Public Version

UNITED STATES INTERNATIONAL TRADE COMMISSION

Washington, D.C.

In the Matter of **CERTAIN PLANT-DERIVED RECOMBINANT HUMAN SERUM ALBUMINS ("rHSA") AND PRODUCTS CONTAINING SAME**	**Inv. No. 337-TA-1238**

INITIAL DETERMINATION ON VIOLATION OF SECTION 337 AND RECOMMENDED DETERMINATION ON REMEDY AND BOND

Administrative Law Judge MaryJoan McNamara

(April 7, 2022)

SELECTED SUMMARY FINDINGS

Pursuant to the Notice of Investigation, 86 Fed. Reg. 6916, dated January 25, 2021, this is the Initial Determination ("ID") of the Investigation in the Matter of Certain Plant-Derived Recombinant Human Serum Albumins ("rHSA") and Products Containing Same, United States International Trade Commission Investigation No. 337-TA-1238. *See* 19 C.F.R. § 210.42(a).

It is a finding of this ID that Complainant Ventria Bioscience Inc. ("Complainant" or "Ventria") has proven by a preponderance of evidence that Respondent Wuhan Healthgen Biotechnology Corp ("Respondent" or "Healthgen") has violated subsection (b) of Section 337 of the Tariff Act of 1930, in the importation into the United States, the sale for importation, or the sale within the United States after importation of certain plant-derived recombinant human serum albumins ("rHSA") and products containing same.

It is a finding of this ID that Healthgen has infringed asserted claims 1 and 11-13 of U.S. Patent No. 10,618,951 ("the '951 patent"). It is also a finding of this ID that the asserted claims of the '951 patent are not invalid.

It is a finding of this ID that one or more of Ventria's domestic industry products have satisfied the technical industry prong of the domestic industry requirement for the '951 patent. It is also a finding of this ID that Ventria has satisfied the economic prong of the domestic industry requirement under Section 337(a)(3)(A), (B), and (C).

This decision recommends: (1) Limited Exclusion Orders with a standard certification provision; and (2) that a 100% bond enter during the Presidential Review Period.

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ABBREVIATIONS

The following shorthand references to the parties, related U.S. agencies, and related proceedings are used in this Initial Determination:

Complainant or Ventria	Complainant Ventria Bioscience Inc.
Respondents	Respondents Wuhan Healthgen Biotechnology Corp.; ScienCell Research Laboratories, Inc.; Aspira Scientific, Inc.; and eEnzyme LLC, collectively
Defaulting Respondents	Aspira Scientific, Inc.; eEnzyme LLC; and ScienCell Research Laboratories, Inc., collectively
Respondent or Healthgen	Wuhan Healthgen Biotechnology Corp.
Staff	Commission Investigative Staff
Parties	Ventria, Healthgen, and Staff, collectively
CBP	U.S. Customs and Border Protection
PTO	U.S. Patent and Trademark Office

The following abbreviations for pleadings, exhibits, briefs, transcripts, and Orders are used in this Initial Determination:

Compl.	Complaint
Resp.	Response of Healthgen to the Notice of Investigation and Complaint Under Section 337 of the Tariff Act of 1930, as Amended
CX	Complainant's exhibit
CDX	Complainant's demonstrative exhibit
CPX	Complainant's physical exhibit
CPBr.	Complainant's Corrected Pre-Hearing Brief
CBr.	Complainant's Initial Post-Hearing Brief
CRBr.	Complainant's Post-Hearing Reply Brief

CPSt.	Complainant's Pre-Hearing Statement
JX	Joint exhibit
RX	Respondent's exhibit
RDX	Respondent's demonstrative exhibit
RPX	Respondent's physical exhibit
RPBr.	Respondent's Corrected Pre-Hearing Brief
RBr.	Respondent's Initial Post-Hearing Brief
RRBr.	Respondent's Post-Hearing Reply Brief
RPSt.	Respondent's Pre-Hearing Statement
SPBr.	Staff's Pre-Hearing Brief
SBr.	Staff's Initial Post-Hearing Brief
SRBr.	Staff's Post-Hearing Reply Brief
SPSt.	Staff's Pre-Hearing Statement
Tr.	Evidentiary hearing transcript
Dep. Tr.	Deposition transcript
COMBr.	Complainant's Opening *Markman* Brief
ROMBr.	Respondent's Opening *Markman* Brief
SOMBr.	Staff's Opening *Markman* Brief
CRMBr.	Complainant's Responsive *Markman* Brief
RRMBr.	Respondent's Responsive *Markman* Brief
SRMBr.	Staff's Responsive *Markman* Brief
Joint CC Chart	Post-Hearing Joint Claim Construction Chart (Doc. ID No. 743262 (May 24, 2021))

***Markman* Order**	Order No. 14 (Aug. 23, 2021)

The following shorthand references to certain products and patents at issue are used in this Initial Determination:

'951 patent	U.S. Patent No. 10,618,951
'461 patent	U.S. Patent No. 8,609,416[1]
Asserted Patent	'951 patent
HSA	Human serum albumin
rHSA	Recombinant human serum albumin
Accused Products or OsrHSA Products	"Cell culture grade" rHSA product and "clinical grade" rHSA product, collectively
DI Products	Cellastim® S; Exbumin®; Optibumin® OptiPEAK®; OptiVERO®; and ITSE™+A, collectively

[1] This patent was terminated from the Investigation. (*See* Section II.A, *infra*.).

I. INITIAL DETERMINATION ON VIOLATION OF SECTION 337, AND RECOMMENDED DETERMINATION ON REMEDY AND BOND

A. Overview

At issue in this Investigation are compositions used to improve the growth of cells outside the body in an artificial environment, i.e., *in vitro*. Cells grown in cell culture have a number of important uses in the biological sciences, such as providing *in vitro* model systems for studying cells outside the body, as well as manufacturing biological compounds (e.g., vaccines). These cells are sustained in an artificial environment by, *inter alia*, cell culture media comprising nutrients (e.g., proteins) that are essential for their growth.

Two (2) widely used growth supplements for cell culture media are fetal bovine serum ("FBS") and bovine serum albumin ("BSA"). In addition to animal sources, serum albumin can also be derived from humans. They contain necessary components, including albumin, which satisfy specific metabolic requirements needed for the culture of cells *in vitro*. Because serum is a naturally derived product from animals or humans, there is a risk of batch-to-batch variability as well as contamination from the animal or human source. Additionally, there have been ethical concerns with respect to harvesting animal serum.

To circumvent such ongoing issues, alternative media have been developed that do not rely on serum components for use in cell culture. These include chemically defined media, serum-free media, or animal-free media. Recombinant proteins, such as recombinant albumin, and other types of synthetic or artificial compounds have also been used in cell culture media instead of native proteins and animal derived components. Recombinant technology involves the introduction of foreign genetic material (transgenes) into a host cell, where the foreign genetic material can be used to produce proteins that would not normally be present in that host cell

(e.g., recombinant albumin).

In the context of recombinant proteins, Ventria Bioscience Inc. ("Complainant" or "Ventria") developed a genetically engineered, plant-based protein-production system called ExpressTec®. This system has enabled Ventria to use the natural life cycle and growth of rice to manufacture recombinant proteins, including the domestic industry recombinant human serum albumin (rHSA) products at issue in this Investigation.

Specifically, the ExpressTec® system inserts a synthetic gene for production of rHSA, the protein of interest in this Investigation, into the rice plant. This allows for the subsequent expression of the rHSA gene in the rice seed of the plant. The stored rice grain is then de-husked and cleaned, and the rHSA protein in the seed is extracted with a water-based buffer. Afterwards, the extracted rHSA protein is purified to the extent desired, and final products are formulated as liquid or lyophilized powder.

Free of animal or human contaminants, these recombinant proteins (rHSA) are an alternative to the use of protein sources, such as FBS, BSA and human serum, in cell and tissue culture.

Such rHSA products have enabled the manufacture of medicines such as immunotherapies used in cancer treatment, gene therapies used to treat genetically inherited diseases, medicines for inflammatory and infectious diseases, and regenerative medicines. Ventria's rHSA products have also been used, *inter alia*, in the production of vaccines.

In this Investigation, the Accused and DI products involve rHSAs described above. Moreover, the Accused Products entail the sale for importation, or the sale within the United States after importation of certain rHSA products derived from rice.

B. Summary of Findings

A summary of this decision's finding is summarized below.

Table No. 1: Summary of Findings

Product	Patent	Claims	Determination
Accused Products[2]	'951 patent	1 and 11-13	Violation
DI Products[3]	'951 patent	1 and 11-13	Satisfied

II. BACKGROUND

A. Institution and Selected Procedural History

On December 15, 2021, Ventria Bioscience Inc. ("Complainant" or "Ventria") filed a complaint ("Complaint") under Section 337 of the Tariff Act of 1930, as amended, 19 U.S.C. § 1337, alleging infringement of claims 1-3 and 11-13 of U.S. Patent No. 10,618,951 ("the '951 patent"),[4] and claims 1-3, 5-7, 10, 12, 18-20, and 22-25 of U.S. Patent No. 8,609,416 ("the '416 patent"). (Doc. ID No. 728108 (Dec. 16, 2020);[5] Compl. at ¶¶ 121-122.). In the Complaint, Ventria also alleged violations of section 337 based on the importation or sale of certain plant-derived rHSAs through false designation of origin. (*See id.* at ¶¶ 128-156.).

The Commission instituted this Investigation pursuant to subsection (b) of Section 337 of the Tariff Act of 1930, as amended, on January 25, 2021. 86 Fed. Reg. 6916 (Jan. 25, 2021).

[2] "Cell culture grade" rHSA product and "clinical grade" rHSA product, collectively.

[3] Cellastim® S; Exbumin®; Optibumin® OptiPEAK®; OptiVERO®; and ITSE™+A, collectively.

[4] JX-0001.

[5] This is the official received date of the original Complaint.

The Notice of Investigation ("NOI") named as complainant: Ventria Bioscience Inc. of Junction City, Kansas ("Complainant" or "Ventria"). *Id.* The NOI named as respondents: Wuhan Healthgen Biotechnology Corp. of Wuhan, China ("Healthgen"); ScienCell Research Laboratories, Inc. of Carlsbad, California; Aspira Scientific, Inc. of Milpitas, California; and eEnzyme LLC of Gaithersburg, Maryland (collectively, the "Respondents").[6] *Id.* at 6917. The Office of Unfair Import Investigations ("Staff," and with Complainant and Healthgen, the "Parties") was also named as a party in this Investigation. *Id.* Of the four Respondents named in the NOI, only Healthgen participated in the Investigation.

On February 23, 2021, Healthgen filed a response to the Complaint and NOI ("Response"). (Doc. ID No. 734917 (Feb. 23, 2021).). In the Response, Healthgen identified five (5) affirmative defenses ("Healthgen's Affirmative Defenses"). (Resp. at 33-34.).

On April 26, 2021, an Order granted Ventria's motion for an order to show cause as to the other three Respondents (the "Defaulting Respondents"). (*See* Order No. 8 (Apr. 26, 2021).). An initial determination ("ID") finding the Defaulting Respondents in default was entered on July 28, 2021. (*See* Order No. 13 (July 28, 2021).).

As the result of two (2) IDs granting Ventria's partial termination of this Investigation with respect to all asserted claims of the '416 patent, claims 2 and 3 of the '951 patent, and the false designation of origin claims against Healthgen,[7] the four (4) remaining claims that are the subject of this decision are claims 1 and 11-13 of the '951 patent. (*See* Order Nos. 12 (July 16,

[6] Two additional entities were named as proposed Respondents in the original Complaint: antibodies-online, Inc. and United States Biological Corporation. (Compl. at ¶ 3.). Ventria withdrew the allegations against both entities prior to institution. (Doc. ID Nos. 729967 (Jan. 8, 2021), 730236 (Jan. 11, 2021).).

[7] The false designation of origin claims against the Defaulting Respondents have not been terminated. (*See* Motion Docket No. 1238-007 at 1 (June 9, 2021); Order No. 12 at 1 (July 16, 2021).).

2021), 29 (Nov. 3, 2021).).

On April 23, 2021, the Parties filed a joint *Markman* hearing proposal. (Doc. ID No. 740824 (Apr. 23, 2021).). A *Markman* hearing was held on May 18, 2021. (*See* Order No. 9 (May 3, 2021); Doc. ID No. 742890 (May 19, 2021).). A *Markman* Order issued construing the claim terms in dispute. (*Markman* Order (Aug. 23, 2021).).

In accordance with the deadline set forth in Order No. 6, Ventria filed two (2) motions *in limine* ("MILs") (Motion Docket Nos. 1238-017 (Sept. 24, 2021), 1238-018 (Sept. 27, 2021)) and Healthgen filed three (3) MILs (Motion Docket Nos. 1238-014 (Sept. 24, 2021), 1238-015 (Sept. 24, 2021), 1238-016 (Sept. 24, 2021)). Ventria's and Healthgen's MILs were denied. (*See* Order Nos. 23 (Oct. 21, 2021), 24 (Oct. 21, 2021).).

The evidentiary hearing ("Hearing") was held on November 4-5, 8-10, 2021.[8] (*See* Order No. 6 at App. A (Feb. 9, 2021).).

B. The Parties

1. Complainant Ventria Bioscience Inc.

Ventria is a corporation organized under the laws of Delaware with its principal place of business in Junction City, Kansas.[9] (*See* Tr. (Deeter)[10] at 142:18-19, 144:18-145:1; Compl. at

[8] Neither Ventria nor Healthgen filed any motions to strike during or after the Hearing.

[9] Ventria notes that "InVitria is a division and brand of Ventria responsible for, among other things, Ventria's rHSA products. Because InVitria is not a separately registered or incorporated legal entity, it is not a named party to this case[.]" (Compl. at ¶ 50.). Ventria also submits that "'Ventria' as used herein [in the Complaint] generally refers to both Ventria and InVitria." (*Id.*).

[10] At the time he provided his testimony on November 4, 2021, Mr. Scott Deeter was the President and CEO of Ventria. (CPSt at 3.). Ventria identified Mr. Deeter as a fact witness to testify about "the Asserted Patent; background of Ventria's business, its technology, and the Domestic Industry Products; the Accused Products and Healthgen's targeting of U.S. customers; Ventria's domestic industry; and any other matters related to Ventria and the Asserted Patent." (*Id.*).

¶ 48.). Ventria operates another facility in Aurora, Colorado. (*See* Tr. (Deeter), at 142:18-19, 144:18-145:1; Compl. at ¶ 48.).

In the Complaint, Ventria described itself as follows:

> Among other accomplishments, Ventria is an established and respected leader in the field of plant-based expression of recombinant proteins. Ventria has invested enormous resources in not only developing and advancing this technology, but also in establishing the industry itself and achieving acceptance of the technology by the wider pharmaceutical and scientific communities. This technology, sometimes referred to as "molecular pharming," involves the production of recombinant protein biologics using plant biology, and it remains a relatively nascent technology and industry. Ventria is recognized as belonging to only a handful of "the very first commercial ventures" in this space.
>
> * * *
>
> Ventria has developed a product family of serum-free, animal-free products that improve the performance and safety of biologic drug manufacturing and final product formulation.
>
> * * *
>
> Ventria develops and manufactures (entirely in the United States) and sells (in the United States and elsewhere) plant-derived rHSA products under three brands: Cellastim® S, Exbumin, and Optibumin®.

(Compl. at ¶¶ 6-7, 9, 51.).

2. Respondent Wuhan Healthgen Biotechnology Corp.

Healthgen is a Chinese corporation based in Wuhan, China. (*See* Resp. at ¶ 54.). Healthgen confirmed that it was co-founded by Dr. Daichang Yang, who previously worked at Ventria. (*See id.* at ¶ 55.). Healthgen also confirmed that it manufactures abroad and sells for importation into the United States products containing plant-derived rHSA, including the product commercially branded as "OsrHSA." (*See id.* at ¶ 2.).

3. Defaulting Respondents

On August 18, 2021, the Commission found Respondents ScienCell Research

Laboratories, Inc. ("ScienCell"), Aspira Scientific, Inc. ("Aspira"), and eEnzyme LLC ("eEnzyme," and with ScienCell and Aspira, the "Defaulting Respondents") in default. (Doc. ID No. 749901 (Aug. 18, 2021).).

According to the Complaint, ScienCell is a corporation organized under the laws of California with its principal place of business in Carlsbad, California. (*See* Compl. at ¶ 68.). Ventria presented evidence demonstrating that ScienCell is or has been a distributor of Healthgen's rice-derived albumin products. (*See id.* at ¶ 69, Ex. 11 (Healthgen website identifying North American distributors); CX-1080C (Cao Dep. Tr.)[11] at 14:21-15:12.).

According to the Complaint, Aspira is a corporation organized under the laws of Delaware with its principal place of business in Milpitas, California. (*See* Compl. at ¶ 70.). Ventria provided evidence showing that Aspira is or has been a distributor of Healthgen's rice-derived albumin products. (*See id.* at ¶ 71, Ex. 11 (Healthgen website identifying North American distributors); CX-1080C (Cao Dep. Tr.) at 14:21-15:12.).

According to the Complaint, eEnzyme is a limited liability company organized under the laws of Maryland with a principal place of business in Gaithersburg, Maryland. (*See* Compl. at ¶ 74.). Ventria presented evidence indicating that eEnzyme is or has been a distributor of Healthgen's rice-derived albumin products. (*See id.* at ¶ 75, Ex. 11 (Healthgen website identifying North American distributors); CX-1080C (Cao Dep. Tr.) at 14:21-15:12.).

III. JURISDICTION, IMPORTATION, AND STANDING

A. The Commission Has Jurisdiction

To have the authority to decide a case, a court or agency must have both subject matter

[11] Ms. Jing Cao, one of Healthgen's corporate representatives, was deposed in this Investigation. (*See* CX-1080C (Cao Dep. Tr.) at 10:15-12:10.). At the time of her deposition, Ms. Cao's job title was "deputy manager of the marketing department." (*See id.* at 17:25-18:5.).

jurisdiction and jurisdiction over either the parties or the property involved. *See Certain Steel Rod Treating Apparatus and Components Thereof*, Inv. No. 337-TA-97, Comm'n Opinion, 215 U.S.P.Q. 229, 231 (U.S.I.T.C. 1981). For the reasons discussed below, the facts support a finding that the Commission has jurisdiction over this Investigation.

1. Subject Matter Jurisdiction

The Commission has subject matter jurisdiction over this Investigation because Ventria alleged that Healthgen has violated 19 U.S.C. §1337(a)(1)(B). *See Amgen v. U. S. Int'l Trade Comm'n*, 902 F.2d 1532, 1536 (Fed. Cir. 1990). Healthgen did not contest that the Commission has subject matter jurisdiction. (*See* RPBr. at 5.).

2. Personal Jurisdiction

Healthgen has appeared and responded to the Complaint and NOI, and fully participated in this Investigation, which included participating in discovery and the Hearing, and by filing motions. Thus, the Commission has personal jurisdiction over Healthgen. *See, e.g., Certain Microfluidic Devices* ("*Microfluidic Devices*"), Inv. No. 337-TA-1068, Initial Determination, 2018 WL 5279172, at *16 (Sept. 20, 2018); *Certain Windshield Wiper Devices and Components Thereof* ("*Wiper Devices*"), Inv. No. 337-TA-881, Initial Determination at 5 (May 8, 2014) (unreviewed in relevant-part) (Doc. ID No. 534255).

3. *In Rem* Jurisdiction

Section 337(a)(1)(B) applies to the "[t]he importation into the United States, the sale for importation, or the sale within the United States after importation" of articles that infringe a valid and enforceable United States patent." 19 U.S.C. § 1337(a)(1)(B). A single instance of importation is sufficient to satisfy the importation requirement of Section 337. *Certain Optical Disc Drives, Components Thereof, and Prods. Containing the Same*, Inv. No. 337-TA-897,

Order No. 101 at 3 (Sept. 22, 2014) (citations omitted) (EDIS Doc. 543438).

Healthgen acknowledged that the Commission has *in rem* jurisdiction and that the importation requirement is satisfied. (*See* RPBr. at 5.). Thus, the Commission has *in rem* jurisdiction over the Accused Products. *See, e.g., Wiper Devices*, Inv. No. 337-TA-881, Initial Determination at 5 (*in rem* jurisdiction exists when importation requirement is satisfied).

B. Ventria Has Standing in the Commission

Jurisdiction also requires standing. *See SiRF Technology, Inc. v. Int'l Trade Comm'n*, 601 F.3d 1319, 1326 (Fed. Cir. 2016) (standing to bring an infringement suit is the same under Commission Rules as it would be in a Federal District Court case); *Certain Optical Disc Drives, Components Thereof and Prods. Containing Same*, Inv. No. 337-TA897, Opinion Remanding the Investigation at 4 (Jan. 7, 2015). Commission Rule 210.12 requires that intellectual property-based complaints filed by a private complainant "include a showing that at least one complainant is the exclusive license of the subject intellectual property." 19 C.F.R. § 210.12(a)(7).

Ventria has standing to bring suit for infringement under Section 337 because Ventria owns by assignment the full right, title and interest in the '951 patent. (*See* Compl. at Ex. 3 (assignments of the '951 patent from inventors to Ventria Bioscience and document formalizing name change of Ventria Bioscience to Ventria Bioscience Inc.).).

IV. OVERVIEW OF RELEVANT TECHNOLOGY

The technical/scientific concepts described below are pertinent to the infringement, technical domestic industry, and validity testimony and evidence that support the analysis discussed in this ID.

A. Albumin

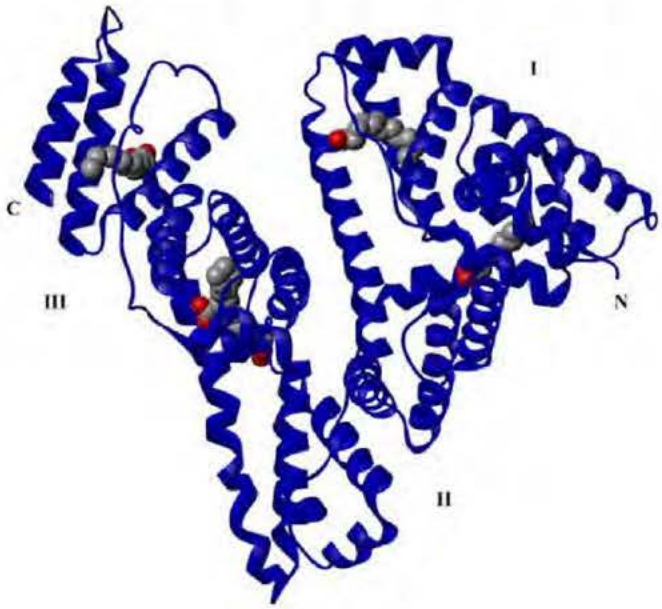
Ventria's expert, Dr. Lisa Wilken,[12] testified that albumin is a protein used extensively in cell culture due to its multiple binding sites that reversibly bind diverse ligands, including lipids, amino acids, hormones, peptides, etc. (Tr. (Wilken) at 316:3-319:17; *see also* JX-0077.0001 (Cellastim S™ Guidelines of Use describing beneficial properties of albumin in cell culture).). By transporting these molecules to cells in culture, albumin improves their growth and productivity. (Tr. (Wilken) at 316:3-319:17; JX-0077.0001.). Dr. Wilken explained that albumin also binds, sequesters, and stabilizes small molecules and ions such as reactive oxygen and nitrogen, serving as an antioxidant. (Tr. (Wilken) at 316:3-319:17.). Ventria provided peer-reviewed literature confirming Dr. Wilken's testimony. (*See* CX-0898;[13] CDX-0001C.0009-10.).

An image of albumin depicting its binding sites and its three-dimensional, folded structure, which was copied from peer-reviewed literature, and upon which Dr. Wilken relied during her expert testimony, is shown below.

[12] When she testified during the Hearing on November 5 and 8-9, 2021, Dr. Lisa Wilken was an Associate Professor in the Department of Biological and Agriculture Engineering at Kansas State University. (CPSt. at Ex. A.). Ventria identified Dr. Wilken as an expert to testify about "the technical background of Asserted Patent; the Accused Products; the Domestic Industry Products; the knowledge of a person of ordinary skill in the art; claim construction; and other issues in connection with infringement, validity, the technical prong of the domestic industry requirement, enforceability, and/or any other technical issue that may arise." (*Id.* at 4.).

[13] Geoffrey L. Francis, *Albumin and mammalian cell culture: implications for biotechnology applications*, CYTOTECHNOLOGY, Apr. 6, 2010 (published).

Figure 1: Crystal Structure of Albumin



(CX-0898; *see also* CDX-0001C.0009-10.).

Relying on peer-reviewed literature, such as CX-0898, Dr. Wilken explained that the image shown above in Figure 1 depicts the "three-dimensional structure of albumin, including . . . the blue peptides or links of amino acids that form the albumin molecule. It is folded into its three-dimensional confirmation [sic] or the structure of this protein." (Tr. (Wilken) at 316:14-22; CX-0898.0002, 0003.).

Specifically, Dr. Wilken testified that the red dots "depict[] an example of a few of the bindings locations of these diverse ligands that we mentioned, the fact that it combines amino acids, lipids, proteins, hormones, and many other molecules. So it's just a representation showing the function of albumin is -- and the value is of a carrier of these molecules." (Tr. (Wilken) at 317:2-9; CX-0898.0002, 0003.). With respect to the gray balls, Dr. Wilken explained that they "model[] the structure of these ligands, and they are bound to the albumin

molecule." (Tr. (Wilken) at 317:10-13; CX-0898.0002, 0003.).

When asked about the importance of albumin's structure, Dr. Wilken testified as follows:

> Q. Why is structure important?
>
> A. [I]t's always important for proteins. ***Structure is the function, and it must be maintained. And, in particular, since [albumin] functions by binding multiple types of molecules, that's derived from its structure***. And so we see 1, 2, and 3 [in Figure 1 above] indicated here. Those are homologous domains, just means domains of the molecule that are similar . . . [a]nd throughout the structure there are many binding sites for various types of molecules . . . that . . . extend throughout the entire protein molecule.

(Tr. (Wilken) at 318:5-22 (emphasis added); *see also* CX-0898.0002, 0003.).

When asked about the impact of altering albumin's structure, Dr. Wilken testified as follows:

> Q. What happens if you alter the structure of an albumin?
>
> A. So if the structure is -- for example, ***if you were to remove a portion of that molecule, the function will certainly be impacted, or the ability to bind and transport these ligands or molecules for the cell culture***.
>
> Q. Is that because it essentially loses a portion of its structure?
>
> A. Yes. So there's binding sites throughout. It's not one particular site. It's multiple sites to carry multiple ligands.

(Tr. (Wilken) at 318:23-319:8 (emphasis added); *see also* CX-0898.0002, 0003.).

B. Recombinant Proteins and Cell Culture

Dr. Wilken explained that recombinant proteins are proteins that result from the expression of recombinant (i.e., non-native) DNA within a host cell or organism, which encodes a recombinant protein that is eventually made by downstream cellular machinery. (Tr. (Wilken) at 321:8-322:11; CDX-0001C.0012; *see also* CX-0898.0002.). Dr. Wilken testified that "[c]ell culture is growth of cells in an environment beyond its natural source . . . . So nutrients are provided through a media for those cells to grow." (Tr. (Wilken) at 319:21-320:1; CDX-

0001C.0011; *see also* CX-0898.0001, 0002.).

She explained that "[c]ell culture is used extensively in research development for studying cells, the function of cells, for production of biological compounds, such as proteins, including therapeutic proteins in vaccines." (Tr. (Wilken) at 320:12-16; CDX-0001C.0011; *see also* CX-0898.0001.). Dr. Wilken added that "cell culture media should have the, what we call, macro nutrients, so the major elements . . . that cells need to grow. It also would include . . . things like albumin, for example, that is beneficial to the cell culture," because albumin has the functionality and "capabilities to bind molecules and deliver them to the cell, or even to pick up molecules that could be detrimental to the cell." (Tr. (Wilken) at 302:22-321:7; *see also* CDX-0001C.0011; CDX-0001C.0009-10; CX-0898.0001, 0002, 0003, 0008, 0009.).

C. Protein Aggregation

As described in the peer-reviewed literature that Ventria provided, protein aggregates are protein-protein interactions that range from the simplest form of a dimer, meaning the interaction of two protein monomers, up to large multimers. (*See* JX-0132;[14] CX-0902.[15]). Both experts agreed that a dimer is the simplest form of an aggregate. (Tr. (Wilken) at 336:13-20; Tr. (DeFilippi)[16] at 1256:23-1257:3, 1257:12-22, 1257:24-1258:7.).

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[14] John den Engelsman et al., *Strategies for the Assessment of Protein Aggregates in Pharmaceutical Biotech Product Development*, PHARMACEUTICAL RESEARCH, Oct. 23, 2010 (published).

[15] Lisa R. Wilken et al., *Recovery and purification of plant-made recombinant proteins*, BIOTECHNOLOGY ADVANCES, Aug. 6, 2011 (available).

[16] When he testified during the Hearing on November 8-9, 2021, Dr. Louis DeFilippi was an independent consultant and the President of Louis DeFilippi, LLC. (RPSt. at 1.). Healthgen identified Dr. DeFilippi as an expert to testify about "the '951 patent, including the technical background and the relevant prior art, the level of knowledge of a person of ordinary skill in the art, invalidity of the '951 patent, the noninfringement of Healthgen's Accused Products, and the technical prong of the Commission's domestic industry requirement." (*Id.*).

Dr. Wilken explained that aggregates can be analyzed using numerous methods including electrophoresis and chromatographic techniques with varying separation and detection principles and unique advantages and disadvantages. (Tr. (Wilken) at 344:6-14, 345:11-21; CDX-0001C.0022; *see also* JX-0132.0004, 0005-07; JX-0060.0006, 0007;[17] CX-0900.0007.[18]). For example, electrophoretic analysis is an effective separation technique commonly used for evaluating aggregation. (Tr. (Wilken) at 351:2-352:1; JX-0132.0005, 0007; JX-0060.0006.).

D. Endotoxin

Dr. Wilken testified that endotoxin is a hydrophobic, lipopolysaccharide component found in the outer membrane of some Gram-negative bacteria that is released upon cell death and lysis. (Tr. (Wilken) at 331:20-332:2; CDX-0001C.0017.). She explained that it is a human pathogen which can also negatively impact the growth or performance of cell cultures and cause significant variation in experimental cell culture data. (Tr. (Wilken) at 332:16-24, 333:10-21; CDX-0001C.0017; JX-0134.0006; CX-0927.). She also added that endotoxins have many documented effects on cell growth and function and many common cell culture systems are known to be sensitive to even low endotoxin levels. (Tr. (Wilken) at 332:16-24, 333:10-21; CDX-0001C.0017; JX-0134.0006.).

Healthgen's expert, Dr. DeFilippi, confirmed that although it was known prior to the invention claimed in the '951 patent that endotoxins were not desirable in cell culture media supplements, no rice-expressed albumin having the low levels of endotoxin and aggregated

[17] Hanns-Christian Mahler et al., *Protein Aggregation: Pathways, Induction Factors and Analysis,* JOURNAL OF PHARMACEUTICAL SCIENCES, Sept. 29, 2008 (published).

[18] Kirsty D. Ratanji et al., *Immunogenicity of therapeutic proteins: Influence of aggregation,* JOURNAL OF IMMUNOTOXICOLOGY, Aug. 6, 2013 (published).

albumin level disclosed in the '951 patent had been developed.

> Q. Okay. And so were endotoxins a concern in cell culture media in particular?
>
> A. Yes. Exactly right. Because these endotoxins, basically, are ubiquitous. It takes a fair amount of work to control the levels. And indeed the FDA recognized you had to control the levels below a certain -- as they say at the bottom, establish an appropriate acceptance limit. You have to be at or below that acceptance limit.
>
> * * *
>
> Q. On the issue of long felt need, you agree that before 2009 the presence of endotoxins in biologically derived products was a major concern, correct?
>
> A. It's always been a major concern, including 2009, and subsequently.
>
> Q. And prior to 2009 there was no rHSA product. I'm sorry. Let me start again. Prior to 2009 there was no rHSA produced in transgenic rice that had less than 1 EU of endotoxin per milligram of albumin, was there?
>
> A. Not in transgenic rice, I don't believe. Other expression systems, there was very low, as we already discussed.
>
> Q. But my question was directed to transgenic rice.
>
> A. Right. And I believe I already answered that. I can answer it again, if you like. That's no problem.

(Tr. (DeFilippi) at 805:15-22, at 979:25-980:15.).

E. Certificates of Analysis

Dr. Wilken testified that a Certificate of Analysis ("COA") is a document listing product attributes that have been measured (e.g., aggregated albumin levels), and measurements that have been and would be expected to maintain. (Tr. (Wilken) at 358:23-359:10.). She explained that the COA typically includes both measured attributes and the method used for such measurements. (*Id.*).

> Q. . . . [C]an you explain to the Court in general what a Certificate of Analysis is?
>
> A. A Certificate of Analysis is usually accompanied with the product, as we see here, and what that does is tell the consumer product attributes or qualities. So this may include, of course, the name of the product, the origin, the source, product

> number, as well as specifications. So these are the attributes of the product. In this case we have five different ones shown here. So it's telling the consumer what they should expect of the product that they receive.

(*Id.* at 358:24-359:10.).

Dr. Wilken also noted that the COA is "important" because it "would be the first information I check receiving a product such as this." (*Id.* at 359: 11-14.). She explained that she would use the COA "for preparation of solutions or to evaluate the suitability of a particular compound or molecule for a particular application, and so we would rely on this data to accurately represent what the product is and how those parameters have been determined." (*Id.* at 359:16-20.).

F. SDS-PAGE

As noted in the peer-reviewed literature Ventria presented, SDS-PAGE (sodium dodecyl sulfate polyacrylamide gel electrophoresis) uses a detergent ("SDS") to disrupt non-covalent interactions within and between proteins and then separates proteins under an electric field based on molecular weight. (JX-0132.0009.). Dr. Wilken explained that the molecular weight of protein species in a sample can be determined by comparison to molecular weight markers that contain a set of proteins with known molecular weights, and relative amounts of protein species can be quantified based on band volume or "band intensity" based on protein staining. (Tr. (Wilken) at 347:1-10, 373:25-374:6, 375:2-6, 453:9-12; *see also* JX-0060.0006, 0007.).

Dr. Wilken confirmed that SDS-PAGE is one of the generally accepted methods of analyzing, characterizing, and quantifying certain product attributes (including aggregates) and is often included in COAs. (Tr. (Wilken) at 344:9-16, 346:11-17, 347:14-21; JX-0132.0009.). The peer-reviewed literature also confirms that the addition of a reducing agent to SDS for protein sample preparation (termed reducing SDS-PAGE) allows for discrimination between protein

aggregates formed by disulfide bonds (a type of covalent bond) and those formed by other non-reducible covalent interactions. (JX-01320009.).

Reducing SDS-PAGE Is an Appropriate Technique to Measure and Quantify Aggregated Albumin.

Healthgen's expert, Dr. DeFilippi, agreed that reducing SDS-PAGE is a "very common technique." (*See, e.g.*, Tr. (DeFilippi) at 856:7-8.). Nevertheless, Healthgen argued that reducing SDS-PAGE is not a suitable technique for quantifying aggregated albumin. Ventria presented compelling evidence to the contrary.

Specifically, and discussed in more detail below: (i) the '951 patent quantifies aggregates in multiple samples of rice-produced rHSA (i.e., Cellastim) using reducing SDS-PAGE and compares their percent aggregate values; (ii) the non-patent literature confirms reducing SDS-PAGE is a standard, recommended method to quantify and characterize aggregates; (iii) Healthgen relied on reducing SDS-PAGE in an effort to show invalidity and noninfringement; (iv) Dr. Wilken personally analyzed aggregates in rice-produced rHSA samples she ran under reducing SDS-PAGE conditions, which she testified can be readily quantified; (v) Healthgen acknowledged in customer communications and internal testing that reducing agents do not "drive up" the amount of monomeric albumin in a sample when compared with HPLC; and (vi) Healthgen quantified what it considered aggregated albumin using SDS-PAGE.

1. The '951 patent uses reducing SDS-PAGE to quantify aggregates in samples of rice-produced rHSA.

The '951 patent uses reducing SDS-PAGE to quantify and compare percentages of proteins and protein complexes in samples of rice-expressed rHSA. (*See* JX-0001 at 70:17-49 (describing the experimental preparation of rHSA samples, including rice-expressed rHSA, for analysis by reducing SDS-PAGE); *see also id.* at 70:22-23 ("The sample was mixed 1:1 with . . .

buffer . . . ***containing reducing agent***") (emphasis added); *id.* at 70:43-47 ("The percent of each contaminating protein in each band was calculated …".). The '951 patent then proceeds to describe, under a heading titled "Results & Discussion" (*id.* at 71:54), the results from the reducing SDS-PAGE experiments described at JX-0001 at 70:17-49. (*See id.* at 72:34-57.). Specifically, the '951 patent states:

> Visual inspection of the gel shows that the new process which meets more rigorous specifications is more consistent among the 3 lots tested. (FIG. 9B, lane 2, 3, 4 vs. lane 6, 7, 8). The banding pattern is significantly different among the three samples from the previous process as compared to the new process. ***Importantly, the new process samples have significantly less aggregates at around 250 KDa than the old process samples have. (Average greater than 2% for the old process, and average less than 1% for the new process)***.

(*Id.* at 72:46-53 (emphasis added).).

Setting aside the question of whether the aggregates identified at 250 kDa consist of individual albumin that satisfies the adopted construction of recombinant mammalian albumin, the '951 patent clearly discloses that reducing SDS-PAGE can and is used to quantify percent aggregates in numerous samples of rice-produced rHSA, including Ventria's DI product, Cellastim. (*Id.*). Dr. DeFilippi acknowledged under cross-examination that the '951 patent reports aggregate quantification by reducing SDS-PAGE. (Tr. (DeFilippi) at 1250:23-1251:4; *see also id.* at 1246:11-13 ("Q. The '951 patent does contain a description for testing of albumin with reducing SDS PAGE, doesn't it? A. Yes.").).

2. <u>Peer-reviewed literature confirms reducing SDS-PAGE is a suitable method for quantifying aggregates</u>.

The peer-reviewed literature of record discloses that reducing SDS-PAGE is a suitable, recommended, analytical technique for quantifying aggregated albumin. For example, den Engelsman (JX-0132) concludes, after reviewing many analytical techniques in detail:

> SEC and ***-PAGE//CE-SDS are methods that are robust enough for reproducible quantification of aggregates and that allow routine use with sufficient sample throughput*** . . . Below we list ***recommendations*** regarding the assessment of protein aggregates in biotech product development: ***Employ robust, quantifiable methods for QC testing***: SEC (quantification of covalent and non-covalent aggregates, but not low-affinity aggregates and larger aggregates); ***SDS-PAGE and/or CE-SDS*** (covalent aggregates).

(JX-0132.0013 (emphases added); *see also id.* at 0005, 0007, 0009 (describing both reducing and nonreducing SDS-PAGE as suitable for quantification of aggregates); JX-0060.0006; Tr. (Wilkens) at 312:2-13, 347:14-21, 351:2-352:1.).

After describing in detail the advantages and disadvantages of numerous techniques for quantification and analysis of aggregates, the authors concluded that "***no single method*** covers the analysis of all aspects of aggregates. As ***each method covers different aggregate characteristics***, the results obtained with a particular method are ***strictly linked to that method***." (JX-0132.0012 (emphases added).).

Healthgen's preferred peer-reviewed literature on the subject, Mahler (JX-0060), arrived at similar conclusions to den Engelsman. (*See, e.g.*, JX-0060.0001 at Abstract ("A major challenge for the analysis of protein aggregates is that no single analytical method exists to cover the entire size range or type of aggregates which may appear. Each analytical method not only shows its specific advantages but also has its limitations."); JX-0132.0004-6; *see also* JX-0060.0018; Tr. (Wilken) at 352:25-353:9, 458:6-11; *see also* JX-0060.0007-8 (discussing reducing SDSPAGE and aggregate quantification using same); JX-0060.0006 at Table 1 (table listing "Frequently Used Methods for Analysis of Protein Aggregation" with "SDS-PAGE" categorized as a "Quantification and/or size estimation" method).).

Despite this guidance from the peer-reviewed literature, Healthgen contended that only certain techniques are appropriate to measure aggregates in this Investigation, namely SEC HPLC. (Tr. (DeFilippi) at 1180:24-1181:10, 1182:14-18; *see also* Tr. at 1382:16-24, 1386:7-16,

1391:5-12, 1395:6-11, 1396:21-1397:3 (closing).). However, as Ventria noted, Dr. DeFilippi acknowledged that the asserted claims do not require any particular technique for determining if the less than 2% aggregated albumin limitation is met, and that there are many techniques that could quantify aggregated albumin. (Tr. (DeFilippi) at 962:25-963:25 ("I don't see any . . . mention of a method or a location where they're performing the method"), 784:16-785:5.). Moreover, the peer-reviewed literature recognizes unequivocally that SEC HPLC has its own limitations when it comes to quantifying aggregates. (*See, e.g.*, JX-0132.0013 ("SEC (quantification of covalent and non-covalent aggregates, ***but not low-affinity aggregates and larger aggregates***") (emphasis added); *id.* at 0008 ("elution position (relative to molecular weight standards) may be used to estimate molecular weight. However, ***any such estimate is an approximation***, as most molecules tend to not be spherical . . . ." (emphasis added).). den Engelsman also states:

> ***There is an upper limit to the size of aggregate detectable by SEC, because larger aggregates can be filtered out by frits in the system or by the column itself***. As a consequence, ***large material (large protein aggregates) may disappear and be overlooked in the analysis***. They also build up on the top of the column and gradually degrade its performance, seen as broadened peaks, poorer resolution and decreased yields (smaller peaks). ***Another form of aggregate that may be missed is that formed by very low affinity intermolecular association***, as these may dissociate into monomers following a change in conditions from those of the sample to those experienced during chromatography[.]

JX-0132.0009 (emphases added); *see also* JX-0060.0006-7 (discussing advantages and disadvantages of SEC HLPC); JX-0060.0018 ("As ***all methods discussed have their own advantages and disadvantages***, there is ***no 'gold standard method'*** for the analysis of protein aggregates in its complexity, though SEC is still considered the most widely used ***despite the limitations discussed***.") (emphases added).).

In sum, the peer-reviewed literature confirms reducing SDS-PAGE can be, and is recommended for, aggregate quantification, and states unequivocally that there is no single "gold standard method" for aggregate quantification. (*See* Tr. (Wilken) at 344:19-24 ("There are -- as

we mentioned, there's advantages and disadvantages to each [method] . . . and there's various aspects that you would look at regarding these methods.").).

3. Dr. DeFilippi relied on reducing SDS-PAGE results to argue both invalidity and non-infringement.

Healthgen's argument that reducing SDS-PAGE is not a valid technique to quantify aggregated albumin is undermined by Dr. DeFilippi's: (i) usage and reliance on Van Urk in his invalidity analysis; and (ii) reliance on reducing SDS-PAGE results in support of his non-infringement arguments.

During the Hearing, Dr. DeFilippi confirmed that paragraph 150 of his opening report indicates Van Urk evaluated its rHSA using SDS-PAGE with a reducing agent. (Tr. (DeFilippi) at 962:21-24.). Additionally, Dr. Defilippi admitted during cross-examination that he was willing to accept Van Urk's use of reducing SDS-PAGE in arriving at some of his opinions. (*Id.* at 959:6-960:3. ("Q. But, in your opinion, in your report -- and by report I mean your opening report, the one on validity, your first report in this case -- the very first line of the paragraph in your report directed toward this, paragraph 150, says that Van Urk evaluated its rHSA using SDS PAGE with a reducing agent, right? That's what it says. A. I'll accept that comment.").). He also provided the following testimony:

> Q. Okay. And do you recall at your deposition under questioning from Ms. Bhattacharyya, you stated that your reliance on reducing SDS PAGE for invalidity in light of your opinion on infringement made your opinion on invalidity a stretch? Do you recall that?
>
> * * *
>
> MR. HENEGHAN: Well, let's play it from the deposition.
>
> * * *
>
> (Video clip played)

> Q. . . . does not identify any other assay for determining the level of aggregation; is that correct?
>
> A. That is correct.
>
> Q. So if there is no other assay to rely upon, I mean, do you really believe that this is an invalidating reference given your positions on infringement?
>
> A. I'd have to go back and look through the patent, would be my honest answer there. As it stands alone, if this is the only proof, then ***that might be a stretch***.
>
> (End of video clip)

(*Id.* at 960:24-962:5 (emphasis added).).

With respect to non-infringement, Dr. DeFilippi relied on data from reducing SDS-PAGE to quantify what he believes is the amount of aggregated albumin in the Accused Products. (*See, e.g.*, Tr. (DeFilippi) at 1169:16-1170:15.).

Such cherry-picking in order to satisfy the argument of the moment is further reason to give Dr. DeFilippi's testimony little weight on this topic.

4. <u>Dr. Wilken personally analyzed aggregates using reducing SDS-PAGE to characterize rice-produced rHSA</u>.

Dr. Wilken is the only expert in this case to perform reducing SDS-PAGE on rice-produced rHSA samples and she testified that she does so routinely in her research.

> Q. And in your work at the university, have you ever used SDS PAGE to measure impurities, such as aggregates, in samples of purified albumin?
>
> A. We use SDS PAGE. It's a standard method. Throughout my under -- or graduate work at Texas A&M, I have many -- probably hundreds of gels, I would say, that I ran. We use those to follow each step of the downstream processing. It's an easy way to assess the performance of both extraction and purification steps. And we – the research has continued at Kansas state. And so that would be a common technique that my researchers use to evaluate our research.

(Tr. (Wilken) at 312:2-13.).

Furthermore, she repeatedly testified that reducing SDS-PAGE is a common technique

that can be used to quantify aggregated albumin samples of rice-produced rHSA. (*See, e.g.*, *id.* at 344:6-24 ("Q. . . . Can you tell us, generally, about techniques that measure protein aggregation? A. So there are numerous different methods that may vary depending on, one, separation technique, so, for example, based on molecular weight, and also based on the detection principle. Q. And is SDS PAGE one of those techniques? A. Yes."), 346:11-17 (discussing den Engelsman's Table III, which lists SDS-PAGE as a technique used to analyze protein aggregates), 347:1-21 (confirming that den Engelman characterizes SDS-PAGE as a suitable technique for the detection and characterization of protein aggregates), 349:14-350:19, 351:6-352:1, 353:10-24.).

5. [redacted] (JX-0062C.0001-2.). In response, [redacted] (*Id.* at 0002.). Figure 2, below, is a copy of a part of the attachment (JX-0063C) to that email thread.

(JX-0063C.0001.).

As Ventria pointed out, in this Healthgen document,

s. (Tr. (Wilken) at 410:8-412:6.). For example,

(*Id.*; *see also* CX-0353C (showing same and confirmed to be

, CX-0883 at ¶ 9.).

Although it is unclear whether Healthgen is referring to

[redacted],[19] [redacted]

[redacted]

[redacted]

(Tr. (DeFilippi) at 854:17-856:3, 1188:7-18, 1201:14-22, 1204:19-15.).[20]

Healthgen argued that its SEC HPLC testing of certain Ventria DI Products showed monomer content being artificially "driven up" in these samples when compared with SDS-PAGE. (Tr. (DeFilippi) at 1188:7-18, 1201:14-22.). However, Dr. Wilken explained that Healthgen's SEC HPLC results were unreliable because, *inter alia*, "there were no standards reported" and as a result "we don't have a particular retention time to link the molecular weight to those results." (Tr. (Wilken) at 542:23-543:21, 465:7-16.). Healthgen's peer-reviewed literature, Mahler, confirms that the lack of standards in Healthgen's SEC HPLC testing could render the data meaningless. (JX-0060.0006 ("***Well characterized, water-soluble and globular proteins are used as calibration standards, which may differ in their elution properties in comparison with the protein of interest***. It has been reported that basing the molecular weight

---

[19] [redacted] (CX-0178C.0004 (emphasis added); *see also* JX-0008.0002 (same).).

[20] Dr. DeFilippi relied on testimony from Ventria's Vice President of Product Development, Dr. Randall Alfano, as allegedly supporting his position on reducing SDS-PAGE. (*See, e.g.*, Tr. (DeFilippi) at 1184:4-1185:20; RX-0007C (Alfano Dep. Tr.) at 10:1-9.). However, Dr. Alfano testified that he did not remember what DTT was, did not know "whether [Ventria] uses an agent, such as heat [or a reducing agent] when performing SDS-PAGE," and was "not familiar with the [SDS-PAGE] methodology at that level." (RX-0007C (Alfano Dep. Tr.) at 31:2-9.). He also testified he was not the right person at Ventria to address the specifics of such testing, and Healthgen counsel's line of questioning confirms he was not "identified [by Ventria] as the person that we could ask about assays." (*Id.* at 31:12-16.). Healthgen failed to mention that Dr. Alfano testified that "SDS-PAGE . . . is still a very viable method for determining . . . aggregation." (*Id.* at 87:19-88:8; *see also id.* at 88:14-89:11, 93:13-94:3 (confirming that SDS-PAGE is "an accurate method of determining the level of aggregation in albumin even if a reducing agent is used in the assay").).

solely on the elution volume has resulted in ***incorrectly identifying peaks as dimers***.") (emphases added); *see also* JX-0132.0008 ("elution position (***relative to molecular weight standards***) may be used to estimate molecular weight") (emphasis added).).

6. Healthgen's internal testing documents quantify what it considers aggregated albumin using reducing SDS-PAGE.

During his direct examination, Dr. DeFilippi relied on RX-0366C, a Testing Record of Healthgen's rHSA product, which Healthgen's counsel confirmed depicts reducing SDS-PAGE results. (Tr. at 1384:22-1385:3 ("And on slide 3 we have another Certificate of Analysis [from RX-0366C], and this is from Healthgen as well. And it shows that when Healthgen uses ***reducing SDS-PAGE*** . . . ." (emphasis added) (closing).). [redacted] (RX-0366C.0012.). Specifically, as shown in the blown-up screen shot of [redacted]

(RX-0366C.0012.).

[redacted] (*Id.* (emphasis added).). Dr. DeFilippi testified during direct examination that [redacted] (Tr. (DeFilippi) at 1270:10-17.). However, he acknowledged on cross-examination [redacted] (*Id.* at 1270:23-1271:9.). Contrary to Dr. DeFilippi's assertions, [redacted]

V. THE ASSERTED PATENT

A. Overview of the Asserted Patent

U.S. Patent No. 10,618,951 ("the '951 patent"), titled "Cell Culture Media Containing Combinations of Proteins," was filed on June 21, 2016, as U.S. Patent Application Serial No. 15/188,478 ("the '478 application"). (JX-0001 at (21), (22), (54).). The '478 application issued as the '951 patent on April 14, 2020, and names Steven Clyde Pettit, Mary Ann Michelle Fernandez Santos, and Ning Huang as the inventors. (*Id.* at (10), (45), (72).). The '478 application is a continuation of U.S. Patent Application Serial No. 12/708,462, filed on February 18, 2020, which has since been abandoned. (*Id.* at (63).). The '951 patent claims priority to U.S. Provisional Application Serial No. 61/154,204, filed on February 20, 2009. (*Id.* at (60).).

The '951 patent relates to compositions for use in cell culture. (*See, e.g., id.* at Abstract.). "Cell culture" is the growth of cells in an artificial environment (e.g., petri dish) under conditions that promote cell survival and/or proliferation. (Doc. ID No. 741045 (Joint Tech. Stip.) at 1 (Apr. 27, 2021).). One component of the artificial environment is the cell culture media, which

is a composition that contains nutrients (e.g., vitamins, carbohydrates, minerals, amino acids, etc.) the cells need to stay alive and grow in the culture. (*Id.* at 2.). Additionally, the cell culture media contains various compounds that maintain other important conditions of the culture, such as pH and salt balance (osmolality). (*Id.*).

Complete media contains all the essential components needed to culture a particular cell type. (*Id.*). A cell culture media *supplement* is designed to be combined with other media components or with a base media formulation for a particular cell type. (*Id.*). Different types of cells have different media requirements. (*Id.*). Moreover, cells can be grown in different types of media depending upon the purpose of the culture. (*Id.*).

Blood serum and serum-derived albumin have been used as components of cell culture media. (*Id.*). Albumin is a protein that is naturally present in animal serum, including human serum. Serum derived from animals is an important source of cell growth and adhesion factors, hormones, lipids, and minerals for cell culture. (Joint Tech. Stip. at 2.). Although albumin derived from animal serum can be used in cell culture, there are concerns regarding potential contamination as well as ethical concerns. (*See id.*). As a result, alternative cell culture media have been developed that do not rely on serum or animal-derived components. Recombinant albumin has been used in cell culture media instead of native proteins and animal-derived components. (*Id.* at 2-3.).

The ’951 patent concerns, in part, recombinant proteins such as recombinant albumin. (*See, e.g.*, JX-0001 at cl. 1.). Recombinant technology involves the introduction of foreign genetic material (transgenes) into a host cell, where the foreign genetic material can be used to produce proteins that would not normally be present in that host cell (e.g., recombinant albumin). (Joint Tech. Stip. at 3.). By using recombinant technology, the DNA of certain cells can be

engineered to include portions of DNA that do not naturally occur in such cells. (*Id.*). For instance, the DNA of a plant cell can be engineered to include foreign DNA. (*Id.*). When expressed by the plant cell's native machinery, this foreign DNA can produce a recombinant protein that the cell would not normally produce. (*Id.*).

B. The Asserted Claims of the Asserted Patent

The asserted claims of the '951 patent generally relate to media supplements or complete media compositions for the growth of cells in cell culture. (*See, e.g.*, JX-0001 at 2:66-3:3.). The recited media supplements or complete media compositions comprise a recombinant mammalian albumin that is produced in a transgenic plant. (*See id.* at cl. 1.). All the claims require that the recombinant mammalian albumin has less than 1 EU (endotoxin unit) of endotoxin per mg of albumin. (*Id.*). As discussed above in Section IV.D, endotoxins are toxins that can associate with cell culture components and cause cell death. (*See id.* at 30:47-53.). The claims also require that the recombinant mammalian albumin has less than 2% aggregated albumin (i.e., non-monomeric albumin) by weight. (*Id.* at cl. 1.).

Additionally, the asserted dependent claims recite, *inter alia*, the inclusion of "at least 0.01% w/w of a heat shock protein" (claim 2), and specifically "a rice heat shock protein" (claim 3). The asserted dependent claims also specify, *inter alia*, that the recombinant mammalian albumin is "a recombinant human serum albumin" (claim 11), and that the transgenic plant is "a transgenic grain" (claim 12), or more specifically, "transgenic rice" (claim 13).

As noted above, at issue in this Investigation are claims 1 and 11-13 of the '951 patent. Independent claim 1, as well as the dependent claims, are reproduced below.[21]

[21] The Parties agreed upon the meaning of the italicized claim terms, which were adopted in the *Markman*

1. *A cell culture media supplement or complete media composition for improving the growth of a cell in cell culture* comprising: a recombinant mammalian albumin wherein said albumin is: i) produced in a transgenic plant; ii) has less than 1 EU of endotoxin/mg of albumin; and iii) less than 2% *aggregated albumin*.

11. The composition of claim 1, wherein said albumin is recombinant human serum albumin.

12. The composition of claim 1, wherein said transgenic plant is a transgenic grain.

13. The composition of claim 12, wherein the transgenic grain is transgenic rice.

(JX-0001 at cls. 1, 11-13.).

VI. THE PRODUCTS AT ISSUE

A. Healthgen's Accused Products

Ventria alleged that Healthgen's rHSA product sold under the brand name OsrHSA infringes claims 1 and 11-13 of the '951 patent. (CBr. at 14-15.). Healthgen's OsrHSA is supplied in both: (i) a powder "cell culture grade" rHSA product; and (ii) a powder and a liquid "clinical grade" rHSA product (collectively, "Accused Products" or "OsrHSA Products"). (*See, e.g.*, JX-0021C.0001-4; CX-0053C.0005; CX-0924.0001-3.). Healthgen refers to the "OsrHSA clinical grade" rHSA product by its internal catalog numbers HYC001C01, HYC001C02, and HYC002C01 (clinical grade lyophilized powder). (*See, e.g.*, CX-0923; CX-0924.0003; JX-0032C.0001-03.). Healthgen refers to the "OsrHSA cell culture grade" rHSA product by its internal catalog numbers HYC002M01, HYC002M02, and HYC002M03. (*See, e.g.*, CX-0924.0001-3; JX-0032C.0004-6; CX-0053C.0007.).

B. Ventria's DI Products

Ventria asserted that the following Ventria products practice one or more claims of the

Order. The Parties disputed the meaning of the underlined claim terms. The disputed terms were analyzed and construed in the *Markman* Order.

Asserted Patent: (i) Cellastim® S ("Cellastim"); (ii) Exbumin® ("Exbumin"); (iii) Optibumin® ("Optibumin"); (iv) OptiPEAK® ("OptiPEAK); (v) OptiVERO® ("OptiVERO"); and (vi) ITSE™+A ("ITSE+A," and with Cellastim, Exbumin, Optibumin, OptiPEAK, and OptiVERO, "DI Products"). (*See, e.g.*, CPBr. at 16; CBr. at 15-16; Compl. at ¶¶ 81-84.).

Ventria described each of the DI Products as follows:

> Cellastim is completely blood-free, rice-expressed rHSA product and is optimized to enhance performance in animal-free cell culture media. Hr'g Tr. 181:20-182:2, 326:17-327:4; JX-0077; JX-0072; JX-0120C-0002, -0005; CDX-0001C:27.
>
> Exbumin is highly purified, is completely blood-free, rice-expressed rHSA product that has passed regulatory approval in the U.S. and Europe as a final-formulation excipient for therapeutic applications. It is one of the few excipients available to improve viral stability for cell culture manufacturing of vaccines and gene therapies. Hr'g Tr. at 166:1-13, 184:6-17; JX-0120C-0002, -0005; CX-0663; CX-0542; CDX-0001C:27.
>
> Optibumin is a liquid product with the highest purity rHSA available on the market. With very low levels of albumin aggregates and lipids, and an exceptionally high concentration of free-thiol/Cys-34 mercapto-albumin, Optibumin is optimized for the most demanding of applications, including cell culture applications. Hr'g Tr. 185:21-186:20, 357:19-358:1; CX-0548; JX-0073; JX-0120C-0002, -0005; CDX-0001C:28.
>
> OptiPEAK HEK293t is provided as a 2-part kit to make a complete cell culture media formulation. Hr'g Tr. 191:17-192:5, 368:3-15. It contains rHSA, and more specifically, [redacted]. Hr'g Tr. 192:3-5. The protein supplement is formulated to be combined with the base media provided in the kit to prepare a complete cell culture media that has been optimized for culturing adherent HEK 293t cells. Hr'g Tr. 191:17-192:5; JX-0120C-0002, -0008; CDX-0001C:31.
>
> OptiPEAK T Lymphocyte is a 2-part kit containing a 100 mL frozen concentrated protein supplement that contains rHSA and more specifically, [redacted]. Hr'g Tr. 192:3-5, 368:3-15. The protein supplement is formulated to be combined with the base media provided in the kit to prepare a complete cell culture media that has been optimized for chemically defined expansion of human T lymphocytes. CX-0545; JX-0120C-0002, -0008; CDX-0001C:31.
>
> OptiVERO is also provided as a 2-part kit to make a complete cell culture media formulation, which includes a concentrated frozen media and protein supplement

with a base media. It contains rHSA, and more specifically, [redacted] Hr'g Tr. 192:6-15, 368:3-15. The protein supplement is formulated to be combined with the base media provided in the kit to prepare a complete cell culture media that has been optimized for culturing VERO cells for virus production. Hr'g Tr. 192:6-15; JX-0120C-0002, -0008; CDX-0001C:31.

ITSE™ + A (also referred to as "ITSE + Albumin Animal-Free") is a cell culture media supplement that contains rHSA, and more specifically [redacted] Hr'g Tr. 192:16-193:1, 368:3-15; JX-0120C-0002, -0007; CDX-0001C:31.

(CBr. at 16-17; *see also* CPBr. at 16-17.).

VII. PERSON OF ORDINARY SKILL IN THE ART

A. Legal Standard

A hypothetical person is a person of ordinary skill and "ordinary creativity." *KSB Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 420 (2007). "Factors that may be considered in determining [the] level of ordinary skill in the art include: (1) the educational level of the inventor[s]; (2) type of problems encountered in the art; (3) prior art solutions to the problems; (4) rapidity with which inventions are made; (5) sophistication of the technology; and (6) educational level of active workers in the field." *Envtl. Designs Ltd. v. Union Oil Co. of California*, 713 F.2d 693, 696-97 (Fed. Cir. 1983) (citations omitted). "These factors are not exhaustive but merely a guide to determining the level of ordinary skill in the art." *Daiichi Sankyo Co. v. Apotex, Inc.*, 501 F.3d 1254, 1256 (Fed. Cir. 2007).). The hypothetical person of skill is also separately presumed to have knowledge of all the relevant prior art in the field. *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 693, 697 (Fed. Cir. 1983).

B. Definition of a Person of Ordinary Skill in the Art

Ventria proposed that at the time the patent was filed, a person of ordinary skill in the art would have had "a Ph.D. in chemistry, biochemistry, biological and agricultural engineering, or chemical engineering, with at least two years of experience involving production and/or

purification of recombinant proteins expressed in plants, such as a recombinant mammalian albumin and/or experience with compositions suitable for use in cell culture media." (COMBr. at 3-4 (citation omitted).).

Healthgen contended that a person of ordinary skill in the art would "possess a Ph.D. in chemistry, biochemistry, or chemical engineering, with at least two years of experience involving production and/or purification of proteins such as a recombinant HSA and/or experience with compositions suitable for use in cell culture media." (ROMBr., Ex. A (DeFilippi Decl.) at ¶ 18.).

Staff argued that one of ordinary skill in the art would have "a Ph.D. in chemistry, biochemistry, biological and agricultural engineering, or chemical engineering, with at least two years of experience involving production and/or purification of recombinant proteins and/or experience with compositions suitable for use in cell culture media." (SOMBr. at 6.).

Because the Parties' definitions were similar, each requiring a Ph.D. in biochemistry and/or chemical fields, and at least two years of experience in similar areas, all proposals were found to be appropriate for a person of ordinary skill in the art. (*Markman* Order at 11.). Thus, the differences among the proposed definitions were not dispositive and had little, if any, effect on the claim construction analysis set forth in the *Markman* Order.

VIII. DIRECT INFRINGEMENT[22]

A. Legal Standard: Literal Infringement

"Determination of infringement is a two-step process which consists of determining the

[22] Ventria did not allege infringement under the doctrine of equivalents ("DOE") or indirect infringement in its Pre-Hearing or Post-Hearing Briefs. (*See* CPBr. at 20-56; CBr. at 38-68.). Thus, any argument Ventria might have made with respect to these issues has been deemed abandoned, withdrawn, or waived under Ground Rules 7.2. and/or 10.1.

scope of the asserted claim (claim construction) and then comparing the accused product . . . to the claim as construed." *Certain Sucralose, Sweeteners Containing Sucralose, and Related Intermediate Compounds Thereof*, Inv. No. 337-TA-604, Comm'n Opinion at 36 (U.S.I.T.C., April 28, 2009) (citing *Litton Sys., Inc. v. Honeywell, Inc*., 140 F.3d 1449, 1454 (Fed. Cir. 1998)).

An accused device literally infringes a patent claim if it contains each limitation recited in the claim exactly. *Litton*, 140 F.3d at 1454. Each patent claim element or limitation is considered material and essential. *London v. Carson Pirie Scott & Co.*, 946 F.2d 1534, 1538 (Fed. Cir. 1991). In a Section 337 investigation, the complainant bears the burden of proving infringement of the asserted patent claims by a preponderance of the evidence. *Enercon GmbH v. Int'l Trade Comm'n,* 151 F.3d 1376, 1384 (Fed. Cir. 1998). If any claim limitation is absent, there is no literal infringement of that claim as a matter of law. *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1247 (Fed. Cir. 2000).

B. The Accused Products Practice Claim 1 of the '951 Patent

1. "A cell culture media supplement or complete media composition for improving the growth of a cell in cell culture comprising"

Healthgen admitted [redacted] Specifically, in response to Complainant's Request for Admission No. 49 (CX-1017C; "RFAs"), which states, [redacted] Healthgen replied in relevant part, [redacted] (CX-1017C at RFA No. 49.). [redacted] (*See, e.g.*, JX-0032C.0004-6; JX-0021C.0002, 0004.). As such, Healthgen's cell culture grade OsrHSA

Products are cell culture medium supplements as claimed. Healthgen's aforementioned characterization of OsrHSA applies equally to the "clinical" and "cell culture" grades of the Accused Products, as a [redacted]. (JX-0021C.0002-3.). JX-0021C further describes the [redacted] (*Id.* at JX-0021C.0002.). JX-0021C also describes the [redacted] (JX-0021C.0003.). Dr. DeFilippi confirmed the foregoing during cross-examination. (Tr. (DeFilippi) at 1245:3-6 ("Q. So both Healthgen's products and the Ventria products that are at issue in this investigation are cell culture media supplements, right? A. Yes."); *see also* RDX-0002C.3.). Therefore, the Accused Products are cell culture medium supplements.

For the foregoing reasons, Ventria has proven by a preponderance of evidence that the Accused Products meet the preamble of claim 1 of the '951 patent.

2. "a recombinant mammalian albumin"

Healthgen admitted in [redacted]. Specifically, in response to RFA No. 46, which states, [redacted] Healthgen replied in relevant part, [redacted] (*Id.*). Similarly, in response to RFA No. 47, which states, [redacted] Healthgen replied in relevant part, [redacted] (CX-1017C at RFA Nos. 46-47.).

Healthgen also confirmed that [redacted] (*Id.* at RFA No. 51.). Recombinant human serum albumin is a species (i.e., a specific form) of recombinant mammalian albumin (*see* JX-0001 at cl. 11), and thus the Accused Products, by Healthgen's own admission, [redacted] which Dr. DeFilippi confirmed during cross-examination. (*See, e.g.*, JX-0032C; Tr. (DeFilippi) at 1245:23-1246:1 ("Q. You agree that both Healthgen's products and Ventria's DI products comprise recombinant human serum albumin, right? A. That is right."); *see also* RDX-0002C.0003.). Therefore, taking into account Healthgen's admissions, Dr. DeFilippi's testimony, and a preponderance of the documentary evidence, the Accused Products comprise a "recombinant mammalian albumin."

For these reasons, Ventria has proven by a preponderance of evidence that the Accused Products meet this limitation of claim 1 of the '951 patent.

3. "wherein said albumin is . . . produced in a transgenic plant"

Healthgen admitted that the [redacted]. Specifically, in response to Complainant's Request for Admission No. 47, which states, [redacted] Healthgen replied in relevant part, [redacted] (CX-1017C at No. 47; *see also* JX-0021C; JX-0032C; CX-0923; CX-0924.). Rice host cells do not naturally produce/express recombinant human serum albumin, and thus must be genetically engineered to produce/express it. (Tr. (Wilken) at 321:9-322:11.). Such genetic engineering results in a transgenic plant. (*Id.*). Thus, by Healthgen's own admission, the Accused Products comprise

recombinant human serum albumin that is "produced in a transgenic plant." Dr. DeFilippi confirmed the foregoing during cross-examination. (Tr. (DeFilippi) at 1244:19-22 ("Q. You agree that Healthgen products and Ventria's DI products are produced in a transgenic rice seed, right? A. This is right."); *see also* RDX-0002C.0003.). Therefore, taking into account Healthgen's admissions, Dr. DeFilippi's testimony, and a preponderance of the documentary evidence, the Accused Products are "produced in a transgenic plant."

Accordingly, Ventria has proven by a preponderance of evidence that the Accused Products meet this limitation of claim 1 of the '951 patent.

4. "wherein said albumin . . . has less than 1 EU of endotoxin/mg of albumin"

Healthgen admitted that the [redacted] Specifically, in response to Complainant's Request for Admission No. 48, which states, [redacted] Healthgen replied in relevant part, [redacted] (CX-1017C at No. 48; *see also* JX-0021C; JX-0032C; CX-0923; CX-0924.). Therefore, taking into account Healthgen's admissions and a preponderance of the documentary evidence, the Accused Products have "less than 1 EU of endotoxin/mg of albumin."

For the reasons discussed above, Ventria has proven by a preponderance of evidence that the Accused Products meet this limitation of claim 1 of the '951 patent.

5. "wherein said albumin . . . has . . . less than 2% aggregated albumin"

a) [redacted]

Healthgen's manufacturing and purification process for the Accused Products is shown in

the following flow chart:

Figure 4: Healthgen's Purification Process

(JX-0010C (annotated, copied from CBr. at 42).).

The flow chart depicts . (*Id.*; *see also* CDX-0001.0042.). In a 2018 peer-reviewed publication authored by Healthgen's CEO, Dr. Daichang Yang, and Healthgen's Vice President of Production, Mr. Bo Shi,[23] the authors described the steps in the OsrHSA purification process as follows: "The main purpose of the first chromatography step is to enrich the target protein and simultaneously remove certain HCPs. ***The subsequent purification steps are mainly performed to remove high-molecular-mass HCPs, polymers, and degraded fragments of***

[23] Mr. Bo Shi, Healthgen's Vice President of Operations, was designated as Healthgen's corporate representative to testify about, *inter alia*, the details of the manufacturing, production, purification, testing, and assembly of the Accused Products. (*See* Tr. (DeFilippi) at 1289:5-23, 1289:24-1290:1; *see also* CX-1081C (Shi Dep. Tr.) at 21:11-15, 23:3-18; 24:9-16, 25:2-11, 142:7-143:5.).

OsrHSA."[24] (JX-0023.0014 (emphasis added).). Thus, Healthgen purifies its OsrHSA in part to remove what Healthgen characterizes as aggregated albumin. Contrary to Dr. DeFilippi's attempts during the Hearing to argue that [redacted] (*see* RDX-0002C.0026), there is no evidence of record that this is the case. The only information Dr. DeFilippi cited in support of his statements that [redacted] (*See* RDX-0002C.0026.).

Mr. Shi, Healthgen's Vice President of Operations and Healthgen's corporate representative designated to testify regarding, *inter alia*, the details of the manufacturing, production, purification, testing, and assembly of the Accused Products, testified and repeatedly agreed that Healthgen's [redacted] (CX-1081C (Shi Dep. Tr.) at 183:5-196:21; *see also* CDX-0001.0043; JX-0047C.0094-95.). Mr. Shi also testified that JX-0047C (marked as CXD-0057 at his deposition) is a [redacted]. (CX-1081C (Shi Dep. Tr.) at 186:3-19.).

[24] HCP is an acronym for "host cell protein." (*See* JX-0023.0004.).

(JX-0047C.0094-95 (annotated); *see also* CX-1081C (Shi Dep. Tr.) at 183:5-196:21; Tr. (Wilken) at 398:6-402:14; CDX-0001.0043-44.).

(JX-0047C.0094-95.). (*Id.*). Mr. Shi testified that (CX-1081C (Shi Dep. Tr.) at 183:5-196:2; JX-0047C.0094-95.).

Dr. DeFilippi testified that he did not review any testimony from Mr. Shi regarding, *inter alia*, the details of the manufacturing, production, purification, testing, and assembly of the Accused Products. (Tr. (DeFilippi) at 1289:5-1291:8.). Nevertheless, Dr. DeFilippi argued

during the Hearing that Dr. Wilken had "confused" Healthgen's [redacted]. (*See* RDX-0002C.0023-24.). However, Dr. DeFilippi admitted that his rebuttal report characterized and referred to Healthgen's [redacted][25] (Tr. (DeFilippi) at 1288:16-25 ("Q. . . . Do you recall in paragraph 71 of your rebuttal report referring to Healthgen's [redacted].). It appears that he did not believe Healthgen's [redacted] was something different from an [redacted] during expert discovery. Thus, his direct testimony on the issue during the Hearing is without merit.

b) Healthgen's OsrHSA "Clinical Grade" Has Less Than 2% Aggregated Albumin

i. Healthgen's Certificates of Analysis Confirm OsrHSA Clinical Grade Has Less than 2% Aggregated Albumin

Ventria presented evidence establishing that Healthgen's clinical grade OsrHSA has less than 2% aggregated albumin. For example, CX-0450, a Healthgen COA for its OsrHSA clinical grade, provides a detailed breakdown of the characteristics of OsrHSA clinical grade. As shown in the image below, the certificate COA is for product code HY001C02, which refers to Healthgen's clinical grade product (*see, e.g.*, CX-0923.0001), for a lot manufactured September 14, 2020, which was analyzed on September 15, 2020, and which has an expiration date of September 13, 2024.

[25] Notably, there is no [redacted] listed on JX-0010C, the only document presented during the Hearing that depicts Healthgen's purification and manufacturing process for the Accused Products.

(CX-0450.0001; JX-0032C.0001 (same); CDX-0001.0047; *see also* JX-0015C.0001-2.).

Page two of CX-0450, shown in the annotated image below, unequivocally confirms that Healthgen's OsrHSA clinical grade has less than 2% aggregated albumin as measured by SEC HPLC.

(CX-0450.0002 (annotated); JX-0032C:0002 (same); Tr. (DeFilippi) at 1277:10-25 (Dr. DeFilippi confirming same); *see also* JX-0015C.0001-2 .

As shown above in Figure 7, SEC HPLC confirms Healthgen's OsrHSA clinical grade is 98.9% monomeric rHSA. (CX-0450.0002.). CX-0450.0002 demonstrates that the maximum amount of aggregated albumin in Healthgen's OsrHSA clinical grade is only 1.1% (i.e., 0.3% polymer plus 0.8 percent dimer), which is well below the 2% threshold of claim 1 of the '951 patent.[26] (*Id.*). Dr. DeFilippi acknowledged that SEC HPLC is a reliable technique to quantify aggregated albumin, which is the same method Healthgen used in CX-0450 to test the aggregated albumin content in OsrHSA clinical grade. (Tr. (DeFilippi) at 1190:16-22; RDX-0002C.0039; *see also* CX-0450.0002.).

In sum, Ventria looked to Healthgen's SEC HPLC data for their OsrHSA clinical grade, which confirmed that the product has less than 2% aggregated albumin. The foregoing evidence establishes that OsrHSA clinical grade has less than 2% aggregated albumin. *C R Bard Inc. v. AngioDynamics, Inc.*, 979 F.3d 1372, 1379 (Fed. Cir. 2020) ("Bard was entitled to rely on AngioDynamics's representations to its customers and to the FDA that the Xcela port [exhibited properties] required by the claims . . . AngioDynamics's statements regarding the capabilities of its own product constituted substantial evidence of those capabilities."); *see also C. & A. Potts & Co. v. Creager*, 155 U.S. 597, 610 (1895) ("Defendants, in their trade circular advertising their own machine, state [its machine infringes Plaintiff's patent] . . . This is a frank and apparently a

[26] CX-0450 (which also begins with bates number) was produced by Healthgen customer, (CX-0885.0008.). In other words, CX-0450 is not merely a Healthgen internal testing document, but a document that Healthgen provides its U.S. customers to represent the characteristics of its OsrHSA clinical grade product.

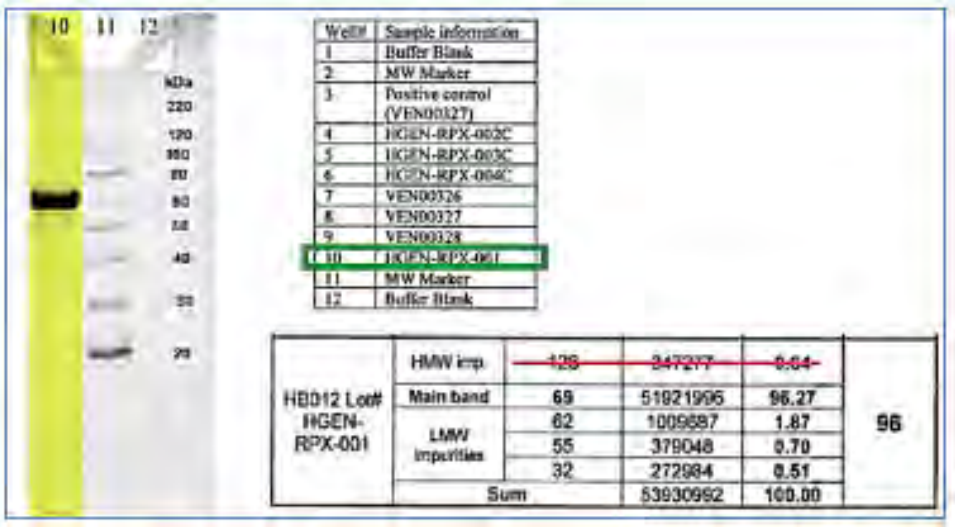
just tribute to the merits of the plaintiff's invention, as well as a distinct admission that their own machine accomplishes the same result.").

ii. Independent Third-Party Testing Confirms OsrHSA Clinical Grade Has Less than 2% Aggregated Albumin

Testing conducted by a reputable third-party laboratory further corroborated that OsrHSA clinical grade has less than 2% aggregated albumin. Specifically, SGS Life Sciences Services ("SGS") tested samples of Healthgen's OsrHSA clinical grade (produced by Healthgen as HGENRPX-001) in May 2021 and June 2021 and memorialized the results of the testing in study reports dated May 19, 2021 (JX-0129), and June 29, 2021 (CX-0904), respectively. Healthgen confirmed via correspondence with Ventria counsel that sample number HGEN-RPX-001 was a sample of Healthgen product HYC001C02, i.e., its OsrHSA clinical grade. (RX-0190C.0001.). The samples of OsrHSA clinical grade were tested using reducing SDS-PAGE to quantify aggregated albumin, if any, in the samples. (JX-0129.0003-5; CX-0904.0003-5; *see also* Tr. (Wilken) at 369:21-25.). As discussed in Section IV.F above, reducing SDS-PAGE is a common technique that is appropriate for quantifying aggregated albumin in a sample. Dr. Wilken testified that she found SGS's testing and protocols acceptable. (Tr. (Wilken) at 370:17-24.). Dr. DeFilippi did not offer any testimony criticizing or disputing SGS's testing conditions or protocols.

The May 2021 testing showed that Healthgen's OsrHSA clinical grade has less than 2% aggregated albumin. As shown in the annotated collection of images below, all of which are taken from JX-0129, Healthgen's OsrHSA clinical grade sample RPX-001 (i.e., HYC001C02) had no more than 0.64%aggregated albumin, i.e., less than 2% aggregated albumin.

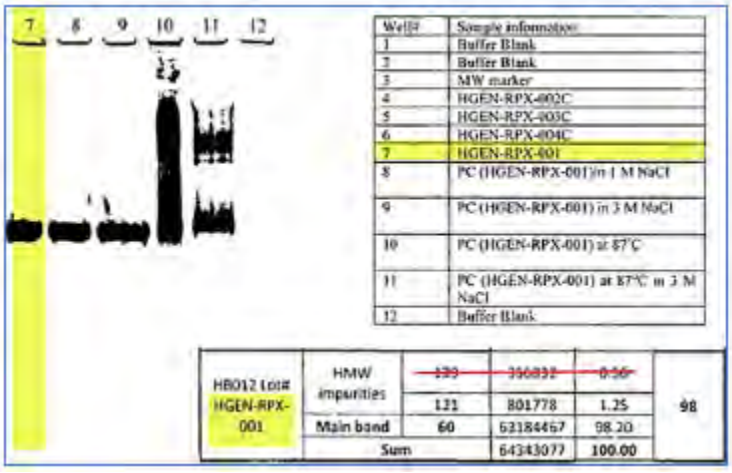
Figure 8: SGS May 2021 Testing Results



(JX-0129.0006-7 (annotated, copied from CBr. at 50); *see also* Tr. (Wilken) at 413:1-414:3; Tr (DeFilippi) at 1198:13-1199:2 (confirming same).).

The June 2021 testing also showed that Healthgen's OsrHSA clinical grade has less than 2% aggregated albumin. As shown in the annotated collection of images below, all of which are taken from CX-0904, Healthgen's OsrHSA clinical grade sample RPX-001 (i.e., HYC001C02) had no more than 1.81% aggregated albumin, i.e., less than 2% aggregated albumin.

Figure 9: SGS June 2021 Testing Results



(CX-0904.0006-7 (annotated, copied from CBr. at 51); *see also* Tr. (Wilken) at 539:11-540:12;

Tr (DeFilippi) at 1199:7-12 (confirming same).).

In sum, three (3) separate test (SEC HPLC, reducing SDS-PAGE under a first set of conditions in May 2021, and reducing SDS-PAGE under a second set of conditions in June 2021) all demonstrated that OsrHSA clinical grade has less than 2% aggregated albumin. Dr. DeFilippi agreed during cross-examination that "three test results on the same batch" of OsrHSA clinical grade "showed results of less than 2 percent aggregated albumin." (Tr. (DeFilippi) at 1279:4-1282:14 ("Q. Okay. ***All three showed results of less than 2 percent aggregated albumin***[?] A. By their particular -- ***by the particular analytical techniques, yes***.") (emphases added).).

For the foregoing reasons, Ventria has proven by a preponderance of evidence that the Accused Products meet this limitation of claim 1 of the '951 patent.

iii. Healthgen's Arguments

1. Effects of shipping, storage, or importation on percentage of aggregated albumin.

Healthgen contended that Ventria improperly relied on "test data from a fresh sample one day after manufacture in China where the percentage of aggregation is at its lowest—data collected at the wrong time[.]" (RRBr. at 29.). According to Healthgen:

> Healthgen evaluated batch no. C001202009001 in China one day after manufacture using SEC-HPLC and provided a sample of that batch to Ventria, who then subjected it to Reducing SDS-PAGE to generate data in the United States on two separate occasions, using two different reducing/bond-breaking agents.

(*Id.* at 30 (citing RDX-0002C.0047; JX-0032C.0001-2; RX-0190C; JX-0129.0004, 0007; CX-0904. 0005, 0007; RDX-0002C.0048).).

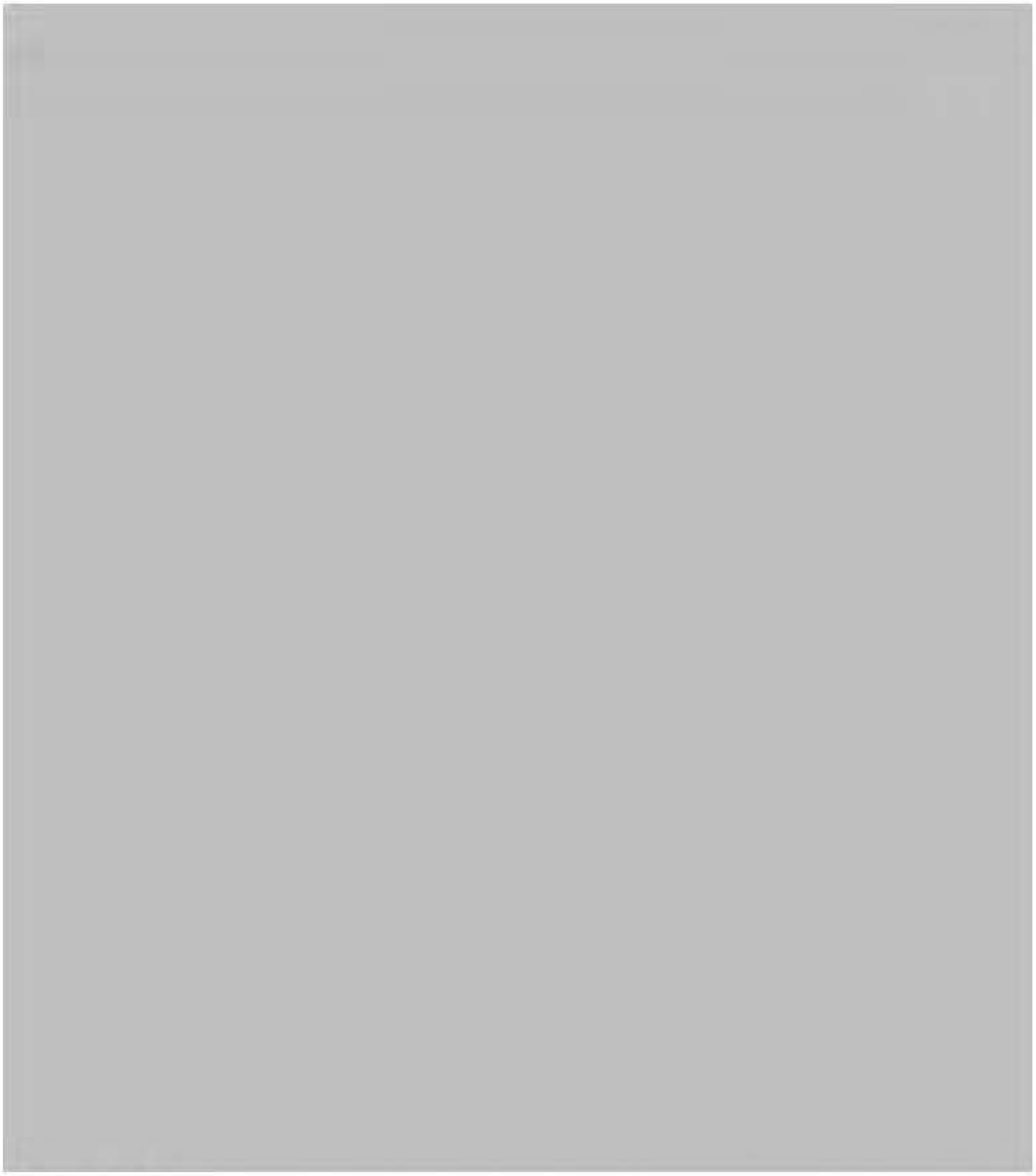
Based on the three (3) data sets, Healthgen asserted that "aggregated albumin increase[d] in Healthgen's liquid sample over time (i.e., during storage) and by shipping." (*Id.* at 31 (citing Tr. (DeFilippi) at 1201:10-1203:10; RDX-0002C.0049-51).).

As an initial matter, Dr. DeFilippi acknowledged during cross-examination that he had no knowledge as to the way Healthgen ships or maintains the stability of its products. (Tr. (DeFilippi) at 1282:21-1283:3.). He also failed to review Healthgen customer communications, including OsrHSA clinical grade data Healthgen prepared for the FDA, that undermines Healthgen's argument that its products were unstable or affected by shipping and handling. (*Id.* at 1273:23-1274:6.).

For example, in an email dated August 14, 2019, Healthgen employee, Ms. Jing Cao, stated the following to customer [redacted] in response to questions about Healthgen's Drug Master File ("DMF") for its OsrHSA clinical grade: [redacted] (JX-0007C.0001.). She attached a filed titled [redacted] (JX-0009C, also [redacted]) to the email. (*Id.*). [redacted] (CX-0882.0004-5.). [redacted] (JX-0009C.0030.). The data supporting that statement is summarized at JX-0009C.0031-33 and concludes with the following table, showing [redacted]

(JX-0009C.0030-33 (annotated).).

The data in Figure 10 also are confirmed in an email dated April 23, 2020, in which Ms. Cao stated to [redacted] that OsrHSA clinical grade data was submitted to the FDA by Healthgen, that [redacted] (CX-0193C.0006-7.). In the same email thread, Ms. Cao later identified multiple sections of Healthgen's DMF for its OsrHSA clinical grade and indicated that DMF Section [redacted] (i.e., JX-0009C) was [redacted] (CX-0193C.0003-4.). As Ventria pointed out, [redacted] which Ms. Cao stated in CX-0193C.0006-7 was used to [redacted] has the following properties according to a Healthgen OsrHSA clinical grade COA that Healthgen provided to [redacted]:



(JX-0015C.0001-2.).

As shown in the emails and DMF-related documents for OsrHSA clinical grade above, Healthgen represented to its U.S. customers and the FDA that its OsrHSA clinical grade has less than 2% aggregated albumin. (JX-0007C.0001; JX-0009C.0001, 0030-33; CX-0193C.0003-4, 0006-7; JX-0015C.0001-2.).

Additionally, Healthgen shared stability study data of its OsrHSA products with its customer, , that states, *inter alia*,

[redacted] (CX-0391C.0013; *see also id.* at 0006-7 (emphasis added).). Healthgen shared similar stability data with its customer, [redacted] in a December 13, 2018 Memorandum, which concluded that [redacted] (CX-0456.0001-2 (emphasis added); *see also* CX-0470C.0001 (email from Ms. Cao stating in relevant part: [redacted]); CX-0474C-0006 (email from Ms. Cao stating in relevant part, [redacted]) (emphasis added); CX-0476C (same); CX-0478C (same).).

Thus, Healthgen's argument that OsrHSA clinical grade is somehow unstable, different after arrival in the U.S., and/or affected by shipping and handling is belied by data it prepared for and submitted to the FDA, stability data it shared with customers, and its own customer communications, which together establish that OsrHSA clinical grade is stable and contains less than 2% aggregated albumin. *Conoco, Inc. v. Energy & Env't Int'l, L.C.*, 460 F.3d 1349, 1362-63 (Fed. Cir. 2006) ("EEI contends that it presented evidence that the accused product was not stable and that the polymer quickly settled out. However, Conoco presented contrary evidence comprising (1) EEI's representations to customers that its product was stable and nonagglomerating, (2) EEI's representations of stability to the PTO, and (3) EEI's concession that the product is stable when injected into the pipeline . . . . Thus, there is sufficient evidence to support the district court's finding [for Conoco].").

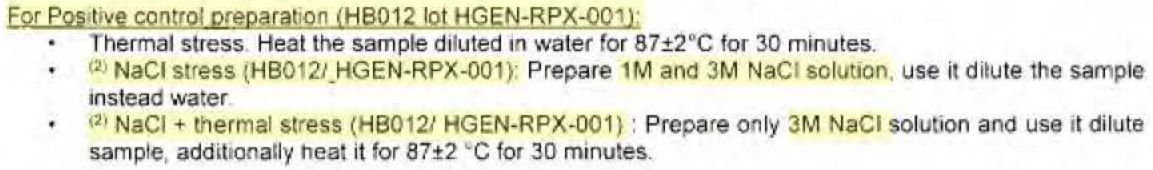
2. The May 2021 and June 2021 SGS Tests.

As Ventria noted, Healthgen's assertion that the May 2021 and June 2021 SGS testing

had "dramatically different" results (RDX-0002C.49) mischaracterizes the evidence. Although the May 2021 and June 2021 tests were both performed using reducing SDS-PAGE, each of their testing conditions were markedly different. Specifically, the May 2021 and June 2021 tests: (i) used different reducing agents (TCEP and DTT, respectively); (ii) had different load volumes; (iii) used different gels; (iv) used different running buffers; and (v) used different electrophoresis conditions. (*Compare* JX-0129.0005 *with* CX-0904-0005.). Thus, as Ventria pointed out, the fact that these tests reported slightly different results is not surprising. Nevertheless, in both cases, the SGS testing showed that OsrHSA clinical grade had less than 2% aggregated albumin, with which Dr. DeFilippi agreed. (Tr. (DeFilippi) at 1282:11-14 ("Q. Okay. All three showed results of less than 2 percent aggregated albumin[?] A. By their particular -- by the particular analytical techniques, yes."); *see also id.* at 1279:4-1282:14.).

Moreover, the June 2021 SGS testing was performed to test whether stressing Healthgen's OsrHSA clinical grade (i.e., RPX-0001) with high salt (sodium chloride or NaCl), alone or in combination with extreme temperature, could cause high molecular weight impurities to form in Healthgen's clinical grade sample, which is shown in the following annotated screenshot from SGS's Study Report for the June 2021 testing.

Figure 12: June 2021 SGS Study Report


For Positive control preparation (HB012 lot HGEN-RPX-001):

- Thermal stress. Heat the sample diluted in water for 87±2°C for 30 minutes.
- (2) NaCl stress (HB012/ HGEN-RPX-001): Prepare 1M and 3M NaCl solution, use it dilute the sample instead water.
- (2) NaCl + thermal stress (HB012/ HGEN-RPX-001) : Prepare only 3M NaCl solution and use it dilute sample, additionally heat it for 87±2 °C for 30 minutes.

(CX-0904.0005 (annotated) (results from the stressed samples at CX-0904.0006-7).).

As Ventria pointed out, it appears that the June 2021 testing was not designed to detect anything more than a main albumin band and any high molecular weight impurities appearing

above the main band in response to substantial salt and heat stressors, which resulted in the lack of any recording of low molecular weight impurities. (CBr. at 58-59.).

c) Healthgen's OsrHSA "Cell Culture Grade" Has Less Than 2% Aggregated Albumin

i. Healthgen's "Tear Sheets" Show OsrHSA Cell Culture Grade Has Less than 2% Aggregated Albumin

During cross-examination, Dr. DeFilippi testified that materials such as sales catalogs and marketing materials are "tear sheets" that "describe[] what the product is to the customer," "you tear it out and hand it to the customer." (Tr. (DeFilippi) at 929:8-931:19.). Healthgen's OsrHSA "tear sheets" describe "what the product is" to U.S. customers: rHSA with less than 2% aggregated albumin.

For example, in response to U.S. customer [redacted] inquiries about [redacted] (CX-0052C.0001), Healthgen attached a document that stated the following:

[redacted]

(CX-0052C.0003; *see also* CDX-0001.0054.).

As shown above, to arrive at a purity of [redacted] for its OsrHSA culture grade, Healthgen stated to [redacted] that it runs OsrHSA culture grade [redacted] (*Id.*).

This means that, according to Healthgen, the [redacted] (*Id.*; *see also* Tr. (Wilken) at 404:14-405:5, 406:11-407:11, 425:4-16; CDX-0001C.0054.). In other words, [redacted] (CX-0883.0002.).

Additional Healthgen documents and communications confirm that OsrHSA culture grade has less than 2% aggregated albumin as measured by [redacted]. For example, CX-0053C, another document produced by a Healthgen customer in this Investigation [redacted], is a Company Overview that Healthgen created. (CX-0053C.). As shown at

CX-0053C.0007, Healthgen described its OsrHSA culture grade in detail, and stated that its purity is [redacted] (CX-0053C.0007 (emphasis added); *see also* CX-0005C.0001 (showing same; produced by Healthgen); CX-0002.0006 (brochure from Healthgen distributor Aspira Scientific stating, with accompanying data, that "[a] detailed analysis . . . confirms Aspira Scientific's rHSA as a single protein at 66.4 kDa"); JX-0019C.0001 (same; produced by Healthgen); CX-0412C; CX-0387C; Tr. (Wilken) at 425:23-428:14; CDX-0001C.0054.). Another customer communication produced by [redacted], an email chain between Healthgen employees and [redacted] personnel, shows that Healthgen's "VP Sales and Marketing at Healthgen" stated in relevant part, [redacted] (CX-0360C.0002-3.).

The foregoing Healthgen representations and other Healthgen customer communications also state that the purity of OsrHSA culture grade is over 99% as determined by SDS-PAGE showing or stating that "[a]ll batches of OsrHSA only have one band," i.e., OsrHSA migrates as a single band on the SDSPAGE gel and that this band corresponds with monomeric rHSA. (*See* JX-0064.0005 (produced by Healthgen customer [redacted]); *see also* CX-0385C.0012 (produced by customer [redacted]); CX-0005C.0001; CX-0052C.0003; CX-0053C.0007-8; JX-0019C.0001; Tr. (Wilken) at 428:15-429:15, 429:16-431:20.). This means, according to Healthgen, that no other bands, be it fragments, aggregated albumin, or other complexes, appear when they run OsrHSA through SDS-PAGE. (*Id.*).

The evidence discussed above, in combination with: (i) Healthgen's [redacted] and its characterization of the same in customer communications; (ii) the properties of Healthgen's [redacted] and Bo Shi's testimony (*see* Section VIII.B.5(a), *supra*); and (iii) Dr. Yang et al.'s characterization of Healthgen's purification process in peer-

reviewed literature (JX-0023.0014) establish by a preponderance of the evidence that OsrHSA culture grade has less than 2% aggregated albumin. *R Bard Inc.*, 979 F.3d at 1379; *see also C & A Potts & Co.*, 155 U.S. at 610; *Conoc Inc.*, 460 F.3d at 1362-63.

ii. Healthgen's Arguments

1. Testing of purportedly representative samples of OsrHSA.

Ventria did not dispute that purportedly representative samples of Healthgen's OsrHSA culture grade that Healthgen provided in this Investigation showed more than 2% aggregated albumin by reducing SDS-PAGE testing that SGS conducted. (*See* JX-0129.0007 (results for HGEN-RPX-0002C, 0003C, 0004C); CX-0904.0007 (same samples run under reducing SDSPAGE).). However, as Ventria noted, this is merely data associated with three samples. (CBr. at 64.). When this data is placed against: (i) Healthgen's and its characterization of the same in customer communications; (ii) the properties of Healthgen's and Bo Shi's testimony (*see* Section VIII.B.5(a), *supra*); and (iii) Dr. Yang et al.'s characterization of Healthgen's purification process in peer-reviewed literature (JX-0023.0014), and viewed in its totality, one can reasonably conclude that the data from these samples are outliers. (Tr. (Wilken) at 492:20-493:21.

A small amount of unfavorable evidence does not outweigh a large amount of evidence that establishes OsrHSA culture grade has less than 2% aggregated albumin. *Jazz Photo Corp. v. U.S.*, 439 F.3d 1344, 1350 (Fed. Cir. 2006) ("We have defined preponderance of the evidence in civil actions to mean 'the greater weight of evidence, evidence which is more convincing than the evidence which is offered in opposition to it."') (quoting *Hale v. Dep't of Transp., Fed. Aviation Admin.*, 772 F.2d 882, 885 (Fed. Cir. 1985)).

2. "Salted" samples and lyophilization.

Dr. DeFilippi testified that: (i) [redacted]; and (ii) lyophilization of OsrHSA culture grade increases aggregation. (Tr. (DeFilippi) at 1175:4-14, 1176:4-11; RDX-0002C.0025-27.). Dr. DeFilippi's demonstratives do not cite to anything but Healthgen's process flowchart (JX-0010), which shows a single process for making its [redacted]. (RDX-0002C.0025-27; Tr. (DeFilippi) at 1299:2-1301:9.). To the contrary, the June 2021 SGS testing indicates that high salt concentrations alone do not increase aggregation in the clinical grade OsrHSA. (CX-0904.0006-7.). CX-0904.0007 shows that all "salted" samples of OsrHSA clinical grade had nearly identical amounts of high molecular weight impurities when compared with an unsalted, unheated control sample. (*Id.* (*compare* HB012 Lot# HGEN-RPX-001 (98% purity) *with* PC in 1M NaCl (99% purity) and PC in 3M NaCl (99% purity)); *see also* CX-0904.0005 ("For Positive control preparation (HB012 lot HGEN-RPX-001) . . . Prepare 1M and 3M NaCl solution, instead [of] water.").).

With respect to alleged aggregation by lyophilization, the evidence shows that Healthgen, in addition to its liquid clinical grade product, also produced an OsrHSA clinical grade powder (i.e., lyophilized) product. (*See* JX-0061C (freeze-dried powder).). Healthgen sold its OsrHSA clinical grade powder to a U.S. customer, [redacted] In correspondence with [redacted] Healthgen's Jing Cao stated that [redacted] (CX-0196C.0007 (Cao referred to as "Abby" in the email chain).). Ms. Cao [redacted]

. (CX-0196C.0007 ; *see also* CX-0923; CX-0924.0003; JX-0032C.0001-3.).

C. The Accused Products Practice Claims 11-13 of the '951 Patent

Claims 11-13 require that the "recombinant mammalian albumin" is rHSA (claim 11), that the transgenic plant is a grain (claim 12), and that the transgenic grain of claim 12 is rice (claim 13). (*See* JX-0001 at cls. 11-13.). Healthgen's admissions and Dr. DeFilippi's testimony undisputedly establish that the Accused Products are rHSA produced in a transgenic rice seed. (CX-1017C at RFA No. 47) ," to which Healthgen replied in relevant part, Tr. (DeFilippi) at 1244:19-22, 1245:23-1246:1).

Accordingly, Ventria has proven by a preponderance of evidence that the Accused Products meet the additional limitations recited in claims 11-13 of the '951 patent.

IX. TECHNICAL PRONG OF THE DOMESTIC INDUSTRY REQUIREMENT

A. Legal Standard

A complainant in a patent-based Section 337 investigation must demonstrate that it is practicing or exploiting the patents at issue. *See* 19 U.S.C. § 1337(a)(2) and (3); *Certain Microsphere Adhesives, Process for Making Same, and Prods. Containing Same, Including Self-Stick Repositionable Notes*, Inv. No. 337-TA-366, Comm'n Op. at 8, Pub. No. 2949 (U.S.I.T.C. Jan. 16, 1996) ("*Microsphere Adhesives*"). "In order to satisfy the technical prong of the domestic industry requirement, it is sufficient to show that the domestic industry practices any claim of that patent, not necessarily an asserted claim of that patent." *Certain Ammonium*

Octamolybdate Isomers ("*Certain Isomers*"), Inv. No. 337-TA-477, Comm'n Op. at 55 (U.S.I.T.C. Jan. 5, 2004).

The test for claim coverage for the purposes of the technical prong of the domestic industry requirement is the same as that for infringement. *Certain Doxorubicin and Preparations Containing Same*, Inv. No. 337-TA-300, Initial Determination at 109, 1990 WL 710463 (U.S.I.T.C. May 21, 1990), *aff'd*, Views of the Commission at 22 (October 31, 1990) ("*Doxorubicin*"). "First, the claims of the patent are construed. Second, the complainant's article or process is examined to determine whether it falls within the scope of the claims." *Id.* The technical prong of the domestic industry can be satisfied either literally or under the doctrine of equivalents. *Certain Dynamic Sequential Gradient Devices and Component Parts Thereof*, Inv. No. 337-TA-335, Initial Determination at 44, Pub. No. 2575 (U.S.I.T.C. Nov. 1992).

B. The DI Products Practice Claim 1 of the '951 Patent

1. Optibumin

Healthgen and Dr. DeFilippi agreed that Optibumin satisfies the technical prong of domestic industry. (Tr. (DeFilippi) at 1243:22-1244:5 ("Q. You agree that Ventria's Optibumin product practices the asserted claims of the '951 patent, right? . . . You agree with that, right? A. Yeah. Q. There's no dispute that Ventria's Optibumin product is a domestic industry product, correct? A. That's my understanding, yes, from what was presented."); *see also id.* at 1244:19-1245:6, 1245:23-1246:1; Tr. at 1404:10-17 (closing); *see also, e.g.*, Tr. (Deeter) at 147:25-148:12; Tr. (Wilken) at 355:15-18, 357:19-358:14, 367:22-368:1; JX-0114C; JX-0091C; JX-0076C.0003; JX-0120C.0002, 0005; JX-0129.0007 (sample VEN00328, which is Optibumin and shows no high molecular weight impurities of any kind); CX-1082; CX-0919; CX-0548.0002-03, JX-0073; CDX-0001C.0032; RDX-0002C.0080.). In view of Healthgen's and Dr.

DeFilippi's admissions, and at least the evidence of record cited above, a preponderance of the evidence establishes Optibumin practices at least claim 1 of the '951 patent and satisfies the technical prong of domestic industry.

2. Cellastim and Exbumin

a) "A cell culture media supplement or complete media composition for improving the growth of a cell in cell culture comprising"

As an initial matter, Healthgen and Dr. DeFilippi did not dispute that Cellastim and Exbumin are cell culture media supplements or complete media compositions.

> Q. And you agree that both Wuhan Healthgen's products and Ventria's DI products are cell culture media supplements, correct?
>
> A. They have products that act as cell culture medium products.
>
> Q. So both Healthgen's products and the Ventria products that are at issue in this investigation are cell culture media supplements, right?
>
> A. Yes.

(Tr. (DeFilippi) at 1244:23-1245:6.).

Ventria also presented evidence and testimony confirming that Cellastim is a cell culture media supplement or complete media composition. (*See* JX-0077 ("Cellastim S . . . has been designed and optimized to boost the performance of ACF T cell medias . . . Albumin is a cell culture supplement that functions as a carrier protein for fatty acids, growth factors, and trace minerals."); CX-0663C ("Exbumin® is used as a media component [redacted]); CX-0542 (same); *see also* JX-0120C.0002, 0005; Tr. (Deeter) at 142:11-17; Tr. (Wilken) at 356:12-20, 356:25-357:3.).

In view of Healthgen's and Dr. DeFilippi's admissions, and at least the evidence of record cited above, Ventria has proven by a preponderance of evidence that Cellastim and

Exbumin meet the preamble of claim 1 of the ’951 patent.

b) “a recombinant mammalian albumin”

As an initial matter, Healthgen and Dr. DeFilippi did not dispute that Cellastim and Exbumin comprise a recombinant mammalian albumin. (Tr. (DeFilippi) at 1245:23-1246:1 (“Q. You agree that both Healthgen’s products and Ventria’s DI products comprise recombinant human serum albumin, right? A. That is right.”); *see also id.* at 1244:6-14.).

Moreover, Ventria presented evidence and testimony confirming that Cellastim and Exbumin comprise a recombinant mammalian albumin. (*See* JX-0077 (“Cellastim S is an animal component free (ACF) human serum albumin (RSA) . . . Cellastim S has the identical amino acid sequence as the major RSA isoform found in human serum.”); JX-0072 (same); CX-0663C (“Exbumin® . . . is a lyophilized animal component free (ACF) recombinant human serum albumin (rHSA)”); CX-0542 (same); *see also* JX-0114C; CX-0919; CX-1082; CX-0542; JX-0116C; JX-0092C; JX-0093C; JX-0094C; JX-0095C; JX-0096C; JX-0076C; CX-0710C; JX-0130C; Tr. (Deeter) at 147:25-148:12; Tr. (Wilken) at 326:17-19, 354:6-13, 356:12-20.).

In view of Healthgen’s and Dr. DeFilippi’s admissions, and at least the evidence of record cited above, Ventria has proven by a preponderance of evidence that Cellastim and Exbumin meet this limitation of claim 1 of the ’951 patent.

c) “wherein said albumin is . . . produced in a transgenic plant”

As an initial matter, Healthgen and Dr. DeFilippi did not dispute that Cellastim and Exbumin are produced in a transgenic plant, specifically transgenic rice seed. (Tr. (DeFilippi) at 1244:19-22 (“Q. You agree that Wuhan Healthgen products and Ventria’s DI Products are produced in a transgenic rice seed, right? A. That is right.”); *see also id.* at 1244:6-14.).

Ventria also presented evidence and testimony which confirms that Cellastim and

Exbumin are produced in a transgenic plant (specifically rice). As Mr. Deeter and Dr. Wilken testified, Cellastim and Exbumin are produced using . (Tr. (Deeter) at 139:9-17, 146:1-11; Tr. (Wilken) at 353:25-354:5; CX-1082.). (CX-0919; *see also* JX-0114C.0001 (Ventria internal document); CX-1082; JX-0120C-0002, 0005; JX-0092C (certificate of analysis stating the species that produced Cellastim is Oryza sativa, i.e., rice); Tr. (Deeter) at 169:18-24; Tr. (Wilken) at 362:4-16.).

In view of Healthgen's and Dr. DeFilippi's admissions, and at least the evidence of record cited above, Ventria has proven by a preponderance of evidence that Cellastim and Exbumin meet this limitation of claim 1 of the '951 patent.

d) "wherein said albumin . . . has less than 1 EU of endotoxin/mg of albumin"

As an initial matter, Healthgen and Dr. DeFilippi did not dispute Cellastim and Exbumin have less than 1 EU endotoxin/mg albumin.

> Q. Okay. And for the Cellastim and Exbumin products, the only limitation that you believe those Ventria products do not meet is the aggregated albumin limitation, correct?
>
> A. Correct.
>
> Q. And if the Cellastim and Exbumin products meet the aggregated albumin limitation, then they are also domestic industry products, right?
>
> A. Yes.

(Tr. (DeFilippi) at 1244:6-14.).

Additionally, the evidence, particularly the certificates of analysis, confirm that Cellastim

has less than 1 EU of endotoxin/mg of albumin. (JX-0092C; JX-0093C; JX-0094C; JX-0095C; JX-0096C; JX-0076C.0001; JX-0116C.0001.). Similarly, the evidence, particularly the certificates of analysis, confirm that Exbumin has less than 1 EU of endotoxin/mg of albumin. (CX-0710C; JX-0076C.0002; JX-0116C.0002; JX-0130C.0001, 0003.).

In view of Healthgen's and Dr. DeFilippi's admissions, and at least the evidence of record cited above, Ventria has proven by a preponderance of evidence that Cellastim and Exbumin meet this limitation of claim 1 of the '951 patent.

e) "wherein said albumin . . . has . . . less than 2% aggregated albumin"

i. Ventria's Testing Shows Cellastim and Exbumin Have Less Than 2% Aggregated Albumin

The May 2021 SGS testing included test results for three (3) samples of Ventria DI Products Cellastim, Exbumin, and Optibumin that were tested by reducing SDS-PAGE. (JX-0129.0003 at Table 1 (listing rHSA samples tested, where VEN00326 corresponds to Cellastim-S (Lot Number P0917; JX-0116C); VEN00327 corresponds to Exbumin (Lot Number P0861; JX-0116C.0002); VEN00328 corresponds to Optibumin); Tr. (Wilken) at 372:14-373:4; CDX-0001C.0032; RDX-0002C.0072.).

Dr. Wilken testified that she found the testing procedure and experimental design of the May 2021 SGS testing acceptable. (Tr. (Wilken) at 370:17-24.). Although Dr. DeFilippi criticized the choice to use reducing SDS-PAGE to quantify and measure aggregated albumin, he did not offer any testimony that indicates that SGS performed the experiment improperly or presented inaccurate data. He agreed during his deposition under cross-examination that he did not "have an issue with" scientists assessing the level of monomeric albumin in a sample using SDS-PAGE under reducing conditions "if they describe the conditions adequately." (Tr.