers to anticipation rather than obviousness. (D.I. 128 at 32-33) It is plaintiff's position that the '620 patent claims are rendered obvious in view of the '112 patent because the '620 patent discloses a narrower range from within the broader range disclosed by the '112 patent, with an identical starting point.

The question of obviousness with respect to a structurally related prior art compound is whether there existed a motivation to modify the known compound to obtain the compound claimed. *See Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356 (Fed. Cir. 2007) (following *KSR*, "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a

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1649 in the '112 patent specification. There are three exemplary proteins disclosed in the '112 patent; two have deletions within the 1649-1689 amino acid range. *See* '112 patent, Table 2. There is nothing in the '112 patent specification that impacts the court's determination. There is no anticipatory disclosure contained in the specification of the '112 patent. *See Atofina*, 441 F.3d at 999 (finding 0.001 to 1.0 percent range did not disclose a 0.1 to 5.0 percent range).

[17]The parties did not specifically address anticipation or obviousness of the invention of '112 patent in view of the invention of '620 patent. The court's analysis with respect to the overlap of disclosed amino acid deletion ranges would result in the same conclusion on this leg of the two-way test.

particular manner to establish prima facie obviousness of a new claimed compound."). According to plaintiff's expert, Dr. Philip Fay, "[t]he interactive binding sites on Factor VIII for binding vWF were known prior to 1985 as residing in the light chain." (D.I. 189 at ¶ 26[18]) Deletion of amino acid residues 741 to 1648 would have been "readily apparent" to one of skill in the art because it was known by November 1984 that the light chain begins at amino acid 1649. (*Id.* at ¶ 70[19])

The evidence of record indicates otherwise. A 1986 article by Toole et al. states that "[t]he B domain is essentially delimited by residues 740 and **1689** that are sites for proteolytic activation of the molecule[.]" (D.I. 139, ex. 9 at 5939[20]) (emphasis added) At his deposition, Dr. Kaufman also stated that, in 1986, the 1649-1689 region was not considered to be part of the C domain (i.e., it was considered to be part of the B domain). (*Id.*, ex. 8 at 43:13-46:12) Dr. Fay acknowledged at trial that he might have been in error in stating that the interactive sites on Factor VIII for binding vWF were known prior to 1985 as residing on the light chain. (D.I. 175 at 379:1-15) In his declaration, Dr. Fay also acknowledges that "it was not known until several years later, through the use of monoclonal antibodies, that amino acid residues 1670-1684 (1689-1703), near the beginning of the light chain, were important for vWF binding." (D.I. 189

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[18]Citing Fass et al., "Monoclonal Antibodies to Porcine Factor VIII Coangulant and Their Use in the Isolation of Active Coangulant Proteins," *Blood*, vol. 59, 1982 at pp. 594-600.

[19]Citing Vehar et al., "Structure of Human Factor VIII," *Nature*, vol. 312, Nov. 1984 at pp. 337-342 (hereinafter, the "Nature article").

[20]Toole et al., "A Large Region (~95 kDa) of Human Factor VIII is Dispensable for *In Vitro* Procoagulant Activity," *Biochemistry*, vol. 83, pp. 5939-5942 (Aug. 1986).

at ¶ 26) Thus, even crediting Dr. Fay's assertion that it was known that the light chain was important for vWF binding – a concept noticeably absent from the '112 patent – it was, by his own admission, not known what specific amino acids were important to maintain. A person of ordinary skill in the art, therefore, would not have appreciated the importance of amino acids 1649-1689 based on the disclosure of the '112 patent, which permitted deletions of that region.[21] In sum, Dr. Fay's conclusion that it would have been "readily apparent" to maintain the entire light chain is not convincing on the record at bar.

2. '112 patent claim 9 and '447 patent claim 1

Plaintiff asserts that '112 patent claim 9 and '447 patent claim 1 interfere. Claim 9 of the '112 patent is a claim to a method for producing the truncated Factor VIII protein claimed in claim 1 of that patent (using the host cell of claim 5), which protein has been discussed previously. Claim 1 of the '447 patent is directed to a composition comprising Factor VIII proteins having the complete A domain and the complete C domain with at least 90% sequence identity.

It is plaintiff's assertion that claim 9 produces two types of proteins – those having complete a3 acidic regions and those not having complete a3 regions – thereby anticipating the composition of the '447 patent. As discussed *supra*, the disclosure of the range of possible (581 to 949-amino acid) deletions in the '112 patent is not a

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[21]At the priority trial, the parties vigorously debated whether Toole conceived preserving the entire a3 acidic region (despite not specifically disclosing a deletion ending at amino acid 1649). The court need not reach priority in view of its findings, however, notes that the evidence was not so clearly in favor of plaintiff on this point so as to possibly buttress its obviousness case.

disclosure of each specific point within the range. *Atofina,* 441 F.3d at 1000. Therefore, the '112 patent does not disclose a recombinant Factor VIII protein having the specific (B-domain) deletion claimed in the '447 patent.

Regarding obviousness, plaintiff asserts only that, to make the proteins of the '447 patent, "one of ordinary skill in the art, knowing the DNA sequence for the full-length human Factor VIII:C protein and using techniques available as of the effective filing date of the '112 patent, would have done so by a method as recited in claim 9 with a reasonable expectation of success." (D.I. 128 at 35) No further analysis or evidentiary support is noted. Plaintiff has not met its burden to demonstrate obviousness on this record. Notwithstanding, the court incorporates by reference its discussion of nonobviousness of the '620 patent claims in view of the '112 patent, *supra*, as the '112 patent fails to render the '447 patent obvious by the same rationale.

3. '112 patent claim 10 and '447 patent claim 1

Claim 10 of the '112 patent recites a truncated human Factor VIII protein lacking one of three permissible amino acid deletion regions (1000-1582, 778-1659, and 778-1694). In the court's order of the same date, the court has defined claim 10 as a closed group. That is, claim 10 encompasses a recombinant protein having one of the three deletions, and no more.

The protein of claim 1 of the '447 patent has complete 1-740 (A domain) and 1649-2332 (C domain) sequences with at least 90% sequence identity within those sequences. Two of the three proteins of claim 10 of the '112 patent maintain the A and C domains, deleting amino acids 1000-1582 and 778-1659 in the B domain. However, these deletions are not in congruence with a complete B domain deletion of claim 1 of

the '447 patent (amino acids 741-1648). The claims, therefore, do not anticipate each other.

Plaintiff primarily focuses on obviousness with respect to this pair of claims. Plaintiff asserts that it would have been obvious to extend the deletion of claim 10 of the '112 patent to encompass the entire B domain, because "those of ordinary skill in the art knew the precise limits of the A and C domains." (D.I. 128 at 37[22]) As discussed previously, Toole himself published in 1986 a statement that the B domain extended through amino acid 1689 – an understanding shared by Kaufman. Dr. Fay was not convincing in his assertion that the light chain had appreciable importance as of 1985. It is not clear, therefore, that ordinary artisans appreciated the "precise" boundary of the C domain. Notwithstanding, plaintiff does not adequately explain a motivation to extend the 1000-1582 and 778-1659 amino acid deletion ranges of claim 10 of the '112 patent in either direction – to include amino acids on the A domain side (741-799 or 741-777) or on the C domain side (through 1649). (D.I. 128 at 36-37)

Viewing conversely the '447 patent as prior art to the '112 patent, Dr. Fay states that an ordinary artisan would understand that, since a protein having the deletion of claim 1 of the '447 patent is active, so too would be a protein having a smaller deletion. (D.I. 119 at ¶ 71) Dr. Fay states that smaller deletions would be "readily apparent" because a person of ordinary skill in the art would have the full DNA sequence (published by Toole in 1984) and "could determine that the enzymes *Sac*I and *Bam*HI cut at about these [Pro-1000 and Asp-1582] sites" would result in '112 patent claim 10

[22]Although plaintiff cites paragraphs 23-24 of Dr. Fay's report in support for this proposition; these sections do not lend support to its argument.

variant (a). (*Id.*) There is a difference between "**could** determine" and a motivation to alter with a reasonable expectation of success. Neither plaintiff nor Dr. Fay further elaborate on why these particular cuts would have been desirable, and the court finds a conclusion of obviousness unwarranted on this record.

4. Conclusion

For the foregoing reasons, the court finds that the two-way test is not satisfied with respect to the pairs of claims identified by plaintiff as interfering claims. The court's conclusions regarding anticipation and obviousness are buttressed by the fact that the '112 patent is listed on the face of the '620 and '447 patents.[23] Insofar as there is no interference-in-fact, the court need not make a priority determination.[24]

V. CONCLUSION

For the foregoing reasons, the court grants defendant's motion to dismiss. An appropriate order shall issue.

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[23]The Federal Circuit has noted that the fact that the PTO did not declare an interference is not controlling, but may be considered by a district court. *Advance Transformer Co. v. Levinson*, 837 F.2d 1081, 1083-84 (Fed. Cir. 1988), *overruled on diff. grounds*, 508 U.S. 83 (1993). The court has declined defendant's invitation to apply a "presumption" of no interference-in-fact in this regard. (D.I. 116 at 24)

[24]Without rendering a decision on priority, the court notes that plaintiff could have sought protection for the alleged interfering (overlapping) subject matter through a continuation-in-part application. It appears as though defendant beat plaintiff to the punch.