PUBLIC VERSION

UNITED STATES INTERNATIONAL TRADE COMMISSION

Washington, D.C.

In the Matter of CERTAIN ANTIVENOM COMPOSITIONS AND PRODUCTS CONTAINING THE SAME	Inv. No. 337-TA-903

ORDER 23: CONSTRUING THE TERMS OF THE ASSERTED CLAIMS OF THE PATENT AT ISSUE

(May 21, 2014)

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I. INTRODUCTION

This Investigation was instituted by the Commission on December 11, 2013 to determine whether certain antivenom compositions and products containing the same infringe U.S. Patent No. 8,048,414 (the "'414 patent").[1] *See* 78 Fed. Reg. 75,372-373 (Dec. 11, 2013). The named respondents are Laboratorios Silanes S.A. de C.V. ("Silanes"), Instituto Bioclon S.A. de C.V. ("Bioclon"), The Silanes Group[2], and Rare Disease Therapeutics, Inc. ("RDT").[3]

Pursuant to Ground Rule 5A, a *Markman* hearing was held April 10, 2014 regarding the interpretation of certain terms of the asserted claims of the patent at issue, namely: claims 1–9, 13, 15–19, 21 and 22 of the '414 patent.

Prior to the hearing, Complainant BTG International Inc. ("BTG"), Respondents, and the Commission Investigative Staff ("Staff") met and conferred in an effort to reduce the number of disputed claim terms to a minimum. The parties also filed initial and reply claim construction briefs, wherein each party offered its construction for the claim terms in dispute, along with support for its proposed interpretation. After the hearing and pursuant to Order No. 6, the parties submitted an updated Joint Claim Construction Chart.[4]

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[1] Complainant BTG International Inc. is the owner, by assignment, of the patent-in-suit. (Compl. at ¶ 57.)

[2] While Respondents insist that the Silanes Group is not a legal entity, they did submit their *Markman* briefs on behalf of the Silanes Group "until it is formally terminated as a Respondent in this Investigation." (RMIB at 1 n.1.)

[3] Respondents Veteria Labs S.A. de C.V. and BioVeteria Life Sciences LLC were terminated from the Investigation on March 11, 2014. (*See* Order No. 14 (Mar. 11, 2014); Notice of Comm'n Determination Not to Review an Initial Determination Partially Terminating the Investigation Based on a Withdrawal of the Compl. (Apr. 1, 2014).)

[4] The claim terms discussed in detail in this Order were identified in the Updated Joint Proposed Claim Construction Chart as being agreed upon or remaining in dispute. For convenience, the briefs and chart submitted by the parties are referred to hereafter as:

CMIB	BTG's Initial *Markman* Brief
CMRB	BTG's Reply *Markman* Brief
RMIB	Respondents' Initial *Markman* Brief
RMRB	Respondents' Reply *Markman* Brief
SMIB	Staff's Initial *Markman* Brief
SMRB	Staff's Reply *Markman* Brief
JC	Updated Joint Proposed Claim Construction Chart

II. IN GENERAL

The claim terms construed in this Order are done so for the purposes of this section 337 Investigation. Those terms not in dispute need not be construed. *See Vanderlande Indus. Nederland BV v. Int'l Trade Comm'n*, 366 F.3d 1311, 1323 (Fed. Cir. 2004) (noting that the administrative law judge need only construe disputed claim terms).

Hereafter, discovery and briefing in this Investigation shall be governed by this construction of the claim terms. **All** other claim terms shall be deemed undisputed and shall be interpreted by the undersigned in accordance with "their ordinary meaning as viewed by one of ordinary skill in the art." *Apex Inc. v. Raritan Computer, Inc.*, 325 F.3d 1364, 1371 (Fed. Cir. 2003), *cert. denied*, 540 U.S. 1073 (2003).

III. RELEVANT LAW

"An infringement analysis entails two steps. The first step is determining the meaning and scope of the patent claims asserted to be infringed. The second step is comparing the properly construed claims to the device accused of infringing." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (*en banc*) (internal citations omitted), *aff'd*, 517 U.S. 370 (1996). Claim construction is a "matter of law exclusively for the court." *Id.* at 970-71. "The construction of claims is simply a way of elaborating the normally terse claim language in order to understand and explain, but not to change, the scope of the claims." *Embrex, Inc. v. Serv. Eng'g Corp.*, 216 F.3d 1343, 1347 (Fed. Cir. 2000).

Claim construction focuses on the intrinsic evidence, which consists of the claims themselves, the specification, and the prosecution history. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (*en banc*); *see also Markman*, 52 F.3d at 979. As the Federal Circuit in *Phillips* explained, courts must analyze each of these components to determine the "ordinary

and customary meaning of a claim term" as understood by a person of ordinary skill in the art at the time of the invention. 415 F.3d at 1313. "Such intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." *Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc.*, 262 F.3d 1258, 1267 (Fed. Cir. 2001).

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude.'" *Phillips*, 415 F.3d at 1312 (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). "Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of particular claims terms." *Id.* at 1314; *see also Interactive Gift Express, Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001) ("In construing claims, the analytical focus must begin and remain centered on the language of the claims themselves, for it is that language that the patentee chose to use to 'particularly point[ ] out and distinctly claim[ ] the subject matter which the patentee regards as his invention.'"). The context in which a term is used in an asserted claim can be "highly instructive." *Phillips*, 415 F.3d at 1314. Additionally, other claims in the same patent, asserted or unasserted, may also provide guidance as to the meaning of a claim term. *Id.*

The specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Id.* at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). "[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Id.* at 1316. "In other cases, the specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor." *Id.* As a general rule, however, the particular examples or

embodiments discussed in the specification are not to be read into the claims as limitations. *Id.* at 1323. In the end, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be . . . the correct construction." *Id.* at 1316 (quoting *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998)).

In addition to the claims and the specification, the prosecution history should be examined, if in evidence. *Id.* at 1317; *see also Liebel-Flarsheim Co. v. Medrad, Inc.,* 358 F.3d 898, 913 (Fed. Cir. 2004). The prosecution history can "often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Phillips*, 415 F.3d at 1317; *see also Chimie v. PPG Indus. Inc.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005) ("The purpose of consulting the prosecution history in construing a claim is to 'exclude any interpretation that was disclaimed during prosecution.'").

When the intrinsic evidence does not establish the meaning of a claim, then extrinsic evidence (*i.e.*, all evidence external to the patent and the prosecution history, including dictionaries, inventor testimony, expert testimony, and learned treatises) may be considered. *Phillips*, 415 F.3d at 1317. Extrinsic evidence is generally viewed as less reliable than the patent itself and its prosecution history in determining how to define claim terms. *Id.* at 1317. "The court may receive extrinsic evidence to educate itself about the invention and the relevant technology, but the court may not use extrinsic evidence to arrive at a claim construction that is clearly at odds with the construction mandated by the intrinsic evidence." *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 977 (Fed. Cir. 1999).

If, after a review of the intrinsic and extrinsic evidence, a claim term remains ambiguous, the claim should be construed so as to maintain its validity. *Phillips*, 415 F.3d at 1327. Claims, however, cannot be judicially rewritten in order to fulfill the axiom of preserving their validity. *See Rhine v. Casio, Inc.*, 183 F.3d 1342, 1345 (Fed. Cir. 1999). Thus, "if the only claim construction that is consistent with the claim's language and the written description renders the claim invalid, then the axiom does not apply and the claim is simply invalid." *Id.*

IV. LEVEL OF ORDINARY SKILL IN THE ART

BTG proposes that a person of ordinary skill in the art would have "at least the qualifications of a bachelors or equivalent degree in biology, biochemistry, or immunology with study or experience involving large-scale proteins or protein chemistry (or equivalent), and some experience with antibodies and snake venom, or equivalent." (CMIB at 8.) BTG contends that this level is consistent with the background and experience of both of the inventors, as well as other experts who submitted declarations during the prosecution of the '414 patent. (*Id.*) BTG believes that Respondents' proposal overstates the necessary qualifications of a person of ordinary skill in the art in protein science or antivenoms as of October 1984. (CMRB at 4.) BTG states that it would concur with Staff's articulation of the level of ordinary skill in the art to the extent it encompasses experience involving venoms and antivenoms. (*Id.*)

Respondents submit that a person of ordinary skill in the art would have an understanding of antibody structure and antigen-antibody interactions. Respondents believe that the education and experience levels of a person of ordinary skill in the art would vary, "with some persons holding a basic Bachelor's degree, but with 5-10 years of relevant work experience, while others would have more advanced degrees, for example a M.D. or a Ph.D. in a relevant field." (RMIB at 10.)

In Staff's view, BTG's and Respondents' proposals are too vague or ambiguous. Staff proposes that a person of ordinary skill in the art is "someone who has a bachelors or equivalent degree in biology, biochemistry, or immunology with at least an additional three years of study or experience involving immunology, large-scale proteins, protein chemistry, or antivenoms." (SMRB at 2.) In response to BTG's concern, Staff submits that "because antivenoms are antibodies, which fall within the purview of immunology, [its] proposal necessarily encompasses experience involving antivenoms." (*Id.*)

Accordingly, as to "one of ordinary skill in the art," the undersigned finds that one of ordinary skill in the art would possess a bachelors or equivalent degree in biology, biochemistry, or immunology with at least an additional three years of study or experience involving immunology, large-scale proteins, protein chemistry, venoms or antivenoms. In addition, one of ordinary skill in the art shall be commensurate with the time of the respective invention, *i.e.*, the effective filing date for the patent-in-suit.

V. THE '414 PATENT

A. Overview

The '414 patent is entitled "Antivenom Composition Containing Fab Fragments." The '414 patent issued on November 1, 2011 to named inventors John B. Sullivan and Findlay E. Russell. The '414 patent is assigned to BTG International Inc. The '414 patent generally relates to compositions for treating snakebite victims and methods for using the same. (*See generally* '414 patent; Compl. at ¶ 61.) The '414 patent also describes methods for purifying antibody fragments utilizing affinity chromatography processes for use in pharmaceutical formations to neutralize the venom of snakes of the *Crotalus* genus. (*Id.*) The '414 patent has 22 claims, of which claims 1, 19, and 20 are the independent claims. Claims 1–9, 13, 15–19, and 21–22 are

asserted against Respondents. The asserted claims read as follows (with the first instance of the disputed terms highlighted in **bold**):

1. An antivenom pharmaceutical composition for treating a snakebite victim, comprising **Fab fragments** which **bind specifically to** a venom of a snake of the *Crotalus* genus and which are **essentially free from contaminating Fc** as determined by immunoelectrophoresis using anti-Fc antibodies, and a pharmaceutically acceptable carrier, **wherein said antivenom pharmaceutical composition neutralizes the lethality of the venom of a snake of the *Crotalus* genus**.

2. The antivenom pharmaceutical composition of claim 1, wherein an antibody source for said Fab fragments is IgG(T).

3. The antivenom pharmaceutical composition of claim 1, wherein an antibody source for said Fab fragments is polyvalent IgG(T).

4. The antivenom pharmaceutical composition of claim 1, wherein the Fab fragments are equine.

5. The antivenom pharmaceutical composition of claim 1, wherein the Fab fragments are obtained from hyperimmune serum.

6. The antivenom pharmaceutical composition of claim 1, wherein the Fab fragments are obtained from animal serum.

7. The antivenom pharmaceutical composition of claim 6, wherein the animal serum has been partially purified by ammonium sulfate precipitation.

8. The antivenom pharmaceutical composition of claim 1, further comprising **$F(ab)_2$ fragments**.

9. The antivenom pharmaceutical composition of claim 1, wherein the Fab fragments are obtained from polyvalent antibodies.

13. The antivenom pharmaceutical composition of claim 12, wherein the population of antibodies is raised to the venom of a snake of the *Crotalus* genus.

15. The antivenom pharmaceutical composition of claim 13, wherein the snake of the *Crotalus* genus is selected from the group consisting of *Crotalus adamanteus, Crotalus atrox*, and *Crotalus durissus.*

16. The antivenom pharmaceutical composition of claim 13, further comprising a population of antibodies raised to a venom of *Bothrops atrox.*

17. The antivenom pharmaceutical composition of claim 1, wherein the composition is in lyophilized form.

18. The antivenom pharmaceutical composition of claim 1, wherein the snakebite victim is a human.

19. An antivenom pharmaceutical composition for treating a human snakebite victim, comprising equine polyvalent Fab and $F(ab)_2$ fragments obtained from the serum of horses hyperimmunized with venom of at least one species of snake that belongs to the *Crotalus* genus, wherein the antivenom pharmaceutical composition **binds to** a venom of a snake of the *Crotalus* genus, wherein the antivenom pharmaceutical composition is essentially free from contaminating Fc, and a pharmaceutically acceptable carrier, wherein the antivenom pharmaceutical composition neutralizes the lethality of the venom of a snake of the *Crotalus* genus.

21. A method of treating envenomation by a snake of the *Crotalus* genus comprising administering the antivenom pharmaceutical composition of any one of claims 1-3, 4, 5-14, and 15-20.

22. The method of claim 21, wherein the antivenom pharmaceutical composition is administered intravenously.

B. Disputed Claim Terms

1. Construction of Disputed Claim Terms

a) "Fab fragments" / "$F(ab)_2$ fragments"

The term "Fab fragments" appears in claims 1–6, 9, and 19. The term "$F(ab)_2$ fragments" appears in claims 8 and 19. The parties disagree on the claim construction of the terms and have proposed the following constructions:

TERM	BTG	RESPONDENTS	STAFF
Fab fragments	"one of two upper fragments of the Y shaped immunoglobulin molecule"	"immunoglobulin fragments that contain one antigen-binding domain, resulting from the proteolytic digestion of immunoglobulins by papain"	"immunoglobulin fragments having a single antigen-binding site, and composed of one light chain, the variable and C_H1 regions of a heavy chain, and at least some portion of the hinge region of said heavy chain, wherein said light and heavy chains

TERM	BTG	RESPONDENTS	STAFF
			are covalently linked by one or more disulfide bonds"
$F(ab)_2$ fragments[5]	"two attached Fab fragments (formed as the V-shaped fragment of the Y shaped immunoglobulin molecule)"	"immunoglobulin fragments that contain two antigen-binding domains, resulting from the proteolytic digestion of immunoglobulins by pepsin" [Silanes Respondents Proposed Construction] "immunoglobulin fragments that contain two antigen-binding domains and a portion of the Fc fragment, resulting from the proteolytic digestion of immunoglobulins by pepsin" [RDT Proposed Construction]	"immunoglobulin fragments having two antigen-binding sites, and composed of two identical Fab fragments, wherein the hinge regions of the identical Fab fragments are covalently linked to each other by two or more disulfide bonds"

BTG contends that its proposed construction is consistent with the claim language, the patent specification, and other intrinsic evidence. (CMIB at 10.) As such, BTG contends that Fab fragments and $F(ab)_2$ fragments are structural limitations covering portions of the IgG molecule. (CMRB at 6.) In particular, BTG asserts that the patent specification structurally defined the claim terms when it stated: "[t]he two upper fragments are each referred to as F(ab) fragments . . . [and] an $F(ab)_2$ fragment is comprised of two attached F(ab) fragments." (CMRB at 6-7; CMIB at 11-13 (citing '414 patent at 1:53-1:61).) BTG also asserts the Federal Circuit used similar structural language in its discussion of the invention. *In re Sullivan*, 498 F.3d 1345, 1347 (Fed. Cir. 2007) (stating "[t]he v-shape portion of the Y-shaped protein is called a $F(ab)_2$ fragment . . . [and] each arm of the v-shaped portion is called, in turn, a Fab fragment."). In

[5] While the Silanes Respondents and RDT have proposed slightly different constructions, they agree on the reasoning for the claim construction for $F(ab)_2$ fragments. (RMIB at 12 n.5.)

addition, BTG claims that Respondents' initial *Markman* brief also used similar structural language. (CMRB at 6-7 (citing RMIB at 5-6).)

BTG asserts that Respondents improperly limit the creation of Fab fragments and $F(ab)_2$ fragments to enzyme digestion by papain and pepsin, respectively. (CMRB at 5-18; CMIB at 9-25.) In support, BTG argues that the plain language of independent claims 1 and 19 does not limit the production of Fab fragments. (CMIB at 11.) BTG also argues that the specification discloses using alternative enzymes in the production of the fragments, which illustrates that the patentee did not limit their production to particular enzymes. (*Id.* at 11-13 (citing '414 patent at 1:41-1:45).) In addition, BTG claims that there was no widely accepted or utilized industry standard that required Fab fragments to be produced by papain and $F(ab)_2$ fragments to be produced by pepsin. (CMRB at 16-18.) Furthermore, BTG asserts that limiting independent claim 1 to Fab fragments produced by papain digestion would make dependent claim 12 wholly redundant and would run afoul of the doctrine of claim differentiation. (CMIB at 11.)

While BTG believes that its proposed construction is closer to how one of ordinary skill in the art understood the claim terms at the time of the invention, it does not object to Staff's proposed construction. (CMIB at 19-20, 24-25.) In fact, BTG admits, "Staff's proposed construction is a more technically descriptive construction." (*Id.*)

Respondents claim that Fab fragments and $F(ab')_2$ fragments are defined by the enzymes used in their production.[6] (RMRB at 5-15; RMIB at 27.) Specifically, Respondents argue that the patentee defined the terms by repeatedly and constantly stating that Fab fragments are produced by papain and $F(ab')_2$ fragments are produced by pepsin. (RMRB at 5-6; RMIB at 13-14, 22-23 (citing '414 patent at 1:61-1:64, 3:54-3:58, 4:49-4:51, FIGs 6 & 8).) In addition, Respondents

[6] Respondents believe a person of ordinary skill in the art would understand the term $F(ab)_2$ fragments to be equivalent to $F(ab')_2$ fragments. (SMRB at 4; RMIB at 11-26; RMRB at 4-15.)

contend that the scientific community, including the World Health Organization (WHO), defined Fab fragments and $F(ab')_2$ fragments by their production enzymes. (*Id.* at 18-22.)

Respondents claim that BTG's and Staff's proposed constructions are overly broad and divorced from the intrinsic evidence. (*Id.* at 12.) Respondents argue that the specification merely explains that other enzymes can be used to split IgG molecules into various pieces. (RMRB at 6 (citing '414 patent at 1:41-1:45).) In addition, Respondents argue that BTG and Staff completely ignore nearly three decades of prosecution history during which the patentee repeatedly distinguished Fab fragments and $F(ab')_2$ fragments based on the enzymes used in their production. (*Id.* at 13; RMIB at 13-17.) Furthermore, Respondents argue that the doctrine of claim differentiation is not absolute and cannot broaden the scope of the claims to encompass more subject matter than what the intrinsic evidence compels. (*Id.* at 22-23.)

Staff contends that the plain and ordinary meaning of the terms is based on the structure of the molecules. (SMIB at 19.) As such, Staff asserts that the term Fab fragments refers to the regions of the antibodies that bind to antigens composed of one constant and one variable domain of each of the heavy and light chains. (*Id.*) Staff also asserts that the term $F(ab)_2$ fragments refers to two identical covalently linked Fab fragments. (*Id.*) Staff therefore argues that its proposed construction is correct because it accurately describes the structure of the molecules, as understood by one of ordinary skill in the art at the time of the invention. (*Id.*)

Staff asserts that BTG's proposed construction is not necessarily incorrect, but it oversimplifies a complex polypeptide protein. (*Id.*) In addition, Staff argues that BTG's proposed construction is silent on the key fact that Fab fragments have one antigen binding site and that $F(ab)_2$ fragments have two antigen binding sites. (*Id.* at 19.) As for Respondents' construction, Staff claims that it improperly limits the creation of Fab fragments and $F(ab)_2$ fragments to

enzyme digestion by papain and pepsin, respectively. (*Id.*) In support, Staff argues that it was well known that various methods could be used to create Fab fragments and $F(ab)_2$ fragments. (SMRB at 4-6.) For example, Staff asserts the patent specification discloses that fragments can be produced using alternative enzymes, such as trypsin, chymotrypsin, and papain. (*Id.*) Staff also argues that the prosecution history cited in Respondents' briefs does not limit the production of the fragments in any manner. (*Id.* at 7.) In addition, Staff claims that the 2010 WHO guidelines fail to accurately reflect the understanding of a person of ordinary skill in the art at the time of the invention. (*Id.* at 7-11.) Moreover, Staff argues that the type of proteolytic digestion is irrelevant to the definition, function, and utility of Fab and $F(ab)_2$ fragments. (SMIB at 21.)

The undersigned finds Respondents' arguments unpersuasive. The plain language of claims 1, 8, and 19 does not limit the production method of Fab fragments or $F(ab)_2$ fragments to papain and pepsin, respectively. ('414 patent at 13:15-14:34.) In fact, the specification and the knowledge of one of ordinary skill in the art illustrates that it was known that Fab fragments and $F(ab)_2$ fragments could be produced by various enzymes, such as trypsin, chymotrypsin, and papain. ('414 patent at 1:39-1:45; Mackessy Decl. at 3-7; *see also* Corbett, Tr. at 6:20-7:10, 25:1-25:25.) In addition, the type of enzyme digestion is irrelevant to the definition, function, and utility of Fab fragments and $F(ab)_2$ fragments.[7] (SMIB at 21.) Furthermore, limiting independent claim 1 to Fab fragments produced by papain digestion would make dependent claim 12 wholly redundant and would run afoul of the doctrine of claim differentiation. *Libel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 910 (Fed. Cir. 2004) (stating "where the limitation that is sought to be 'read into' an independent claim already appears in a dependent claim, the doctrine of claim differentiation is at its strongest.").

[7] The structural and chemical differences between Fab fragments and F(ab') fragments has a negligible effect on the primary function of the fragments. (*See* Alberts, *supra*, at 963-980; *see also* SMIB at 8-13; Corbett, Tr. at 22:8-23:2.)

Turning to BTG's and Staff's proposed constructions, the undersigned finds that BTG's proposed construction oversimplifies a complex structure of amino acids and fails to address the key functional aspect of the Fab fragments and $F(ab)_2$ fragments (*i.e.,* number of antigen-binding sites). (Koo, Tr. at 46:3-46-18.) The specification structurally defines a whole antibody molecule as three fragments connected in a Y shape. ('414 patent at 1:51-1:61.) The V-shape portion of the Y-shape molecule is called a $F(ab)_2$ fragment and has two antigen-binding sites, while each arm of the V-shape molecule is called a Fab fragment and has a single antigen-binding site. ('414 patent at 1:51-1:61; Mackessy Decl. at 3-7; Kossiakoff Decl. at 4-6; *see also* Bruce Alberts et al., Molecular Biology of the Cell 951–1012 (1st ed. 1983); Corbett, Tr. at 5:13-6:19.) The Fab fragments and $F(ab)_2$ fragments are further comprised of heavy and light polypeptide chains having variable and constant domains, which are covalently linked by disulfide bonds. (Mackessy Decl. at 3-7; Kossiakoff Decl. at 4-6; *see also* Corbett, Tr. at 5:13-6:19.) The alteration of the variable domains of the light and heavy chains and the flexibility of the disulfide bonds allows Fab fragments and $F(ab)_2$ fragments to neutralize millions of foreign antigens. (Alberts, *supra*, at 951-1012; *see also* Corbett, Tr. at 5:13-6:19.) Thus, the undersigned finds Staff's proposed construction more accurately and technically describes the complex structure of Fab fragments and $F(ab)_2$ fragments. (CMIB at 19-20, 24-25; *see also* Corbett, Tr. at 10:20-10:23.)

Accordingly, the undersigned hereby construes "Fab fragments" as "***immunoglobulin fragments having a single antigen-binding site, and composed of one light chain, the variable and C_H1 regions of a heavy chain, and at least some portion of the hinge region of said heavy chain, wherein said light and heavy chains are covalently linked by one or more disulfide bonds***" and "$F(ab)_2$ fragments" as "***immunoglobulin fragments having two antigen-binding***

sites, and composed of two identical Fab fragments, wherein the hinge regions of the identical Fab fragments are covalently linked to each other by two or more disulfide bonds."

b) "bind specifically to" / "binds to"

The term "bind specifically to" appears in claim 1 of the '414 patent and the term "binds to" appears in claim 19 of the '414 patent. The parties agree that these terms should be given the same construction. (CMRB at 18; RMIB at 27, 31-32; SMIB at 31.) However, the parties disagree on the claim construction of said terms and have proposed the following:

BTG	RESPONDENTS	STAFF
Plain and ordinary meaning, *i.e.* "capable of binding to"	"have been affinity purified against"	Plain and ordinary meaning, *i.e.* "capable of binding to"

BTG argues that the '414 patent does not recite any special definition for the term "binds" because it is well-understood in the art. (CMIB at 27.) BTG contends that declarations submitted during prosecution also make clear that there is no special meaning for the concept of binding. (*Id.* (citing BTG Exs. C and D).) Moreover, BTG argues that the language of the claims does not require that binding be caused by affinity purification. (*Id.* at 28.)

BTG submits that Respondents' proposed construction improperly requires affinity purification and that Respondents fail to show that the patentees redefined or disavowed the ordinary meaning of "bind." (CMIB at 28; CMRB at 20-21.) According to BTG, while the '414 patent describes various processes that use affinity chromatography, these are merely examples and do not redefine what it means for the antivenom composition to bind to the venom. (CMIB at 28-29.) Additionally, BTG contends that the disclosure of exemplary processes of affinity purification was a separate invention claimed in a separate patent. (Corbett, Tr. at 73:17-24.) BTG also argues that Respondents' proposed construction improperly excludes preferred embodiments and conflicts with dependent claims that expressly include purification processes. (CMRB at 21-22.)

Respondents contend that their proposed construction is consistent with the specification, which repeatedly states that an affinity purification step is a required feature of the "invention." (RMIB at 29-32; RMRB at 16-17.) Additionally, Respondents assert that the inventors distinguished their invention from the prior art on the basis of affinity purification. (RMIB at 31.)

According to Respondents, BTG's and Staff's proposed construction improperly broadens the scope of the claims. (RMIB at 32.) Respondents submit that BTG's and Staff's proposed construction "could and most certainly would encompass antibodies that were 'capable of' binding to the venom of a snake but incapable of neutralizing it." (RMRB at 18; *see also* Yonan, Tr. at 84:16-19 ("BTG and the Staff are saying 'specifically bind' or 'bind,' just means that it's capable of doing it; not that it actually has to do it.").)

In support of its proposed construction, Staff claims that one of ordinary skill in the art would understand the concept of an antibody binding to an antigen. (SMIB at 31; SMRB at 15.) However, while Staff argues that Respondents' proposed construction improperly limits the term to affinity purification, Staff admits that its proposed construction of "capable of binding to" may be too broad. (Koo, Tr. at 97:23-98:3.)

The undersigned finds that the terms "bind specifically to" and "binds to" should be construed in accordance with their plain and ordinary meaning because these terms are well-understood by one of ordinary skill in the art. (*See* BTG Ex. B at ¶ 28 ("I have reviewed the '414 Patent and it very clearly uses the term 'bind to' in its plain and ordinary sense."); Koo, Tr. at 97:23-25; *see also Phillips*, 415 F.3d at 1312 ("We have frequently stated that the words of a claim 'are generally given their ordinary and customary meaning.'").) The undersigned, however, rejects BTG's and Staff's position that the plain and ordinary meaning of these terms is

"capable of binding to." As Respondents note, and as Staff acknowledges, construing these terms using the words "capable of" is inaccurate because it would not require actual binding, and as a result, would improperly broaden the scope of the claims. (*See* Yonan, Tr. at 84:16-19; Koo, Tr. at 97:25-98:3.)

The undersigned rejects Respondents' proposed construction because the plain language of claims 1 and 19 does not warrant limiting these terms to affinity purification. (*See* '414 patent at 13:17-24, 14:21-34.) Indeed, when the patentees intended to limit the claims to certain purification processes, they did so explicitly. (*See id.* at 13:36-38 (claiming "wherein the animal serum has been partially purified by ammonium sulfate precipitation").) Furthermore, while affinity purification is disclosed in the specification, it is merely an example, which should not be imported as a limitation in these terms. (BTG Ex. B at ¶ 29; *Phillips*, 415 F.3d at 1323 ("although the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments"); *see also* Corbett, Tr. at 73:17-23 (noting that affinity purification is a separate invention disclosed in the specification, which is claimed in a separate patent).)

Accordingly, the undersigned hereby construes the terms "bind specifically to" and "binds to" according to their plain and ordinary meaning.

c) "the [or said] antivenom pharmaceutical composition neutralizes the lethality of the venom of a snake of the *Crotalus* genus"

The phrase "the [or said] antivenom pharmaceutical composition neutralizes the lethality of the venom of a snake of the *Crotalus* genus" appears in all of the asserted claims of the '414 patent. The parties disagree on the proper claim construction and have proposed the following constructions:

BTG	RESPONDENTS	STAFF
Plain and ordinary meaning, *i.e.*, "the [or said] composition capable of administration for treatment mitigates the toxic effects caused by the venom of a snake of the *Crotalus* genus that could otherwise result in the death of a snakebite victim"	"it is required that the Fab fragments in each dose confer a significant protective effect when administered to a *Crotalus* snakebite victim"	Plain and ordinary meaning, *i.e.*, "the [or said] composition capable of administration for treatment mitigates the toxic effects caused by the venom of a snake of the *Crotalus* genus that could otherwise result in the death of a snakebite victim"

BTG and the Staff agree that this term should be given its plain and ordinary meaning – *i.e.*, the composition "mitigates the toxic effects caused by the venom of a snake of the *Crotalus* genus that could otherwise result in the death of a snakebite victim." (CMIB at 30; SMIB at 33.) BTG and Staff submit that the plain language of the claim only requires that the composition as a whole exhibit a neutralizing effect, not that the lethality-neutralizing capabilities be linked directly to the Fab fragments within the pharmaceutical composition. (CMIB at 30; CMRB at 23-24; SMIB at 33.)

BTG and Staff object to Respondents' proposed construction, arguing that it improperly seeks to limit the term to require that only the Fab fragments neutralize the lethality of the snake venom. (CMIB at 30, 32 ("The claim does ***not*** require that the 'Fab fragments,' by themselves, neutralize the lethality of the venom, and Respondents' construction would improperly re-write the claim language in such a manner.") (emphasis original); SMIB at 33.) BTG and Staff assert that nothing in the prosecution history, the specification or the claims requires that the Fab fragments and only the Fab fragments neutralize the lethality of the venom. (CMRB at 24-25; SMRB at 17-18.) BTG and Staff also contend that Respondents' proposed construction violates the doctrine of claim differentiation for it renders claim 1 "essentially identical" to claim 20. (CMIB at 32-33; CMRB at 25-26 ("Respondents' proposed constructions would improperly require that Fab fragments be specifically responsible for neutralizing the lethality of the snake

venom in each of claims 1, 19, and 20—even though the claims are drafted differently and are of clearly different scope."); SMIB at 33-34; SMRB at 18.)

Respondents assert that both the specification and the prosecution history dictate that the Fab fragments in the composition, not the composition as a whole, neutralize the lethality of the snake venom. (RMIB at 34-36.) Specifically, Respondents argue that to overcome an obviousness rejection during prosecution, the inventors amended the claims to make clear it is the lethality-neutralizing ability of the Fab fragments that distinguishes the claimed invention from the prior art. (RMIB at 36-38; RMRB at 19-20.) Respondents also claim that statements in the specification about the effectiveness of Fab fragments to neutralize the lethality of a venomous snakebite illustrate that the Fab fragments in the composition must not only exhibit a protective effect, but also that this protective effect must be significant. (RMIB at 35.) Respondents therefore contend that their construction "is consistent with the inventors' repeated assertions . . . that the claimed Fab fragments unexpectedly exhibited the sought-after pharmaceutical activity." (*Id.* at 38.)

Respondents accuse BTG and Staff of ignoring the prosecution history and in particular, the patentees' repeated assertions that the claimed Fab fragments neutralize the lethality of the snake venom.[8] (RMRB at 20.) Respondents believe that BTG's and Staff's proposed construction would impermissibly broaden the claims beyond the scope argued by the inventors during prosecution and thus, should be rejected. (RMIB at 38.)

As the Federal Circuit has stated, "[c]laim construction . . . begins and ends in all cases with the actual words of the claim." *Renishaw PLC*, 158 F.3d at 1248; *see also Phillips*, 415 at 1314; *Vitronics*, 90 F.3d at 1582 ("First, we look to the words of the claims themselves, both

[8] Respondents assert that BTG's and Staff's claim differentiation argument is "entirely academic and refutable" since claim 20 is not asserted in this Investigation. (RMRB at 20.)

asserted and nonasserted, to define the scope of the patented invention.") (internal citations omitted). "The words of a claim 'are generally given their ordinary and customary meaning.'" *Phillips*, 415 F.3d at 1312 (quoting *Vitronics*, 90 F.3d at 1582); *see also Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1323 (Fed Cir. 2003) ("We indulge a 'heavy presumption' that claim terms carry their full ordinary and customary meaning, unless the patentee unequivocally imparted a novel meaning to those terms or expressly relinquished claim scope during prosecution.") (internal citations omitted). Here, claims 1 and 19 unambiguously state that the "***antivenom pharmaceutical composition*** neutralizes the lethality of the venom . . . ." ('414 patent at 13:22-23, 14:32-33 (emphasis added).) In other words, it is the composition as a whole – not the Fab fragments – that confers the lethality neutralizing effect. (*Id.*; *see also id.* at 2:2-3 ("Furthermore, F(ab) and $F(ab)_2$ fragments may sometimes be utilized together.").) Thus, the plain language of claims 1 and 19 does not warrant limiting this term in the manner proposed by Respondents.[9]

Furthermore, Respondents have not provided any reason to deviate from the plain and ordinary meaning of this term. First, the portions of the specification and prosecution history cited by Respondents do not amount to a "clear and unmistakable" disavowal of claim scope. *Revolution Eyewear, Inc. v. Aspex Eyewear, Inc.*, 563 F.3d 1358 (Fed. Cir. 2009) ("Our cases recognize that 'the specification may reveal an intentional disclaimer, or disavowal of claim scope by the inventor.' . . . Importantly, any limitation based on such disclaimer must be shown with reasonable clarity and deliberateness.") (internal citations omitted); *Purdue Pharma L.P. v. Endo Pharms., Inc.*, 438 F.3d 1123, 1136 (Fed. Cir. 2006) ("A patentee may limit the meaning of

[9] In fact, when the patentees wanted to limit the claims to the Fab fragments (and not the composition as a whole) neutralizing the lethality of the snake venom, they explicitly stated so – *i.e.*, "wherein said ***Fab fragments*** neutralize the lethality of the venom of a snake of the *Crotalus* genus in the absence of IgG and F(ab)2." (*See* '414 patent at 14:40-42 (emphasis added).)

a claim term by making a clear and unmistakable disavowal of scope during prosecution."); *Epistar Corp. v. U.S. Int'l Trade Comm'n*, 566 F.3d 1321, 1334 (Fed. Cir. 2009) ("[the accused infringer] must . . . overcome a heavy presumption that claim terms carry their full ordinary and customary meaning, unless it can show the patentee expressly relinquished claim scope."). As Staff noted in its briefing, "the patentee's arguments to the PTO is not simply that it was unexpected that Fab fragments would have a positive pharmaceutical effect of neutralizing and eliminating venom from the body, but it was unexpected that the Fab fragments do not cause a redistribution of venom with deleterious effects." (SMIB at 18; *see also* Koo, Tr. at 114:18-21 (stating that what was novel about the invention was that the Fab fragments "actually did not cause harm by carrying venom particles where they should not be going.") Second, construing the term according to Respondents' proposed construction would render the scope of claim 20 to be identical to claim 1 and as noted *supra*, Respondents have not set forth evidence of a clear disavowal of claim scope that would overcome the strong presumption of claim differentiation. *See InterDigital Commc'ns, LLC v. Int'l Trade Comm'n*, 690 F.3d 1318, 1324 (Fed. Cir. 2012); *RF Del., Inc. v. Pac. Keystone Techs., Inc.*, 326 F.3d 1255, 1263 (Fed. Cir. 2003) ("Under the doctrine of claim differentiation, each claim in a patent is presumptively different in scope.") (internal citations omitted).

Accordingly, the undersigned hereby construes the term "the [or said] antivenom pharmaceutical composition neutralizes the lethality of the venom of a snake of the Crotalus genus" in accordance with its plain and ordinary meaning.

d) "essentially free from contaminating Fc"

The term "essentially free from contaminating Fc" appears in claims 1 and 19. As an initial matter, the parties agree that the phrase "essentially free" means a "small" or "little" amount. (Yonan, Tr. at 129:25-130:2; CMIB at 25-26; SMIB at 28 (citing '414 patent at 9:55-9:56).) In addition, BTG and Staff have proposed the exact same constructions for the term "essentially free from contaminating Fc," but they disagree on whether "contaminating Fc" includes both Fc fragments and whole IgG molecules with Fc portions. (SMRB at 13; SMIB at 28.) Furthermore, while Respondents and Staff contend that "contaminating Fc" includes both Fc fragments and whole IgG molecules with Fc portions, they disagree on whether the term "domain" should be included. (SMRB at 12-14; SMIB at 28-30; *see also* RMRB at 21-22.)

BTG	RESPONDENTS	STAFF
"not more than a small, but detectable, amount of Fc"	"contains little or no immunoglobulin proteins with an Fc domain"	"not more than a small, but detectable, amount of Fc"

According to BTG, the plain and unambiguous meaning of "contaminating Fc" includes only Fc fragments. (CMRB at 28.) Thus, BTG objects to Respondents' and Staff's inclusion of both Fc fragments and whole IgG molecules with Fc portions. (*Id.* at 26-28.) BTG argues that the term "Fc" implies that it only encompasses Fc fragments because it is an abbreviation for crystallizing fragment. (Loughran, Tr. at 136:19-136:20.) BTG also argues that the specification defined "Fc" as "Fc fragments" by using the terms interchangeably. (*Id.* at 136:11-137:7 (comparing '414 patent at 1:54-1:59, 3:53-3:58, 4:23-24, and 5:16-5:18 with '414 patent at 9:54-9:56, and 10:13-10:24).) Furthermore, BTG claims the "term Fc is separate and distinct from a whole IgG molecule, which is a term that is utilized in claim 20." (*Id.* at 128:11-128:25 (stating that different claim terms are presumed to have different meanings).)

Respondents and Staff argue that one of ordinary skill in the art would understand that "contaminating Fc" should encompass both cleaved Fc fragments and whole IgG molecules with Fc regions.[10] (RMIB at 40 (citing Kossiakoff Dec. at 8); SMIB at 28.) In addition, Respondents and Staff contend that the plain language of the claims does not limit "contaminating Fc" to only Fc fragments. (RMIB at 39; SMIB at 28-30.) Furthermore, Respondents and Staff claim that when the patentees referred to a fragment of a molecule, they consistently used the modifying term "fragment." (RMIB at 40; SMRB at 12.) Moreover, Respondents and Staff assert that the test used by the patentees to determine if the compound was essentially free from contaminating Fc is sensitive to both Fc fragments and whole IgG molecules with Fc regions. (RMIB at 41; SMRB at 13-14; *see also* Koo, Tr. at 133:13-134:13.)

Respondents and Staff agree that BTG improperly limits "contaminating Fc" to only Fc fragments. (RMRB at 21; SMRB at 13.) According to Respondents and Staff, limiting "contaminating Fc" to only Fc fragments would go against the concept of the invention, as whole IgG molecules with Fc regions have the potential to cause serum sickness just like Fc fragments. (Yonan, Tr. at 139:3-139:8; SMRB at 14.) In addition, Respondents and Staff assert that BTG improperly reads the term "fragments" into the claims. (Yonan, Tr. at 130:14-130:18, 131:11-131:22; SMIB at 29-30.)

The undersigned finds that the specification and the knowledge of one of ordinary skill in the art illustrate that "contaminating Fc" refers to both Fc fragments and whole IgG molecules with Fc portions.[11] (Alberts, *supra*, at 951-1012; Kossiakoff Dec. at 8; *see also* '414 patent at

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[10] Staff asserts that it does not ultimately matter whether "contaminating Fc" only refers to Fc fragments or whole IgG molecules with Fc regions because both will be eliminated from the pharmaceutical compound by immunoelectrophoresis. (Koo, Tr. at 132:25-134:18; SMRB at 13-14.) The undersigned finds this argument unpersuasive, as the limitation referring to immunoelectrophoresis only appears in claim 1 and the term "contaminating Fc" appears in claims 1 and 19. ('414 patent at 13:16-14:34; *see* Loughran, Tr. at 135:16-135:24.)

[11] The undersigned rejects Respondents' proposed construction because "Fc domain" is ambiguous and unnecessary. *See Harris Corp. v. IXYS Corp.*, 114 F.3d 1149, 1152 (Fed. Cir. 1997) (refusing to read in terms that would

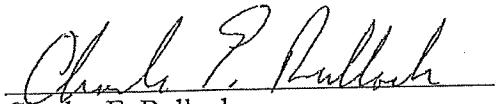
2:52-3:18, 9:51-9:62.) In addition, limiting "contaminating Fc" to only Fc fragments would undercut the inventive aspect of the patent, as both Fc fragments and whole IgG molecules with Fc portions have a potential to cause serum sickness. (Yonan, Tr. at 139:3-139:8; Koo, Tr. at 139:21-139:24; *see also* '414 patent at 6:47-6:51; Loughran, Tr. at 126:9-126:13.) Furthermore, the plain language of the claims does not limit "contaminating Fc" to only Fc fragments. *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365-69 (Fed. Cir. 2012) (stating the patentee is entitled to the full scope of the plain and ordinary meaning of the term).

Accordingly, the undersigned hereby construes "essentially free from contaminating Fc" as ***"not more than a small, but detectable, amount of Fc, which includes Fc fragments and whole IgG molecules with Fc portions."***

Within seven days of the date of this document, each party shall submit to the Office of the Administrative Law Judges a statement as to whether or not it seeks to have any portion of this document deleted from the public version. The parties' submissions may be made by facsimile and/or hard copy by the aforementioned date.

Any party seeking to have any portion of this document deleted from the public version thereof must submit to this office a copy of this document with red brackets indicating any portion asserted to contain confidential business information. The parties' submissions concerning the public version of this document need not be filed with the Commission Secretary.

SO ORDERED.



Charles E. Bullock
Chief Administrative Law Judge

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contribute nothing but meaningless verbiage); *InterDigital Commc'ns, LLC v. Int'l Trade Comm'n*, 690 F.3d 1318, 1324 ("Claim terms are generally given their ordinary meaning as understood by persons skilled in the art in question at the time of the invention").

CERTAIN ANTIVENOM COMPOSITIONS AND PRODUCTS CONTAINING THE SAME **337-TA-903**

PUBLIC CERTIFICATE OF SERVICE

I, Lisa R. Barton, hereby certify that the attached **PUBLIC VERSION ORDER NO. 23** has been served by hand upon the Commission Investigative Attorney, **Brian Koo, Esq.**, and the following parties as indicated, on June 3, 2014.

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