

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.

TABLE OF CONTENTS

I.	INITIAL DETERMINATION ON VIOLATION OF SECTION 337, AND RECOMMENDED DETERMINATION ON REMEDY AND BOND	1
A.	Overview	1
B.	Summary of Findings.....	3
II.	BACKGROUND	3
A.	Institution and Selected Procedural History	3
B.	The Parties	5
1.	Complainant Ventria Bioscience Inc.	5
2.	Respondent Wuhan Healthgen Biotechnology Corp.	6
3.	Defaulting Respondents	6
III.	JURISDICTION, IMPORTATION, AND STANDING	7
A.	The Commission Has Jurisdiction	7
1.	Subject Matter Jurisdiction	8
2.	Personal Jurisdiction	8
3.	<i>In Rem</i> Jurisdiction	8
B.	Ventria Has Standing in the Commission.....	9
IV.	OVERVIEW OF RELEVANT TECHNOLOGY	9
A.	Albumin	10
B.	Recombinant Proteins and Cell Culture.....	12
C.	Protein Aggregation	13
D.	Endotoxin.....	14
E.	Certificates of Analysis.....	15
F.	SDS-PAGE	16
V.	THE ASSERTED PATENT	27
A.	Overview of the Asserted Patent.....	27
B.	The Asserted Claims of the Asserted Patent.....	29
VI.	THE PRODUCTS AT ISSUE	30
A.	Healthgen’s Accused Products	30
B.	Ventria’s DI Products	30
VII.	PERSON OF ORDINARY SKILL IN THE ART	32

A.	Legal Standard	32
B.	Definition of a Person of Ordinary Skill in the Art	32
VIII.	DIRECT INFRINGEMENT	33
A.	Legal Standard: Literal Infringement.....	33
B.	The Accused Products Practice Claim 1 of the '951 Patent	34
1.	“A cell culture media supplement or complete media composition for improving the growth of a cell in cell culture comprising”	34
2.	“a recombinant mammalian albumin”	35
3.	“wherein said albumin is . . . produced in a transgenic plant”	36
4.	“wherein said albumin . . . has less than 1 EU of endotoxin/mg of albumin”	37
5.	“wherein said albumin . . . has . . . less than 2% aggregated albumin”	37
a)		37
b)	Healthgen’s OsrHSA “Clinical Grade” Has Less Than 2% Aggregated Albumin.....	41
i.	Healthgen’s Certificates of Analysis Confirm OsrHSA Clinical Grade Has Less than 2% Aggregated Albumin.....	41
ii.	Independent Third-Party Testing Confirms OsrHSA Clinical Grade Has Less than 2% Aggregated Albumin	44
iii.	Healthgen’s Arguments	46
c)	Healthgen’s OsrHSA “Cell Culture Grade” Has Less Than 2% Aggregated Albumin	52
i.	Healthgen’s “Tear Sheets” Show OsrHSA Cell Culture Grade Has Less than 2% Aggregated Albumin	52
ii.	Healthgen’s Arguments	55
C.	The Accused Products Practice Claims 11-13 of the '951 Patent	57
IX.	TECHNICAL PRONG OF THE DOMESTIC INDUSTRY REQUIREMENT	57
A.	Legal Standard	57
B.	The DI Products Practice Claim 1 of the '951 Patent.....	58
1.	Optibumin	58

2.	Cellastim and Exbumin.....	59
a)	“A cell culture media supplement or complete media composition for improving the growth of a cell in cell culture comprising”	59
b)	“a recombinant mammalian albumin”	60
c)	“wherein said albumin is . . . produced in a transgenic plant”	60
d)	“wherein said albumin . . . has less than 1 EU of endotoxin/mg of albumin”	61
e)	“wherein said albumin . . . has . . . less than 2% aggregated albumin”	62
i.	Ventria’s Testing Shows Cellastim and Exbumin Have Less Than 2% Aggregated Albumin	62
ii.	Healthgen’s Testing Shows Cellastim and Exbumin Have Less Than 2% aggregated albumin.....	67
3.	OptiPEAK HEK293t, OptiPEAK T Lymphocyte, OptiVERO, and ITSE™ + A	71
X.	INVALIDITY	71
A.	Legal Standards.....	71
1.	Anticipation.....	71
2.	Obviousness	72
B.	The Scope and Content of the Prior Art.....	74
C.	The Prior Art References Do Not Anticipate the Asserted Claims of the ’951 Patent.....	76
1.	Claim 1	76
a)	Healthgen Failed to Demonstrate that Each Claim Element Is Present in Either Van Urk or Berezenko.....	76
b)	Healthgen Failed to Demonstrate Each Claim Limitation Is Present in the Combination Claimed in the ’951 Patent, or that a Person of Ordinary Skill in the Art Would at Once Envisage Such a Combination	80
c)	A Person of Ordinary Skill in the Art Would Understand Disclosures Specific to Yeast-Derived rHSA Would Not Read on Plant-Derived rHSA.....	81
d)	The Substance of Both References Was Already Considered by the PTO	85
e)	Neither Reference Enables the Production of the Claimed	

	Product	87
2.	Claim 11	88
3.	Claims 12 and 13	88
D.	The Prior Art References Do Not Render Obvious the Asserted Claims of the '951 Patent	89
1.	A Person of Ordinary Skill in the Art Would Not Be Motivated to Combine Deeter with Van Urk or Berezenko	89
2.	Deeter in View of Van Urk or Berezenko	91
	a) Claim 1	91
	b) Claim 11	94
3.	Deeter and/or Huang in View of Van Urk or Berezenko.....	94
	a) Claims 12 and 13	94
4.	Secondary Considerations.....	95
XI.	ECONOMIC PRONG OF THE DOMESTIC INDUSTRY REQUIREMENT	95
A.	Legal Standard	95
B.	Economic Prong Overview	100
C.	Ventria's Sales-Based Allocation Method is Reasonable.....	100
D.	Ventria Has Satisfied the Economic Prong of the Domestic Industry Requirement Under Subsections 337(a)(3)(A), (B), and (C)	101
E.	Ventria Has Satisfied the Economic Prong of the Domestic Industry Requirement Even if Investments Only in Optibumin® are Considered	107
XII.	RECOMMENDATION ON REMEDY AND BOND.....	111
A.	Legal Standard	112
B.	A General Exclusion Order Is Not Warranted.....	113
	1. A GEO Is Not Warranted Under 19 U.S.C. § 1337(d)(2)(A).....	114
	2. A GEO Is Not Warranted Under 19 U.S.C. § 1337(d)(2)(B)	118
C.	Limited Exclusion Orders Are Warranted	121
D.	Cease and Desist Orders Are Not Warranted	122
E.	Bond During the Presidential Review Period Is Warranted	123
XIII.	WAIVER OR WITHDRAWAL OF RESPONDENT'S DEFENSES.....	127
XIV.	CONCLUSIONS OF FACT OR LAW: THIS INITIAL DETERMINATION FINDS A SECTION 337 VIOLATION BASED UPON INFRINGEMENT OF U.S. PATENT NO. 10,618,951	127

XV. CONCLUSION AND ORDER	129
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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 <i>Markman</i> Brief
ROMBr.	Respondent's Opening <i>Markman</i> Brief
SOMBr.	Staff's Opening <i>Markman</i> Brief
CRMBr.	Complainant's Responsive <i>Markman</i> Brief
RRMBr.	Respondent's Responsive <i>Markman</i> Brief
SRMBr.	Staff's Responsive <i>Markman</i> 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.

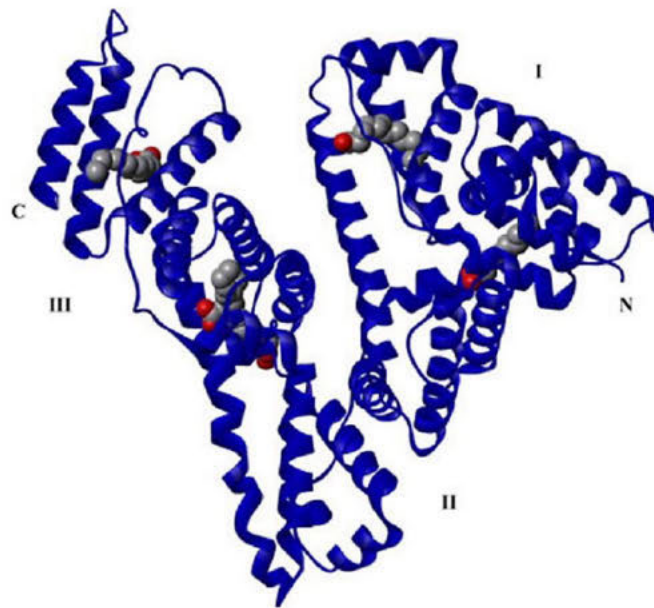
A. Albumin

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*, CYTOTECNOLOGY, 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.).

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. (RPSSt. 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. Peer-reviewed literature confirms reducing SDS-PAGE is a suitable method for quantifying aggregates.

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. (Wilkins) 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 SDS-PAGE 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 HPLC); 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. Dr. Wilken personally analyzed aggregates using reducing SDS-PAGE to characterize rice-produced rHSA.

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.

(JX-0062C.0001-2.). In response,

(*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, [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] s. (Tr. (Wilken) at 410:8-

412:6.). For example, [REDACTED]

[REDACTED] (*Id.*; see also

CX-0353C (showing same and confirmed to be [REDACTED]

[REDACTED], CX-0883 at ¶ 9.).

Although it is unclear whether Healthgen is referring to [REDACTED]

[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]
[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]

[REDACTED] (RX-0366C.0012.). Specifically, as shown in the blown-up screen shot of [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



(RX-0366C.0012.).

[REDACTED]

[REDACTED]

[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]

[REDACTED]

[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]
[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]
[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 INFRINGEMENT²²

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]

[REDACTED] Healthgen replied in relevant part, [REDACTED]

[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]

[REDACTED]. (JX-0021C.0002-3.). JX-0021C further describes the [REDACTED]

[REDACTED] (*Id.* at JX-0021C.0002.). JX-0021C also describes the [REDACTED]

[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]
[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]
[REDACTED] Healthgen replied in relevant part, [REDACTED]
[REDACTED] (CX-1017C at RFA Nos. 46-47.).

Healthgen also confirmed that [REDACTED]

[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]

[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]

[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]

[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

[REDACTED]. (*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]

[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]

[REDACTED]

[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]

[REDACTED]

[REDACTED]

[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]

[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.).

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] (JX-0047C.0094-95.). [REDACTED]

[REDACTED] (*Id.*). Mr. Shi testified that [REDACTED]

[REDACTED]

[REDACTED] (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]
[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]
[REDACTED]
[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 [REDACTED]

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

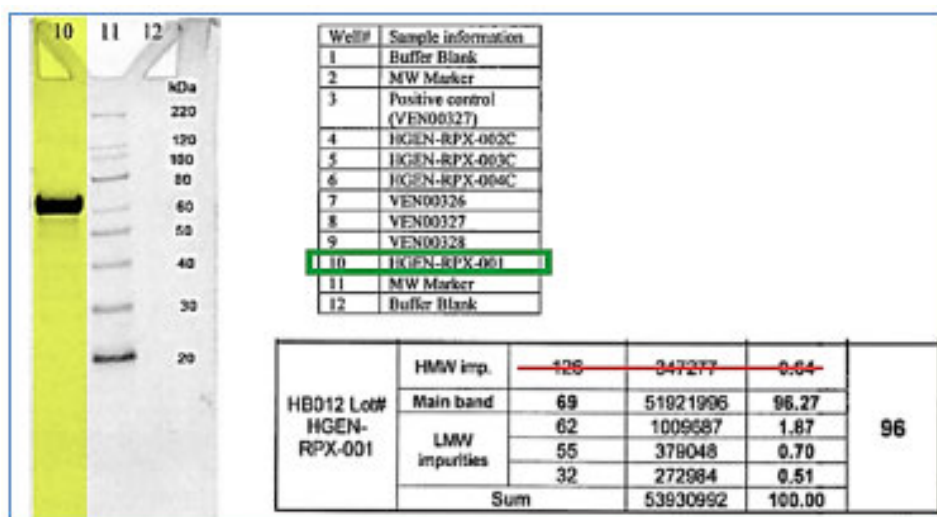
²⁶ CX-0450 (which also begins with bates number [REDACTED]) was produced by Healthgen customer, [REDACTED] (CX-0885.0008.). In other words, CX-0450 is not merely a Healthgen internal testing document, but a document that Healthgen provides its U.S. customers to represent the characteristics of its OsrHSA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

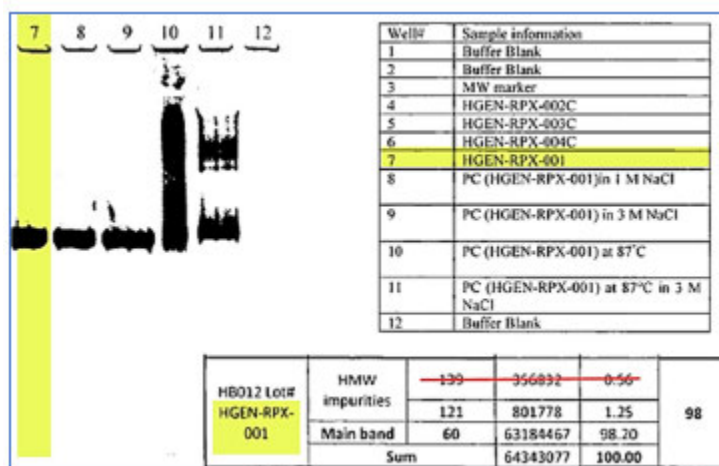
Testing conducted by a reputable third-party laboratory further corroborated that OsrHSA clinical grade has less than 2% aggregated albumin. Specifically, SGS Life Sciences Services (“SGS”) tested samples of Healthgen’s OsrHSA clinical grade (produced by Healthgen as HGENRPX-001) in May 2021 and June 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]

[REDACTED] (JX-0007C.0001.). She attached a filed titled [REDACTED] [REDACTED] (JX-0009C, also [REDACTED]) to the email. (*Id.*) [REDACTED]

[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]

[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]

[REDACTED]

[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, [REDACTED], that states, *inter alia*, [REDACTED]

[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]

[REDACTED] (CX-0456.0001-2 (emphasis added); *see also* CX-0470C.0001 (email from Ms. Cao stating in relevant part: [REDACTED]

[REDACTED]); CX-0474C-0006 (email from Ms. Cao stating in relevant part, [REDACTED]

[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 $87\pm 2^{\circ}\text{C}$ 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 $87\pm 2^{\circ}\text{C}$ 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] [REDACTED] (CX-0052C.0001), Healthgen attached a document that stated the following:



(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]

[REDACTED]

[REDACTED] (*Id.*).

This means that, according to Healthgen, the [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[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]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[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]

[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] [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 SDS-PAGE)). However, as Ventria noted, this is merely data associated with three samples. (CBr. at 64.). When this data is placed against: (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), 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]
[REDACTED]
[REDACTED] (CX-0196C.0007 (Cao referred to as “Abby” in the email chain).). Ms. Cao [REDACTED]
[REDACTED]

[REDACTED]

[REDACTED]. (CX-0196C.0007 [REDACTED])

[REDACTED]; 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) [REDACTED]

[REDACTED],” to which Healthgen replied in relevant part, [REDACTED]

[REDACTED] 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 [REDACTED]. (Tr.

(Deeter) at 139:9-17, 146:1-11; Tr. (Wilken) at 353:25-354:5; CX-1082.). [REDACTED]

[REDACTED] (CX-0919; *see*

also JX-0114C.0001 (Ventria internal document [REDACTED]

[REDACTED]); 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

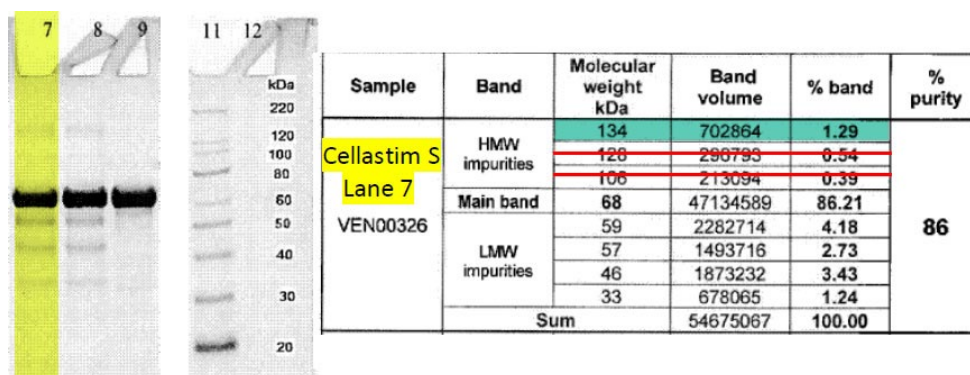
The May 2021 SGS testing included test results for three (3) samples of Ventria DI Products Cellastim, Exbumin, and Optibumin that were tested by reducing SDS-PAGE. (JX-0129.0003 at Table 1 (listing rHSA samples tested, where VEN00326 corresponds to Cellastim-S (Lot Number P0917; JX-0116C); VEN00327 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.

(DeFilippi) at 1253:14-1254:4.).

With respect to the May 2021 SGS results shown at JX-0129.0007, Dr. Wilken explained that a “Main band” for a given sample in Table 4 corresponds with the percentage of monomeric rHSA present in the sample (based on the “band volume”) at the molecular weight (kDa) listed. (Tr. (Wilken) at 374:9-376:4.). She testified that any species (rows) falling above the “Main band” correspond with the percentage of high molecular weight (“HMW”) impurities present in the sample at the molecular weights (kDa) listed, and that any species (rows) falling below the “Main band” correspond with the percentage of low molecular weight (“LMW”) impurities present in the sample at the molecular weights (kDa) listed. (*Id.*).

Cellastim. The results from the May 2021 SGS testing show that Cellastim has less than 2% aggregated albumin. As set forth below in the annotated screenshot from JX-0129.0007, Cellastim has a main band at 68 kDa, i.e., the weight of an rHSA monomer. (Tr. (Wilken) at 375:14-376:4.). Dr. Wilken testified that in view of the weight of the main band (68 kDa), she would expect an albumin dimer—the simplest form of an aggregate—to appear at 136 kDa (68 x 2). (*Id.*). The closest band to 136 kDa that SGS quantified was a high molecular weight impurity band of 134 kDa. (Tr. (Wilken) at 376:5-8.). If only the 134 kDa band is counted as dimeric rHSA (i.e., aggregated albumin), as Dr. Wilken did, the sample of Cellastim has only 1.29% aggregated albumin. (*Id.*). Dr. Wilken also testified that even if both the band at 134 kDa and the band at 128 kDa are included as “aggregated albumin, the sample of Cellastim only has 1.83% aggregated albumin. (*Id.* at 378:7-12.). Dr. DeFilippi agreed. (Tr. (DeFilippi) at 1275:19-1276:19.).

Figure 14: May 2021 SGS Test Results for Cellastim

(JX-0129.0007 (annotated, copied from CBr. at 74).).

However, Dr. Wilken testified it would be inappropriate to count the impurities measured at 128 and 106 kDa in the Cellastim sample as aggregated albumin in view of the adopted construction for “recombinant mammalian albumin” and its necessary implications on the scope of “aggregated albumin.” (Tr. (Wilken) at 376:9-378:6.). Specifically, Dr. Wilken explained that the impurities measured at 128 and 106 kDa would comprise fragmented proteins that would necessarily fail to qualify as recombinant mammalian albumin fragments that “retain the biological or therapeutic activity of native mammalian albumin” because of the number of amino acids such fragmented proteins would be missing in view of the expected weight of an rHSA dimer (136 kDa) and the resulting loss in function. (*Id.* at 377:11-378:6.).

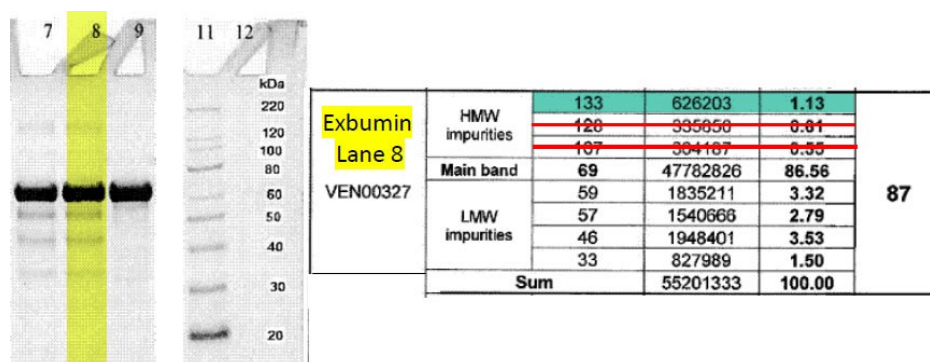
For example, the band at 106 kDa would consist of, at best, a 68 kDa monomer and a 38 kDa fragmented protein (the sum of which is 106 kDa), or two fragmented proteins of 53 kDa (same). Dr. Wilken testified and the evidence shows that because albumin has about 585 amino acids (*see, e.g.*, CX-0898.0002), in both scenarios described above, the fragmented proteins would lack a significant number of amino acids compared with native rHSA (roughly 130 amino acids less for the 53 kDa fragmented protein $((68 - 53) / 68)$ and multiplied by 585), and roughly

258 amino acids less for the 38 kDa fragmented protein $((68 - 38) / 68)$ and multiplied by 585), and thus would necessarily lose a significant portion of their structure and function. (Tr. (Wilken) at 377:23-378:6.). As Dr. Wilken explained, such fragmented proteins are not “recombinant mammalian albumin” and thus cannot form “aggregated albumin” as claimed. (*Id.*). Dr. Wilken provided similar testimony with respect to the band at 128 kDa. (*Id.* at 377:11-22.).

To count all HMW bands as “aggregated albumin,” as Dr. DeFilippi did, ignores the construction of “recombinant mammalian albumin” and the fact the claimed compositions must serve as cell culture medium supplements or complete media compositions.

Thus, the May 2021 SGS testing shows Cellastim has less than 2% aggregated albumin.

Exbumin. The results from the May 2021 SGS testing also show that Exbumin has less than 2% aggregated albumin. As set forth below in the annotated screenshot from JX-0129.0007-8, Exbumin has a main band at 69 kDa, i.e., the weight of an rHSA monomer. Dr. Wilken testified that in view of the weight of the main band (69 kDa), she would expect an albumin dimer to appear at 138 kDa (69 x 2). The closest band to 138 kDa that SGS quantified was a high molecular weight impurity band of 133 kDa. (Tr. (Wilken) at 378:16-23.). If only the 133 kDa band is counted as dimeric rHSA (i.e., aggregated albumin), as Dr. Wilken did, the sample of Exbumin has only 1.13% aggregated albumin. (*Id.* at 378:16-23.). Dr. DeFilippi agreed that even if the bands at 133 kDa and 128 kDa are included as “aggregated albumin, the sample of Exbumin only has 1.74% aggregated albumin. (Tr. (DeFilippi) at 1276:20-1277:9.).

Figure 15: SGS May 2021 Test Results for Exbumin

(JX-0129.0007-8 (annotated, copied from CBr. at 76).).

Similar to her opinion with respect to the data for Cellastim, Dr. Wilken testified that it would be inappropriate to count the impurities measured at 128 and 107 kDa in the Exbumin sample as aggregated albumin in view of the adopted construction for “recombinant mammalian albumin” and its necessary implications on the scope of “aggregated albumin.” (Tr. (Wilken) at 378:24-379:7.). Dr. Wilken testified the impurities measured at 128 and 107 kDa, would comprise fragmented proteins that would necessarily fail to qualify as recombinant mammalian albumin fragments that “retain the biological or therapeutic activity of native mammalian albumin” because of the number of amino acids such fragmented proteins would be missing in view of the expected weight of an rHSA dimer (138 kDa) and the resulting loss in function. (*Id.*).

For example, the band at 107 kDa would consist of, at best, a 69 kDa monomer and a 38 kDa fragmented protein (the sum of which is 107 kDa), or two fragmented proteins of 53.5 kDa (same). Dr. Wilken testified and the evidence shows that because albumin has about 585 amino acids (*see, e.g.,* CX-0898.0002), in both scenarios described above, the fragmented proteins would lack a significant number of amino acids compared with native rHSA (roughly 131 amino

acids less for the 53 kDa fragmented protein $((69 - 53.5) / 68)$ and multiplied by 585), and roughly 262 amino acids less for the 38 kDa fragmented protein $((69 - 38) / 68)$ and multiplied by 585), and thus would necessarily lose a significant portion of their structure and function. (Tr. (Wilken) at 377:13-378:6, 378:24-379:7.). Such fragmented proteins are not “recombinant mammalian albumin” and thus cannot form “aggregated albumin” as claimed. (*Id.*). Dr. Wilken provided similar testimony with respect to the band at 128 kDa. (*Id.*).

Thus, the May 2021 SGS testing shows Exbumin has less than 2% aggregated albumin.

ii. Healthgen’s Testing Shows Cellastim and Exbumin Have Less Than 2% aggregated albumin

Healthgen also tested two samples each of Cellastim and Exbumin under reducing and nonreducing SDS-PAGE. (Tr. (Wilken) at 379:18-380:11; RX-0310, RX-0311.). As shown in the annotated image from RX-0311, below, even under Healthgen’s interpretation of the scope of “aggregated albumin” (i.e., adding up all HMW bands that appear above the main, monomeric rHSA band), both samples of Cellastim tested by reducing SDS-PAGE had below 2 percent aggregated albumin (1.5% and 1.0%, respectively), while one sample of Exbumin had below 2 percent aggregated albumin (1.4% with the other exactly at 2%). Dr. DeFilippi agreed. (Tr. (DeFilippi) at 1252:10-16 (“Q. So the two Exbumin samples, example [sic] 1 was right at 2 percent, and sample 2 was at 1.4 percent of aggregated albumin, correct? A. By this technique, correct. Q. And for Cellastim, both samples were below 2 percent, correct? A. By this technique, correct.”); *see also id.* at 1254:7-17.).

Figure 16: Healthgen Test Results for Cellastim and Exbumin Under Reducing Conditions

REDUCING GEL			REDUCING GEL		
Cellastim S (2 µg), reduced, sample 1			Exbumin (2 µg), reduced, sample 1		
Band No.	Molecular Weight (kDa)	Band %	Band No.	Molecular Weight (kDa)	Band %
1	147.7	1.3	1	149.6	1.2
2	102.3	0.2	2	102.4	0.8
3	60.1	87.9	3	60.2	87.7
4	52.0	5.7	4	52.1	6.5
5	42.5	4.9	5	42.5	3.7

Cellastim S (2 µg), reduced, sample 2			Exbumin (2 µg), reduced, sample 2		
Band No.	Molecular Weight (kDa)	Band %	Band No.	Molecular Weight (kDa)	Band %
1	153.4	0.8	1	155.5	1.1
2	103.4	0.2	2	103.4	0.3
3	60.6	88.6	3	60.9	89.1
4	52.2	6.0	4	52.6	5.2
5	42.6	4.3	5	42.9	4.3

(RX-0311.0002-3.).

Since this ID finds that reducing SDS-PAGE is an appropriate technique to measure aggregated albumin (*see* Section IV.F, *supra*), Dr. DeFilippi’s testimony confirms that Cellastim and Exbumin have less than 2% aggregated albumin and therefore satisfy the technical prong of domestic industry. Moreover, using the correct scope of “aggregated albumin” and applying it to Healthgen’s reducing SDS-PAGE data, the results show that both samples of Cellastim and both samples of Exbumin had less than 2% aggregated albumin. (Tr. (Wilken) at 382:1-384:17; *see also id.* at 384:18-386:21.).

For example, under reducing SDS-PAGE, Exbumin sample 2 has a main band at 60.9 kDa, i.e., the weight of an rHSA monomer. Dr. Wilken testified that in view of the weight of the main band (60.9 kDa), one would expect an albumin dimer to appear at 121.8 kDa. (*Id.* at 385:24-386:5.). Since there is no band near 121.8 kDa, Dr. Wilken selected the closest impurity to the value of the expected dimer at 121.8 kDa that was least twice the weight of the main band. (*Id.* at 385:24-386:5; CDX-0001C.0034-35.). If only the 155.5 kDa band is counted as dimeric

rHSA (i.e., aggregated albumin), which Dr. Wilken did, the sample of Exbumin has only 1.1% aggregated albumin.

As with the SGS data described above, Dr. Wilken testified that it would be inappropriate to count all HMW impurities measured in Exbumin sample 2 as aggregated albumin in view of the adopted construction for “recombinant mammalian albumin” and its necessary implications on the scope of “aggregated albumin.” (Tr. (Wilken) at 385:24-386:13, 377:23-378:6; 385:24-386:13.).

For example, the band at 103.4 kDa would consist of, at best, a 60.9 kDa monomer and a 42.5 kDa fragmented protein (the sum of which is 103.4 kDa), or two fragmented proteins of 51.7 kDa (same). Dr. Wilken testified and the evidence demonstrates that because albumin has about 585 amino acids (*see, e.g.*, CX-0898.0002), in both scenarios described above, the fragmented proteins would lack a significant number of amino acids compared with native rHSA (roughly 88 amino acids less for the 51.7 kDa fragmented protein $((60.9 - 51.7) / 68)$ and multiplied by 585), and roughly 176 amino acids less for the 42.5 kDa fragmented protein $((60.9 - 42.5) / 60.9)$ and multiplied by 585), and thus would necessarily lose a significant portion of their structure and function. (Tr. (Wilken) at 377:23-378:6.). As Dr. Wilken testified, such fragmented proteins are not “recombinant mammalian albumin” and thus cannot form “aggregated albumin” as claimed. (*Id.*). Dr. Wilken conducted a similar exercise with other samples tested under reducing SDS-PAGE by Healthgen, and confirmed they have less than 2% aggregated albumin as measured by reducing SDS-PAGE. (*Id.*). at 384:3-17; 385:24-386:13.).

Using a similar analysis, Dr. Wilken concluded that both samples of Cellastim tested under nonreducing SDS-PAGE conditions have less than 2% aggregated albumin. (*Id.* at 382:1-384:17.). For example, under nonreducing conditions, as shown in the annotated image of RX-

0311.0002-3 below, the main band for Cellastim sample 1 runs at about 52.5 kDa and thus the anticipated dimer would be around 105 kDa.

Figure 17: Healthgen Test Results for Cellastim and Exbumin Under Non-Reducing Conditions

NON-REDUCING GEL			NON-REDUCING GEL		
Cellastim S (2 µg), non-reduced, sample 1			Exbumin (2 µg), non-reduced, sample 1		
Band No.	Molecular Weight (kDa)	Band %	Band No.	Molecular Weight (kDa)	Band %
1	118.2	2.5	1	117.4	3.4
2	109.3	1.9	2	107.8	3.0
3	52.5	83.9	3	52.4	82.2
4	44.4	6.5	4	44.4	5.8
5	34.6	5.2	5	34.6	5.6

Cellastim S (2 µg), non-reduced, sample 2			Exbumin (2 µg), non-reduced, sample 2		
Band No.	Molecular Weight (kDa)	Band %	Band No.	Molecular Weight (kDa)	Band %
1	124.0	2.2	1	121.4	2.0
2	114.0	1.1	2	112.4	1.4
3	52.7	87.1	3	52.6	86.5
4	44.1	6.0	4	43.9	6.6
5	34.4	3.6	5	34.4	3.5

(RX-0311.0002-3 (annotated, copied from CBr. at 81.).

The nonreducing SDS-PAGE data for Cellastim sample 1 indicates there are two HMW impurity bands at about 118.2 and 109.3 kDa. (Tr. (Wilken) at 382:25-384:2.). Dr. Wilken explained that if the 109.3 kDa is the dimeric band of albumin, which she selected because it is the band that is closest to the value of the expected dimer at 105 kDa that is at least twice the weight of the main band, then the Cellastim sample 1 has 1.9 percent aggregated albumin as tested by nonreducing SDS-PAGE. (*Id.* at 382:25-383:15.). Dr. Wilken testified that the 118.2 kDa band “doesn’t appear to represent formation of aggregates of the albumin monomer” and thus does not fall under the proper scope of “aggregated albumin” in view of the adopted construction for “recombinant mammalian albumin.” (*Id.*). Dr. Wilken conducted a similar exercise with Cellastim sample 2 and Exbumin sample 2, and confirmed they have less than 2% aggregated albumin as measured by reducing SDS-PAGE. (*Id.* at 384:3-17; 385:24-386:13.).

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

3. OptiPEAK HEK293t, OptiPEAK T Lymphocyte, OptiVERO, and ITSE™ + A

Dr. DeFilippi conceded that if Cellastim satisfies the technical prong of domestic industry, Ventria products OptiPEAK HEK293t, OptiPEAK T Lymphocyte, OptiVERO, and ITSE™ + A would also satisfy the technical prong of domestic industry. (Tr. (DeFilippi) at 1244:15-18 (“Q. And if Cellastim meets the aggregated albumin limitation, then OptiVERO, OptiPEAK, and ITSE + A Ventria products also are domestic industry products, right? A. I think one could conclude that.”)).

As Mr. Deeter and Dr. Wilken confirmed, each of these complete media products [REDACTED]. (Tr. (Deeter) at 148:4-12, 192:3-10; Tr. (Wilken) at 368:2-15.). Thus, they practice the asserted claims for the same reasons set forth above for Cellastim. (Tr. (Wilken) at 368:16-369:1.).

X. INVALIDITY

A. Legal Standards

1. Anticipation

A determination that a patent is invalid as being anticipated under 35 U.S.C. § 102 requires a finding, based upon clear and convincing evidence, that each and every limitation is found either expressly or inherently in a single prior art reference. *See Celeritas Techs. Inc. v. Rockwell Int’l Corp.*, 150 F.3d 1354, 1361 (Fed. Cir. 1998). Anticipation is a question of fact, including whether a limitation, or element, is inherent in the prior art. *In re Gleave*, 560 F.3d 1331, 1334-35 (Fed. Cir. 2009). The limitations must be arranged or combined the same way as in the claimed invention, although an identity of terminology is not required. *Id.* at 1334 (“the

reference need not satisfy an *ipsissimis verbis* test”); MPEP § 2131.

In addition, the prior art reference’s disclosure must enable one of ordinary skill in the art to practice the claimed invention “without undue experimentation.” *Gleave*, 560 F.3d at 1334-

35. A prior art reference that allegedly anticipates the claims of a patent is presumed enabled; however, a patentee may present evidence of nonenablement to overcome this presumption.

Impax Labs., Inc. v. Aventis Pharmaceuticals Inc., 468 F.3d 1366, 1382 (Fed. Cir. 2006).

“[W]hether a prior art reference is enabling is a question of law based upon underlying factual findings.” *Gleave*, 560 F.3d at 1335.

2. Obviousness

Under 35 U.S.C. § 103(a), a patent is valid unless “the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made” to a person having ordinary skill in the art. 35 U.S.C. § 103(a). The ultimate question of obviousness is a question of law, but “it is well understood that there are factual issues underlying the ultimate obviousness decision.”

Richardson-Vicks, 122 F.3d 1476, 1479 (Fed. Cir. 1997) (citing *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17 (1966)).

After claim construction, “[t]he second step in an obviousness inquiry is to determine whether the claimed invention would have been obvious as a legal matter, based on underlying factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the differences between the claimed invention and the prior art, and (4) secondary considerations of non-obviousness.” *Smiths Indus. Med. Sys., Inc. v. Vital Signs, Inc.*, 183 F.3d 1347, 1354 (Fed. Cir. 1999) (citing *Graham*, 383 U.S. at 17). The existence of secondary considerations of non-obviousness does not control the obviousness determination; a

court must consider “the totality of the evidence” before reaching a decision on obviousness.

Richardson-Vicks, 122 F.3d at 1483.

The Supreme Court clarified the obviousness inquiry in *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 389 (2007). The Supreme Court said:

When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. *Sakraida* and *Anderson’s-Black Rock* are illustrative—a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

Following these principles may be more difficult in other cases than it is here because the claimed subject matter may involve more than the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement. Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit.

* * *

The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents. The diversity of inventive pursuits and of modern technology counsels against limiting the analysis in this way. In many fields it may be that there is little discussion of obvious techniques or combinations, and it often may be the case that market demand, rather than scientific literature, will drive design trends. Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility.

KSR, 550 U.S. at 417-19.

The Federal Circuit has since held that when a patent challenger contends that a patent is invalid for obviousness based on a combination of several prior art references, “the burden falls

on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed process, and would have had a reasonable expectation of success in doing so.”

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

The TSM²⁷ test, flexibly applied, merely assures that the obviousness test proceeds on the basis of evidence--teachings, suggestions (a tellingly broad term), or motivations (an equally broad term)--that arise before the time of invention as the statute requires. As *KSR* requires, those teachings, suggestions, or motivations need not always be written references but may be found within the knowledge and creativity of ordinarily skilled artisans.

Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 520 F.3d 1358, 1365 (Fed. Cir. 2008).

B. The Scope and Content of the Prior Art

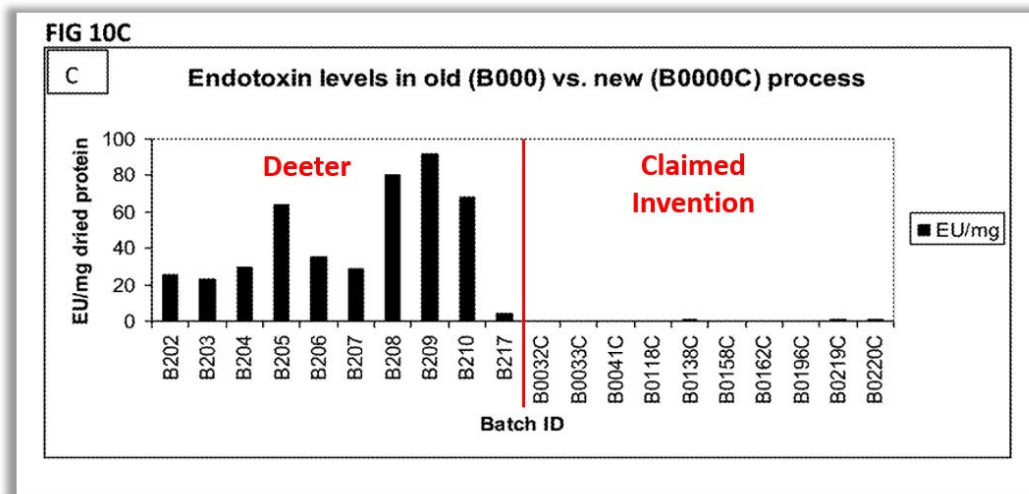
Both Van Urk and Berezenko relate to albumin produced by recombinant *yeast*, and not albumin produced by a recombinant *plant*, as claimed in the '951 patent. In contrast, Deeter relates to Ventria's own first-generation rice-derived rHSA products (aka “old Cellastim”), a reference and product that was expressly cited during prosecution of the '951 patent, and which lacks key elements of the claimed invention, as recognized by the examiner. (Tr. (Wilken) at 1032:17-1034:23, 1062:9-1063:19; JX-0002.0053, 0661, 0664, 0686, 0704, 0705, 0726-28.).

Deeter was cited multiple times during prosecution of the '951 patent as allegedly rendering the claimed albumin compositions obvious. (Tr. (Wilken) at 1062:14-20.) The applicant overcame the rejections by demonstrating unequivocally through *data and evidence* that the claimed recombinant albumin compositions were patentable over the recombinant

²⁷ TSM is an acronym that stands for teaching, suggestion, motivation.

albumin compositions disclosed in Deeter because of the claimed recombinant albumin compositions' unique structural and functional characteristics as compared with that reference. (JX-0002.0661, 0664, 0704-05; Tr. (Wilken) at 1062:21-1063:19.). The same distinctions are also reflected in the '951 patent. (See JX-0001 at Example 6, Fig.10C, Tables E3-E4.). That is, the '951 patent, as filed, contained a significant amount of comparative data distinguishing the rHSA claimed in the '951 patent from the rHSA disclosed in Deeter. For example, the endotoxin levels for the majority of the old Cellastim (Deeter) products that were tested had levels ranging from 23.1 EU/mg up to 91.8 EU/mg (average of 45.0 EU/mg), whereas those of the claimed invention were consistently less than 1 EU/mg, as shown in the annotated version of '951 patent Figure 10C below.

Figure 18: Figure 10C of the '951 Patent



(JX-0001 at Fig. 10C (annotated, copied from CRBr. at 25).).

Cell viability was also seen to decrease dose-dependently when using the old Cellastim (Deeter) in cell culture. (*Id.* at Tables E3, E4.). As applicant's declarant explained, through the invention of the '951 patent, Ventria was able to achieve the claimed albumin compositions with

consistent endotoxin levels for every batch tested below 1 EU/mg, and which avoided the dose-dependent negative impact on cell viability of Deeter. (JX-0002.0709-13.). As a result, the examiner withdrew its objections based on Deeter, noting that the data demonstrates “the compositions of Deeter et. al. are incapable of achieving the claimed less than 1 EU of endotoxin/mg of albumin and that the levels of endotoxins in the cell culture medium were not appreciated at the time of Deeter’s invention.” (JX-0002.0726-27; *see also* Tr. (Wilken) at 1070:12-24.).

Healthgen asserted Huang against claims 12 and 13 only. As Dr. Wilken explained, the Huang reference does not provide additional information with respect to Healthgen’s allegations beyond that which is already disclosed in Deeter. (Tr. (Wilken) at 1073:12-15.). Huang merely discusses methods of improving the upstream process of producing rHSA in a rice cell culture that is secreted into the media, i.e., improving production, and not on achieving any composition capable of encompassing the claims of the ’951 patent. (*Id.* at 1073:16-22; JX-0028.). As with Deeter and Berezenko (and the substance of Van Urk), the Huang reference was before the examiner during prosecution. (JX-0001.0003.).

C. The Prior Art References Do Not Anticipate the Asserted Claims of the ’951 Patent

1. Claim 1

a) Healthgen Failed to Demonstrate that Each Claim Element Is Present in Either Van Urk or Berezenko

As an initial matter, Healthgen failed to demonstrate that each of the claim limitations is present in either Van Urk or Berezenko. For example, Healthgen asserted that both Van Urk and Berezenko disclose a cell culture media supplement comprising a recombinant mammalian albumin that is produced in a transgenic plant. (RBr. at 7-9, 18-19.). However, Dr. Wilken

explained that “neither the Van Urk nor Berezenko [references] . . . disclose any proteins produced in a transgenic plant, specifically recombinant mammalian albumin in a transgenic plant, certainly not a recombinant human serum albumin in a transgenic plant, certainly not in transgenic grain or transgenic rice.” (Tr. (Wilken) at 1066:12-18.). Dr. DeFilippi acknowledged that the “Van Urk reference, like Berezenko, is directed to a human serum albumin product derived from yeast.” (Tr. (deFilippi) at 951:20-23.).

Berezenko does not disclose any recombinant mammalian albumin produced in a transgenic plant *at all*, for use in a cell culture media or otherwise. The only Berezenko quotation Healthgen cited as support for its alleged disclosure of the plant limitation is the following: “Many expression systems are known, including . . . plant cells.” (RBr. at 19; JX-0027 at 3:39-43.). However, as Ventria pointed out, this quote does not say that such expression systems can be used for recombinant mammalian proteins, nor does it say that any such proteins can be used to create a cell culture media supplement. (CRBr. at 5.). It simply discloses the statement that expression systems in plants were known.²⁸

Likewise, Healthgen failed to show that Van Urk discloses a cell culture media supplement or complete media composition comprising a recombinant mammalian albumin that is produced in a transgenic plant. Van Urk’s disclosure with respect to cell culture is purely aspirational, stating that it “*may* be fulfil [sic] various roles” and “*may* be used.” (JX-0030.0025 (emphases added).). Van Urk does not contain any disclosure, plant-related or otherwise, of any such albumin actually being used as a cell culture media supplement. (*See generally*, JX-0030.).

Healthgen has also asserted that both references disclose a recombinant mammalian

²⁸ The word “plant” only appears in one other portion of Berezenko, in the context of a manufacturing facility (i.e., manufacturing plant), not “plant,” the organism. (JX-0027 at 31:35-40.).

albumin for use in a cell culture comprising less than 1 EU of endotoxin/mg of albumin. (RBr. at 7-9, 11-14, 18-19, 21-22.). Critically, Healthgen failed to demonstrate the recited endotoxin level in either reference. For example, endotoxin is mentioned in only two (2) passages of Van Urk. One passage is in the Examples, which merely indicates a “solution of drug product” was assayed for endotoxin levels. (JX-0030.0074.). Van Urk does not indicate what this “solution of drug product” is (“drug product” is only mentioned in this one passage without an antecedent basis), or provide details concerning the “solution of drug product’s” composition, how it was made, or how it was purified. (*Id.*). The second mention is similarly deficient. Healthgen asserted that Van Urk discloses the albumin as being “‘essentially free’ of endotoxin.” (RBr. at 12.). As Ventria noted, the quote is incomplete and misleading. Rather than stating that the disclosed product is specifically free of endotoxin, Van Urk instead states that the albumin is characterized as being essentially free of any number of optional characteristics, including the word “or” directly prior to the word “endotoxin,” denoting these characteristics are not necessarily present. The full quotation is as follows:

Figure 19: Quotation from Van Urk

The albumin is also characterised by extremely low levels of, or by being essentially free of, aluminium, lactate, citrate, metals, non-albumin human proteins, such as immunoglobulins, pre-kallikrein activator, transferrin, α_1 -acid glycoprotein, haemoglobin and blood clotting factors, prokaryotic proteins, fragments of albumin, albumin aggregates or polymers, or endotoxin, bilirubin, haem, yeast proteins, animal proteins and viruses. By essentially free is meant below detectable levels.

(JX-0030.0023 (annotated, copied from CRBr. at 6).).

There is no disclosure here of recombinant mammalian albumin for use in a cell culture that actually contains such levels of endotoxin. Moreover, the quoted section specifically relates to “fungal cell[s],” and not transgenic plants. (*Id.*).

The disclosures of Van Urk also do not show data that demonstrate that the yeast compositions are endotoxin-free, much less that it has less than 1 EU of endotoxin/mg of albumin. (*Id.*). Nor is there any evidence that the disclosure of “no detectable endotoxin” is with respect to a specific type of *yeast*-derived rHSA. The statement was made with respect to an unknown product, as part of a list of potential characteristics, many of which are merely aspirational, as Dr. Wilken explained. (Tr. (Wilken) at 1067:23-1068:8.). Similarly, endotoxin is mentioned only twice in Berezenko, both in the context of non-descript, aspirational statements of potential characteristics, noting there can be “extremely low levels of, or . . . being essentially free of” a laundry list of possible substances, of which endotoxin is only one (JX-0027 at 1:42-48), and “[t]he medium for rHA production [in yeast-derived Example 1] *can be* ultrafiltered (10,000 Mol. Wt. cut-off) to remove endotoxins.” (*Id.* at 7:15-20 (emphasis added); Tr. (Wilken) at 1068:22–1069:4.). Berezenko does not show any data associated with its claim that the yeast compositions are endotoxin-free, much less that it has less than 1 EU of endotoxin/mg of albumin. (*See generally*, JX-0027.). Thus, Berezenko fails to disclose any formulations that actually have less than 1 EU endotoxin/mg of albumin. (*Id.*).

Healthgen also failed to demonstrate that Van Urk discloses recombinant albumin comprising less than 2% aggregated albumin, yeast-derived or otherwise. Dr. DeFilippi based his opinion on a single sentence from Van Urk that concerns the monomer content of the yeast-derived rHSA as tested by reducing SDS-PAGE, a test which he otherwise has asserted is inappropriate for quantification of aggregate or monomer albumin content. (CBr. at 31-33.). During the Hearing, Dr. DeFilippi contradicted himself, asserting that the analysis in Van Urk was not based on reducing SDS-PAGE. However, during cross-examination, he acknowledged that given his position on infringement, his invalidity opinion is a “bit of a stretch.” (Tr.

(DeFilippi) at 959:22-963:25.). Dr. DeFilippi's inconsistent assertion that "Van Urk did not purport to quantify the level of aggregated albumin using Reducing SDS-PAGE" has been given little, if any, weight. Thus, Healthgen failed to present any evidence regarding the monomer content disclosed in Van Urk. (RBr. at 15; *see also* CBr. at 31-33.).

For the foregoing reasons, Healthgen failed to prove by clear and convincing evidence that claim 1 is anticipated by Van Urk or Berezenko.

b) Healthgen Failed to Demonstrate Each Claim Limitation Is Present in the Combination Claimed in the '951 Patent, or that a Person of Ordinary Skill in the Art Would at Once Envisage Such a Combination

Healthgen's anticipation argument fails for the separate reason that Healthgen failed to demonstrate that each limitation is present in either Van Urk or Berezenko in the combination claimed in the '951 patent, or that one of ordinary skill would at once envisage such a combination. *See Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1381 (Fed. Cir. 2015). It is not enough for Healthgen to argue that the expression of recombinant proteins in plants was allegedly disclosed, and that certain disclosed yeast-derived products allegedly had less than 1 EU of endotoxin and less than 2% aggregates. To meet its burden, Healthgen must demonstrate, by clear and convincing evidence, that Van Urk and Berezenko specifically disclose a cell culture media supplement comprising a recombinant mammalian albumin that is produced in a transgenic plant, and which itself having been produced in a transgenic plant also contains less than 1EU endotoxin/mg albumin and less than 2% aggregated albumin. Healthgen failed to do so because each of the alleged statements with respect to aggregates and endotoxin from Van Urk and Berezenko relate to yeast-derived rHSA, not plant-derived rHSA, and a person of ordinary skill would recognize the inapplicability of yeast-related disclosures to plant-

derived proteins.

For example, literature published before and after the invention date, the prosecution history of the '951 patent, statements by Healthgen inventors with respect to their own rice-produced rHSA, the knowledge of a person of ordinary skill at the time of the invention, the disclosure and data set forth in the '951 patent, and the testimony of Dr. Wilken all establish that “recombinant mammalian albumin” “produced in a transgenic plant” confers the claimed albumin compositions with markedly different structural properties when compared with recombinant mammalian albumin produced in non-plant host cells, including animals and yeast (such as those of Van Urk and Berezenko). (*See* Section X.C.1(c)-(d), *infra*; Tr. (Wilken) at 1047:21-23.).

One of ordinary skill would understand that the teachings of Van Urk or Berezenko with respect to endotoxin or albumin levels (to the extent there are any) would be specific to yeast-derived recombinant albumin and, therefore, inapplicable to plant-derived recombinant albumin. (*See* Section X.C.1(c), *infra*). Thus, that Van Urk and Berezenko mention the word “plant” does not change the fact that neither contains teachings or disclosure of the specific combination of claim elements present in claim 1 of the '951 patent.

c) A Person of Ordinary Skill in the Art Would Understand Disclosures Specific to Yeast-Derived rHSA Would Not Read on Plant-Derived rHSA

As Dr. Wilken explained, plants and yeast are from entirely different kingdoms, and have significant structural and functional differences. (Tr. (Wilken) at 1022:21–1023:14.). Whereas plants are multicellular organisms and are autotrophs, meaning they harness energy from the sun, yeast are unicellular heterotrophs. (*Id.* at 1023:15-25.). These differences greatly alter their physiology, and in turn present a “different profile of impurities,” which necessarily alters the

methods used to purify the recombinant protein away from such impurities. (*Id.* at 1025:9-12.). Even within the same host organism, extraction methods and downstream processing steps such as purification methods vary greatly based on where the recombinant protein is expressed. (*Id.* at 1025:13-20, 1029:2-15.). For example, some methods of generating recombinant proteins, such as that of the DI products practicing the '951 patent, utilize a seed-based expression system, whereby the recombinant protein is expressed within the plant seed, but not in the other parts of the plant such as the leaves or roots. (*Id.* at 1028:14-20, 1029:16-20.). Other plant-based expression systems accumulate the recombinant protein elsewhere, such as the leaves. (*Id.* at 1029:2-6.). As Dr. Wilken explained, "if you express something within a seed, that's going to be -- it would look differently than if you express it within a leaf. That's because we have different impurities and we need to address those impurities differently." (*Id.* at 1025:13-20.). Thus, even within the same host organism, the choice of expression system can greatly alter the required downstream processing steps, such as the particular techniques required for purification. (*Id.* at 1025:13-20, 1029:2-15.).

Dr. Wilken explained that yeast-derived recombinant proteins such as those of Van Urk and Berezenko are grown in an extracellular bio-reactor based system, rather than extracted from the tissue of a plant grown in a field. (*Id.* at 1026:1-1027:5, 1029:21-1030:3.). She testified that in such bio-reactor systems, the recombinant protein is grown in a cell culture in a lab, in media which contains the nutrients required for those cells to grow, with the recombinant protein being secreted directly into the media. (*Id.* at 1026:1-9, 1026:22-1027:13.). As the cell culture grows, it consumes some of those nutrients, resulting in depleted media. Dr. Wilken explained that this means the media (containing the recombinant protein) has depleted a certain amount of the nutrients but will also contain waste products. (*Id.* at 1029:19-1030:19.). This results in a "very

different” impurity profile than would be associated with plant-based recombinant proteins. (*Id.*). Furthermore, Dr Wilken explained that bio-reactor expression systems are accomplished under conditions in which the laboratory workers can sterilize the media prior to inoculating the culture, which allows for control over the process and any potential contaminants that may be introduced. (*Id.* at 1026:10-17.). In contrast, as Dr. Wilken explained, seed-based proteins derived from plants are grown in a field, where they are exposed to bacteria and therefore, endotoxins. (*Id.* at 331:23–332:15.). Consequently, the process of growing yeast-based recombinant proteins in a lab will “certainly” result in a different background of impurities than expected from a rice-seed based expression system. (*Id.* at 1030:14-19.).

Furthermore, Dr. Wilken testified that due to albumin’s numerous fatty acid binding sites, there are a wide variety of fatty acids with differing characteristics that can bind to these sites on the albumin, with the type of fatty acid differing based on the production system, e.g., rice or yeast.

Q. What kind of fatty acids do we find bound to albumin?

A. Those would be based on the production system.

Q. What do you mean they are based on the production system?

A. Those fatty acids are coming from whatever, for example, yeast or potentially rice. Those -- that is where the fatty acids are introduced into the HSA.

Q. Do you expect, as one of skill in the art, to have different molecules, different substances, bound to those fatty acid binding sites dependent on which host the recombinant human serum albumin was produced in?

A. Absolutely. There’s a wide variety of various fatty acids and fatty acid structure. It’s a general term that has certain characteristics, but that how many – how long the carbon chain is and the particular either saturated or unsaturated, the bonds present, would depend on what organism is producing those fatty acids.

(*Id.* at 1037:10-1038:2.).

She explained that these fatty acids have been demonstrated to co-purify, i.e., remain with the albumin when extracted from the host, leaving a fingerprint on the final product composition and impacting the overall function and performance of the product. (*Id.* at 1038:3-17.).

Dr. Wilken also explained that the difference between yeast-based rHSA systems such as those of Van Urk and Berezenko, and plant-based systems such as that of the '951 patent, directly affects the real-world extraction and purification techniques required to prepare properly functioning albumin products, and to separate the recombinant proteins from those varying impurities. (*Id.* at 1042:4-22; CX-0901-0003.). For example, Dr. Wilken testified that yeast-based and rice-based recombinant albumin have been shown to have different isoelectric points, which is a factor that is “very important” to a skilled artisan because it can affect the interactions between the “product and any impurity present in the extract,” as well as impact “charge-based separation” techniques. (Tr. (Wilken) at 1042:4- 22.). She stated that the isoelectric point is the pH for which a protein carries a net zero charge. (*Id.* at 1043:1-7.). Dr. Wilken clarified that if the pH rises above the isoelectric point, the protein will carry a negative charge, and if below the isoelectric point, it will carry a positive charge. (*Id.*). She also explained that purification techniques, including the chromatography methods Healthgen asserted would be employed to remove endotoxin, utilize *electric charge to accomplish the separation*, and as a result, the laboratory worker needs to select the proper pH to provide the charge needed to purify or extract the protein from the various impurities. (*Id.* at 1043:8-17; RBr. at 36 (“purification processes described in Van Urk and Berezenko, e.g., DEAE-Sepharose chromatography, which *separates endotoxins from recombinant albumin by the difference in their charges*”) (emphasis added).).

Given the foregoing, the recovery and purification of recombinant proteins and the

identification of extraction conditions remains the subject of intense experimentation that is typically done on a case-by-case basis because it depends on the particular expression system being used as well as the requirements and intended applications of the recombinant protein. (CX-1051; JX-0139.). As of the priority date for the '951 patent, and thereafter, the industry recognized significant advancements were needed with respect to downstream processing for plant-based recombinant systems. (CX-0901.0013; Tr. (Wilken) at 1058:19-1060:1.). Notably, in 2018, Healthgen's President, Daichang Yang, authored a book chapter discussing the challenges associated with developing downstream processing techniques (e.g., purification) for the recovery of rHSA. (JX-0023.0004; Tr. (Wilken) at 1057:3–1058:1.). As Dr. Wilken explained, there is no “one-size-fits-all approach” for developing downstream processes (e.g., purification methods) for recombinant proteins. (Tr. (Wilken) at 1056:6-1057:2; *see also* JX-0139.). There are multiple production platforms, expression strategies and extraction and purification processes which result in differing outcomes depending on the methods used. (CX-0901; CX-0896.). Thus, a person of ordinary skill would have understood that plant and yeast-derived rHSA are not interchangeable, and that any given finding or technique used with yeast would not inform or read upon plants. (Tr. (Wilken) at 1071:1-24.).

d) The Substance of Both References Was Already Considered by the PTO

The claims of the '951 patent have already survived a challenge based on the same assertion Healthgen made: that they are anticipated by prior art disclosures which are specific to yeast-derived rHSA.

For example, the patent examiner initially rejected certain claims as anticipated by the Berezenko reference. (JX-0002.0562; Tr. (Wilken) at 1060:22-1062:6.). In overcoming this and

other rejections, the applicant argued that “those skilled in the art would immediately recognize that the recombinant albumin produced in a transgenic plant will be different from a naturally occurring mammalian albumin” for numerous reasons, and that this difference is “exemplified by the data” disclosed in the application. (JX-0002.0662.). The applicant also explained that the Berezenko reference relates to the yeast-derived Novozymes CellPrime product for which comparative data was disclosed. (*Id.* at 0663-64.). Such data showed the difference between the claimed plant-derived rHSA and Berezenko’s yeast-derived rHSA, including data that Ventria’s plant-derived rHSA is five-times more active in promoting cell viability than the yeast-derived HSA. (JX-0001.0021; JX-0002.0663-64; Tr. (Wilken) at 1047:24-1049:15, 1061:10–1062:6.). In recognition of the difference between the two (2) systems, the examiner withdrew the rejection, and acknowledged that the specification and data contained therein demonstrated the “mammalian albumin produced in a transgenic plant has differential effects on the cultured cells in comparison to other expression systems,” and that the products of the patent are “distinct” from those of the prior art. (JX-0002.0686, 0687; JX-0002.0661; JX-0002.0727-28.). Thus, the evidence shows the PTO was well-aware of and had expressly considered yeast-derived rHSA systems, including that of Berezenko.

Healthgen asserted that Van Urk was not considered by the PTO. However, Healthgen did not dispute that the substance from Van Urk upon which Healthgen relied was also contained in Berezenko. First, the disclosed technology in Van Urk is from the same applicant (Delta Biotechnology Limited) and research group whose work in yeast-derived albumin (Berezenko) was the basis for the examiner’s initial anticipation rejection. (Tr. (DeFilippi) at 929:23-930:12; JX-0027.0001; JX-0030.0001.). Second, as Dr. Wilken explained, the content of both references is consistent with one another. (Tr. (Wilken) at 1065:15-1066:9.). Moreover, Dr. DeFilippi

acknowledged that the portions of Van Urk upon which he relied for his opinions on anticipation are “very similar” to those of Berezenko. (Tr. (DeFilippi) at 951:24–952:2, 956:6-9.

e) Neither Reference Enables the Production of the Claimed Product

To be anticipatory, a reference must not only disclose each element as arranged and combined in the claim, but must also enable the asserted claim, such that a person of ordinary skill in the art “can practice the subject matter based on the reference, without undue experimentation.” *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1082 (Fed. Cir. 2008) (citations omitted). As Dr. Wilken explained, neither Van Urk nor Berezenko accomplish this because there are no details or guidance in either disclosure that would put one of ordinary skill in possession of the claimed albumin compositions without burdening them with undue experimentation. (Tr. (Wilken) at 1066:22-1067:4.).

Van Urk only mentions the term “plant” five (5) times in passing throughout its 103-page disclosure, while Berezenko only mentions the term “plant” in passing, each time in the context of general, laundry-list statements alleging the teachings are applicable to any type of organism—plant, bacteria, animal, etc.—without accompanying data, instructions, evidence, disclosure, or experiments demonstrating how such non-yeast organisms can be genetically modified to express rHSA, and that said rHSA could successfully be produced, extracted, and purified therefrom. (*Id.* at 1067:6-22, 1068:10-20; JX-0030 at 16:13-19; JX-0027 at 31:27-41, 3:39-46.). The only working examples in each reference involve rHSA derived from yeast. (JX-0030 at 15:5-9; JX-0027 at 1:11-17, 2:13, 5:10-32:67; Tr. (Wilken) at 1067:12-22, 1068:13-16.). None of the examples describes the transfection, growth, production, extraction, or purification of rHSA from any other organism, including other types of yeast. (*See generally*, JX-0030; JX-

0027.).

Moreover, both references disclose numerous permutations without any guidance as to which of the possibilities for transfection, production, extraction, and purification would result in the claimed plant-derived compositions. (JX-0027 at 11-12, 12:65-13:7, 16:63-17:4, 18:55-66; JX-0030 at 5:1-11, 6:8-17, 7:14-27.). As Dr. Wilken explained, there is no “one-size-fits-all approach” for developing downstream processes for recombinant proteins. (Tr. (Wilken) at 1056:6-1057:2.). Even years after the priority date for the ’951 patent, there remained a significant amount of experimental design required to properly express and purify recombinant proteins, with such designs typically being done on a case-by-case basis. (*See* Section X.C.1; *see generally* Tr. (Deeter) at 151:22-154:23.).

2. Claim 11

Claim 11, which depends from claim 1, further limits the claimed recombinant mammalian albumin to rHSA. (JX-0001 at cl. 11.). As discussed above in Section X.C.1, neither Van Urk nor Berezenko disclose the claimed recombinant mammalian albumin, and therefore also do not disclose rHSA.

Accordingly, Healthgen failed to prove by clear and convincing evidence that claim 11 of the ’951 patent is anticipated by Van Urk or Berezenko.

3. Claims 12 and 13

Claim 12 recites: The composition of claim 1, wherein said transgenic plant is a transgenic grain. (JX-0001 at cl. 12.). Claim 13 further limits said transgenic grain to transgenic rice. (*Id.* at cl. 13.). Healthgen is no longer asserting that Berezenko anticipates claims 12 or 13, or that Van Urk anticipates claim 13. (Tr. (DeFilippi) at 933:12-22, 951:14-19.). Healthgen’s sole argument with respect to the alleged anticipation of these dependent claims is that Van Urk

anticipates claim 12. As discussed above in Section X.C.1, Van Urk does not disclose a recombinant, plant-produced protein, much less the claimed plant-produced recombinant mammalian albumin compositions. For the same reasons, Van Urk does not disclose a recombinant mammalian albumin produced in a transgenic grain, which is a specific type of plant.

Notably, the term “grain” is not mentioned even once in Van Urk. (*See generally*, JX-0030.). As Dr. Wilken explained, Van Urk fails to “disclose any proteins produced in a transgenic plant . . . [and] certainly not in transgenic grain.” (Tr. (Wilken) at 1066:12-18.). Healthgen argued that Van Urk meets the transgenic grain limitation because it contains the word “corn (maize).” (RBr. at 17.). Importantly, Healthgen’s argument directly contradicts Dr. DeFilippi’s admission that Van Urk does not disclose a process for obtaining rHSA from said corn.

Q. But Van Urk has no -- explains no process specifically for expressing the product from the corn, does it?

A. From the point of view of genetics and expression, he does not specifically describe the genetics -- the way to get the gene into corn. I believe that is correct.

For the reasons discussed above, Healthgen failed to prove by clear and convincing evidence that claims 12 and 13 of the ’951 patent are anticipated by Van Urk.

D. The Prior Art References Do Not Render Obvious the Asserted Claims of the ’951 Patent

1. A Person of Ordinary Skill in the Art Would Not Be Motivated to Combine Deeter with Van Urk or Berezenko

To prove obviousness based on a combination of references, Healthgen must explain why a person of skill in the art would have been motivated to combine specific references and reasonably expect success in achieving the claimed invention. *Personal Web Techs. LLC v.*

Apple, Inc., 848 F.3d 987, 993 (Fed. Cir. 2017). For the following reasons, Healthgen failed to meet its burden.

As discussed above in Section X.B, although Deeter is directed to old Cellastim, a plant-derived HSA product, Van Urk and Berezenko concern the purification of yeast-derived HSA. Given the vast differences between plant-derived and yeast-derived products, a POSA would not look to the disclosures of Van Urk or Berezenko, which call out purification steps specific to particular yeast-derived impurities. (Tr. (Wilken) at 1071:8-13; Section X.C.1(c).)

For example, both Van Urk and Berezenko confirm that their purification steps are tailored specifically to yeast and removing yeast contaminants/impurities. Van Urk states that the steps in its purification process are designed to “give increased yeast antigen clearance” (JX-0030.0001), and then describes how multiple steps in its purification process “removes yeast antigens.” (*Id.* at 0056.). Similarly, Berezenko states that “rHA is concentrated and purified with respect to at least yeast antigens,” and proceeds to make similar statements regarding the purpose of its affinity, anion exchange, and gel permeation chromatography steps. (JX-0027.0013.).

Dr. Wilken explained that in contrast with terrestrial systems (e.g., plants grown in a field), the yeast-specific proteins of Van Urk and Berezenko are grown in a bio-reactor and secreted directly into the media, which alters the profile contaminants introduced through the process. (Tr. (Wilken) at 1026:1-17, 1029:19-20.). Accordingly, it “would not be suitable to apply one particular system to the other” given the “need to discriminate between the properties of the impurities and the recombinant protein.” (*Id.* at 1071:8-19.).

Healthgen failed to demonstrate why a person of ordinary skill in the art would have been motivated to modify the “entirely plant-based” compositions of Deeter with any alleged

purification techniques disclosed in Van Urk and Berezenko for yeast-derived rHSA. Dr. DeFilippi testified that he could not recall having seen any peer-reviewed literature discussing the use of a purification system designed for one transgenic species for a different transgenic species. (Tr. (DeFilippi) at 950:20-25.). As explained above in Section X.C.1(c), given the stark differences between recombinant proteins produced in a transgenic plant from yeast-derived proteins, one of ordinary skill would not look to disclosures focused solely on yeast-produced proteins in an attempt to modify the plant-specific disclosure of Deeter.

2. Deeter in View of Van Urk or Berezenko

a) Claim 1

Deeter does not disclose a recombinant mammalian albumin produced in a transgenic plant which has less than 1 EU endotoxin/mg albumin, nor do Van Urk or Berezenko. (*See* Section X.C.1, *supra.*). As Dr. DeFilippi acknowledged, before 2009, there was no rHSA produced in transgenic rice that was free from endotoxin or had less than 1EU of endotoxin per milligram of albumin, including the product of Deeter. (Tr. (DeFilippi) at 980:7-12.).

Healthgen argued that both Van Urk and Berezenko describe purification processes that achieved less than 1EU of endotoxin/mg of HSA, and that a person of ordinary skill would expect that further purifying the rHSA of Deeter would result in rHSA containing less than 1 EU endotoxin/mg albumin. (RBr. at 40-43.). This is incorrect. As discussed above, endotoxin is only mentioned in a single passage of Van Urk, which merely indicates a “solution of drug product” was assayed for endotoxin while Berezenko merely indicates the medium for rHA production “*can be*” filtered to remove endotoxins. (*See* Section X.C.1, *supra.*). Neither reference describes any yeast-derived rHSA (much less plant-derived) being free of or having any particular level of endotoxins, or which of the limitless sets of yeast-specific purification

permutations would allegedly result in rHSA with the level of endotoxins claimed in the '951 patent. (*Id.*). Neither reference provides data associated with a claim that either composition may allegedly be free of or have low levels of endotoxin. (*Id.*).

Dr. Wilken explained that plant-derived and yeast-derived HSA will have different impurity profiles, which will alter their isoelectric points and, in turn, will fundamentally alter the purification process and ability to separate albumin from such impurities based on electric charge. (*See* Section X.C.1(c) *supra*; Tr. (Wilken) at 1042:4–1043:17.). This includes the separation of endotoxin from albumin, which Healthgen acknowledged is accomplished “by the differences in their charges.” (RBr. at 36.). Thus, one of ordinary skill would not expect that the processes of Van Urk or Berezenko would be applicable to the removal of endotoxin from the plant-derived proteins of Deeter, much less to the claimed limit of 1 EU/mg albumin. (Tr. (Wilken) at 1069:9-1070:3.).

Healthgen contended that the isoelectric point is irrelevant because “Ventria’s own cited document shows that” certain albumin has consistent isoelectric values. (RBr. at 40 n.9.). However, Healthgen did not cite to any Ventria documents in support. Instead, Healthgen cited to one of its own internal documents that does not relate to a comparison of yeast-derived and plant-derived HSA, but rather the isoelectric point of Healthgen’s infringing plant-based OsrHSA and certain plasma-derived HSA. (JX-0009C.0028 (“Results show that OsrHSA and pHSA have...”)).

Moreover, Healthgen failed to provide any evidence that purification of the product of Deeter with any alleged process of Van Urk or Berezenko would result in the claimed composition. Healthgen asserted, based solely on Dr. DeFilippi’s testimony and without any documentary support, that a process which removed endotoxin from albumin would be expected

to work regardless of whether the albumin was produced in rice or yeast.²⁹ (RBr. at 40.).

Healthgen's failure to provide documentary support for this position is informative, particularly given the fact that Dr. DeFilippi admitted he "do[es] not" have "experience producing or purifying recombinant proteins in plants." (Tr. (DeFilippi) at 920:19-21.).

Deeter also does not disclose a recombinant mammalian albumin produced in a transgenic plant having less than 2% aggregated albumin (and Healthgen has not asserted otherwise), nor do either Van Urk or Berezenko. (Tr. (Wilken) at 1072:17-1073:2; RBr. at 24-44.). There is no disclosure of data or results confirming "there may be up to 1% dimeric albumin," much less disclosure or examples in Van Urk that tie the allegedly low aggregated albumin levels of its yeast products to a plant-produced recombinant mammalian albumin. (JX-0030; Section X.C.1, *supra*.). There also is no disclosure in Berezenko of a plant composition possessing the less than 2% aggregated albumin. (Section X.C.1, *supra*.).

Healthgen's assertion that "Deeter's recombinant albumin, as purified by method [sic] disclosed in Van Urk or Berezenko, would remain a 'cell culture media supplement'" is also incorrect. (RBr. at 38.). Healthgen does not cite to anything in support of its assertion that the result of this combination would "remain" a cell culture media supplement. (*Id.*). As discussed above, a person of ordinary skill in the art would not expect the teachings with respect to yeast-derived rHSA to be applicable to plant-derived rHSA. (See Section X.C.1(c), X.D.1; Tr. (Wilken) at 1056:6-1057:2.). Healthgen failed to offer any evidence as to what steps or

²⁹ Healthgen asserted that the Matejtschuk reference demonstrates Van Urk or Berezenko combined with Deeter would result in a plant-derived recombinant protein with less than 1 EU endotoxin/mg albumin. (RBr. at 27 (citing RX-0024.0006).). According to Healthgen, Matejtschuk utilized the same "DEAE-Sephrose" chromatography purification technique of Van Urk and Berezenko, to "consistently lower[]" endotoxin concentrations in albumin" derived from *plasma*. (RBr. at 27, 42-43; RX-0024.0002, 0006.). However, as Ventria noted, Healthgen did not raise this argument in its Pre-Hearing Brief. (CRBr. at 34 n.8.). Thus, this argument has been waived under Ground Rule 7.2.

conditions one of ordinary skill would alter, employ, remove, and/or add from Deeter in view of Van Urk or Berezenko to arrive at any composition achieving less than 2% aggregated albumin, much less, one that would remain a cell culture media supplement. (*See* Section X.C.1(e), *supra.*). In sum, Healthgen failed to demonstrate that the already purified product of Deeter, subsequently purified by the methods of Van Urk or Berezenko, could be used as a cell culture media supplement, or would contain less than 2% aggregated albumin, particularly given the fact that both references indicate the steps in their processes were designed for the removal of “yeast antigens.” (*Id.*; JX-0030.0045-46; JX-0027.0013.).

For these reasons, Healthgen failed to prove by clear and convincing evidence that claim 1 would have been obvious over Deeter in view of Van Urk or Berezenko.

b) Claim 11

Claim 11 depends from claim 1, and further requires the composition of claim 1, wherein said albumin is recombinant human serum albumin. As discussed above, neither combination discloses the claimed recombinant mammalian albumin, and therefore also cannot disclose the claimed recombinant human serum albumin. (*See* Section X.D.1(a), *supra.*).

For these reasons, Healthgen failed to prove by clear and convincing evidence that claim 11 would have been obvious over Deeter in view of Van Urk or Berezenko.

3. Deeter and/or Huang in View of Van Urk or Berezenko

a) Claims 12 and 13

Claims 12 depends from claim 1, and further limits said transgenic plant to a transgenic grain. Claim 13 further limits said transgenic grain to a transgenic rice. As discussed above, no combination of Van Urk and/or Berezenko with Deeter discloses the claimed plant-produced recombinant mammalian albumin compositions. (*See* Section X.D.1(a), *supra.*). Thus, they also

fail to disclose a recombinant mammalian albumin produced in a transgenic grain, much less a transgenic rice.

Healthgen argued claims 12 and 13 are obvious when the combination of Van Urk or Berezenko with Deeter is further combined with Huang. (RBr. at 28-33.). However, the Huang reference does not add anything beyond the already deficient disclosures of Van Urk, Berezenko, and Deeter, and therefore fails to render claims 12 and 13 obvious for the same reasons previously discussed. (Tr. (Wilken) at 1073:12-15; JX-0028.). Rather, Huang merely discusses methods of improving the upstream process of producing rHSA in a rice cell culture that is secreted into the media, i.e., improving production, not on purifying or achieving any composition of said rHSA capable of encompassing the claims of the '951 patent. (Tr. (Wilken) at 1073:16-22; JX-0028.). As with Deeter and Berezenko (and the substance of Van Urk), the Huang reference was in front of the Examiner during prosecution of the '951 patent, and the examiner was not persuaded its disclosure rendered any claim obvious. (JX-0001.0003.).

For these reasons, Healthgen failed to prove by clear and convincing evidence that claims 12 and 13 would have been obvious over Deeter and/or Huang in view of Van Urk or Berezenko.

4. Secondary Considerations

Because this determination finds that the '951 patent is not obvious, secondary considerations need not be examined.

XI. ECONOMIC PRONG OF THE DOMESTIC INDUSTRY REQUIREMENT

A. Legal Standard

The Commission may only find a violation of Section 337 “if an industry in the United States relating to the articles protected by the patent . . . exists or is in the process of being established.” 19 U.S.C. § 1337(a)(2) (emphases added). Typically, a complainant must show

that a domestic industry existed at the time the complaint was filed. *See Motiva LLC v. Int'l Trade Comm'n*, 716 F.3d 596, 601 n.6 (Fed. Cir. 2013).

The domestic industry requirement consists of a “technical prong” and an “economic prong.” *See, e.g., Certain Elec. Devices, Including Wireless Commc'n Devices, Portable Music & Data Processing Devices, & Tablet Computs.*, Inv. No. 337-TA-794, Order No. 88, 2012 WL 2484219, at *3 (June 6, 2012); *Certain Unified Commc'ns Sys., Prods. Used with Such Sys., and Components Thereof*, Inv. No. 337-TA-598, Order No. 9 at 2 (Sept. 5, 2007) (“*Communications Systems*”). A complainant satisfies the “technical prong” of the domestic industry requirement when it proves that its activities relate to an article “protected by the patent.” *See Communications Systems*, Order No. 9 at 2. A complainant satisfies the “economic prong” of the domestic industry requirement when it demonstrates that the economic activities set forth in subsections (A), (B), and/or (C) of Section 337(a)(3) have taken place or are taking place with respect to the protected articles. *See id.*

Subsection 337(a)(3) states that:

(3) For purposes of paragraph (2), and industry in the United States shall be considered to exist if there is in the United States, with respect to the articles protected by the patent, copyright, trademark, mask work, or design concerned –

- (A) significant investment in plant and equipment;
- (B) significant employment of labor, or capital; or
- (C) substantial investment in its exploitation, including engineering, research and development, or licensing.

19 U.S.C. § 1337(a)(3).

Because the criteria are listed in the disjunctive, satisfaction of any one of them will be sufficient to meet the economic prong of the domestic industry requirement. *Certain Integrated Circuits, Chipsets and Prods. Containing Same*, Inv. No. 337-TA-428, Order No. 10, Initial

Determination (May 4, 2000) (“*Integrated Circuits*”) (unreviewed). Establishment of the “economic prong” is not dependent on any “minimum monetary expenditure” and there is no need for a complainant “to define the industry itself in absolute mathematical terms.” *Certain Stringed Musical Instruments and Components Thereof*, Inv. No. 337-TA-586, Comm’n Op. at 25-26 (May 16, 2008) (“*Stringed Instruments*”). However, a complainant must substantiate the nature and the significance of its activities with respect to the articles protected by the patent at issue. *Certain Printing and Imaging Devices and Components Thereof*, Inv. No. 337-TA-690, Comm’n Op. at 30 (Feb. 17, 2011) (“*Imaging Devices*”).

The Commission has interpreted Sections 337(a)(3)(A) and (B) to concern “investments in plant and equipment and labor and capital with respect to the *articles* protected by the patent.” *Certain Ground Fault Circuit Interrupters and Prods. Containing Same*, Inv. No. 337-TA-739, 2012 WL 2394435, at *50, Comm’n Op. at 78 (June 8, 2012) (“*Circuit Interrupters*”) (emphasis in original) (quoting 19 U.S.C. §§ 1337(a)(3)(A), (B)).

When a complainant proceeds under Section 337(a)(3)(C), it is not sufficient for the “substantial investment” under subsection (C) to merely relate to articles protected by the asserted patents. Rather, “the complainant must establish that there is a nexus between the claimed investment and asserted patent regardless of whether the domestic- industry showing is based on licensing, engineering, research and development.” *Certain Integrated Circuit Chips & Prods. Containing*, Inv. No. 337-TA-845, Final Initial Determination, 2013 WL 3463385, at *14 (June 7, 2013).

In addition, the Commission has definitively stated that investments in plant and equipment or labor and capital that relate to engineering and research and development (“R&D”) (that are expressly identified under subsection (C)), are properly considered under subsections

(A) and (B):

The statutory text of section 337 does not limit sections 337(a)(3)(A) and (B) to investments related to manufacturing or any other type of industry. It only requires that the domestic investments in plant and equipment, and employment of labor or capital be “with respect to the articles protected by the patent.” 19 U.S.C. § 1337(a)(3). Moreover, even though subsection (C) expressly identifies “engineering” and “research and development” as exemplary investments in the “exploitation” of the patent, that language does not unambiguously narrow subsections (A) and (B) to exclude those same types of investments.

Certain Solid State Storage Drives, Stacked Elecs. Components, and Prods. Containing Same, Inv. No. 337-TA-1097, Comm’n Op. at 8 (June 29, 2018) (“*Storage Drives*”); *see also, e.g., Certain Marine Sonar Imaging Devices, Including Downscan and Sidescan Devices, Prods. Containing the Same, and Components Thereof*, Inv. No. 337-TA-921, Comm’n Op. at 57-64 (Jan. 6, 2016) (“*Sonar Imaging Devices*”).

There is no mathematical threshold test or a “rigid formula” for determining whether a domestic industry exists. *Certain Male Prophylactic Devices, Inc.*, Inv. No. 337-TA-292, Comm’n Op. at 39, USITC Pub. 2390 (June 1991) (“*Male Prophylactic Devices*”). However, to determine whether investments are “significant” or “substantial,” the actual amounts of a complainant’s investments or a quantitative analysis must be performed. *Lelo Inc. v. Int’l Trade Comm’n*, 786 F.3d 879, 883-84 (Fed. Cir. 2015). Even after *Lelo*, which requires some quantification of a complainant’s investments, there is still no bright line as to a threshold amount that might satisfy an economic industry requirement.

It is the complainant’s burden to show by a preponderance of evidence that each prong of the domestic industry requirement is satisfied. *Certain Prods. Containing Interactive Program Guide and Parental Control Tech.*, Inv. No. 337-TA-845, Final Initial Determination, 2013 WL 3463385, at *14 (June 7, 2013.). Moreover, the Commission makes its determination by “an

examination of the facts in each investigation, the article of commerce, and the realities of the marketplace.” *Male Prophylactic Devices*, Comm’n Op. at 39 (quoting *Certain Double Sided-Floppy Disk Drives and Components Thereof*, Inv. No. 337-TA-215, Comm’n Op. at 17, USITC Pub. 1859 (May 1986)). “Commission precedent permits complainants to present evidence of their U.S. investments using methods and approaches that are appropriate to the facts of a particular investigation; such methods and approaches may include a comparison between complainant’s domestic investments to the complainant’s foreign investments to inform the contextual analysis for determining whether the claimed domestic investments are significant or substantial.” *Certain Movable Barrier Operator Sys. and Components Thereof*, Inv. No. 337-TA-1118, Comm’n Op. at 23 (Jan. 12, 2021) (internal citations omitted).

In addition, as the Commission explained, it has looked to several different “contextual indicators” to determine if a complainant’s investments and expenditures are sufficient to constitute a domestic industry. See *Certain Bone Cements, Components Thereof and Prods. Containing the Same*, Inv. No. 337-TA-1153, Comm’n Op. at 26 (Jan. 25, 2021). The Commission stated:

For instance, one methodological approach the Commission has used in both pre- and post-1988 investigations is “comparing complainant’s domestic expenditures to its foreign expenditures.” Another approach, among others, is to consider “the value added to the article in the United States by the domestic activities.” Indeed, Commission decisions have accepted a “value-added” analysis to assess whether an industry in the United States exists. Moreover, the Federal Circuit in *Schaper* compared the investments in the United States with “the total production process of [the domestic industry products],” and found that there was not “significant value added” to the products in the United States. In sum, as discussed above, the Commission’s determination as to the existence of a domestic industry must be assessed according to a highly fact-specific assessment of the “nature and significance” of the complainant’s domestic activities.

Id. at 26-27 (internal citations omitted).

B. Economic Prong Overview

On August 13, 2021, Ventria filed a corrected motion for summary determination (“MSD”) that it satisfies the economic prong of the domestic industry (“DI”) requirement under 19 U.S.C. §§ 1337(a)(3)(A), (B), and (C) through its domestic investments in plant and equipment, labor and capital, and research and development (“R&D”) relating to the DI Products. (Motion Docket No. 1238-009 (Aug. 13, 2021); MSD at 1; *see also* CBr. at 82-84.). On August 25, 2021, Healthgen filed an opposition (“MSD Opposition”) to Ventria’s MSD. (Doc. ID No. 750292 (Aug. 25, 2021).). On September 3, 2021, Ventria filed a motion for leave to file a reply in support of its MSD. (Motion Docket No. 1238-010 (Sept. 3, 2021).). On September 10, 2021, Healthgen filed an opposition to Ventria’s motion for leave. (Doc. ID No. 751442 (Sept. 10, 2021).). On September 30, 2021, Ventria’s motion for leave (1238-010) was granted. (Order No. 21 at 7 (Sept. 30, 2021)).

For the reasons discussed below, Ventria has met its burden to show that its investments satisfy the economic prong of the DI requirement under 19 U.S.C. § 1337(a)(3)(A), (B), and (C).

C. Ventria’s Sales-Based Allocation Method is Reasonable

Ventria contended that in the ordinary course of business, it does not allocate expenditures to particular products. (CBr. at 84.). Ventria therefore uses a sales-based allocation method to provide a quantitative approximation of investments attributable to the DI Products. (*Id.*; Tr. (LaMotta)³⁰ at 668:20-671:16.). Such a sales-based allocation method has been accepted as a reasonable methodology by the Commission. *See, e.g., Certain Mobile Device*

³⁰ Mr. Ryan LaMotta is Ventria’s expert witness on domestic industry, remedy, and bond. (Tr. (LaMotta) at 647:15-24.). He has a BBA and MBA from Baylor University, is a Director of ASQ Consulting Group, and has experience in accounting and financial analysis. (*Id.* at 645:24-647:18.).

Holders and Components Thereof, Inv. No. 337-TA-1028, Comm’n Op. at 18-19 (Mar. 22, 2018); *Certain Robotic Vacuum Cleaning Devices and Components Thereof Such as Spare Parts*, Inv. No. 337-TA-1057, Order No. 39 at 17 (Feb. 13, 2018), *aff’d by* Comm’n Op. (Aug. 1, 2018). In addition, Healthgen’s expert, Mr. Reed,³¹ agreed that it was a reasonable allocation methodology. (See Tr. (Reed) at 1314:8-1315:2).

As shown in Table 1 below, sales of Ventria’s DI Products as a percentage of its total sales ranged between about [REDACTED] from 2015-2020.

Table 1: DI Product Sales as a Percentage of Total Sales



(See CBr. at 84-85; CX-0975C.).

D. Ventria Has Satisfied the Economic Prong of the Domestic Industry Requirement Under Subsections 337(a)(3)(A), (B), and (C)

Ventria asserted that it has invested a total of [REDACTED] relating to its six DI Products. (See Tr. (LaMotta) at 666:16-667:6.). As an initial matter, rather than addressing whether Ventria’s claimed investments in the six DI Products meet the economic prong of the DI requirement, Healthgen instead argued that Ventria erred “by including investments in products that do not practice any claim of the ’951 patent.” (See RRB. at 64-65.). Specifically, Healthgen’s argument that Ventria does not satisfy the economic prong of the DI requirement is

³¹ Mr. Brett Reed is Healthgen’s expert witness on domestic industry and remedy. (See Tr. (Reed) at 1303:2-4.). He has a bachelor’s degree from the University of California at Irvine, a master’s degree from UCLA, and is a director at Competition Economics, LLC, an economic consulting firm, working primarily on intellectual property matters and commercial damages. (*Id.* at 1303:18-1307:21.).

limited to challenging Ventria's investments in one DI Product – Optibumin®. (*See id.* at 64-74 (“Under a proper economic prong analysis, Ventria may only claim investments in Optibumin and not in the five other, non-practicing products.”); Tr. (Reed) at 1340:7-12.). Thus, pursuant to Ground Rules 7.2 and/or 10.1, Healthgen has waived any arguments that Ventria's investments in all six DI Products are not significant or substantial.³²

From 2015-2020, Ventria has invested [REDACTED] in plant and equipment relating to the six DI Products. (*See* Tr. (LaMotta) at 666:16-667:2.). Ventria incurred a total of [REDACTED] in plant and equipment expenditures attributable to all products that included the cost of [REDACTED], approximately [REDACTED] of farmland in [REDACTED] where Ventria plants, cultivates, and harvests the proprietary rice from which the recombinant proteins are expressed, equipment used to test and manufacture the DI Products, equipment used for R&D, and agricultural machinery such as tractors, combines, planters, trucks, and irrigation needed to plant, cultivate, and harvest the rice from which the DI Products are produced. (*See* Tr. (LaMotta) at 674:1-675:15; CDX-0002C at 25; CX-0776C; CX-0786C; CX-0794C; CX-0797C; CX-0867C; Tr. (Deeter) at 184:3-5; 185:3-5; 187:7-8; 193:2-10; 194:3-197:15; CDX-0005C at 15; Tr. (Curl)³³ at 622:10-625:3; CX-0825C; CX-0828C; CX-0830C; CX-0831C; CX-0832C; CX-0833C.).

As shown in Table 2 below, applying Ventria's sales-based allocation results in

[REDACTED] of those investments attributable to the DI Products.

³² This waiver does not affect Healthgen's arguments with respect to the technical prong of the domestic industry requirement.

³³ Mr. Marcus Hofer-Curl, a fact witness for Ventria, is the Director of Product Applications at Ventria and has worked there about three and a half years. (Tr. (Curl) at 579:25-580:9.).

Table 2: Investments in Plant and Equipment Allocated to DI Products


(See CBr. at 86; CDX-0002C at 25; CX-0776C; CX-0786C; CX-0794C; CX-0797C; CX-0867C.).

From 2015-2020, Ventria also invested [REDACTED] in labor relating to the six DI Products. (See Tr. (LaMotta) at 666:16-667:4, 678:10-679:17.). During that time period, Ventria incurred a total of [REDACTED] in labor costs. (See CX-0766C; CDX-0002C at 31.). Ventria has a diverse employee base engaged in R&D, laboratory work, rice breeding, farming, and manufacturing the rHSA products, which is entirely located in the United States. (See Tr. (Deeter) at 197:24-198:1, 198:13-16; Tr. (LaMotta) at 679:23-680:19, 681:14-15.). Ventria's path of growth in the United States is demonstrated by the fact that it has grown from around [REDACTED] employees 20 years ago, to [REDACTED] employees in 2015, and [REDACTED] employees in 2020. (See Tr. (Deeter) at 197:17-23; Tr. (LaMotta) at 679:23-680:3.). In addition, almost all of Ventria's employees work with the rHSA technology that supports the DI Products.³⁴ (See Tr. (Deeter) at 198:2-5.). For example, employees at the Kansas facility [REDACTED] (See *id.* at 180:10-181:5.). Employees at the Kansas facility also [REDACTED] (See *id.* at 181:6-19.).

³⁴ Moreover, Ventria has outsourced many tasks that may not necessarily qualify toward a domestic industry. (See Tr. (Deeter) at 198:4-16 [REDACTED])

[REDACTED] Ventria therefore asserted that "costs for any non-cognizable work are not included in Ventria's claimed labor costs." (CBr. at 86-87.).

As shown in Table 3 below, applying Ventria's sales-based allocation results in

[REDACTED] of its labor investments attributable to the DI Products.

Table 3: Investments in Labor and Capital Allocated to DI Products



(See CBr. at 87; CDX-0002C at 31; CX-0766C.).

From 2015-2020, Ventria also invested [REDACTED] in research and development relating to the six DI Products.³⁵ (See Tr. (LaMotta) at 666:23-667:6, 683:5-8; CDX-0002C at 36.). Ventria tracks its R&D expenditures on its financial statements under the [REDACTED] line item, which includes raw materials used in R&D initiatives as well as costs associated with R&D personnel. (See CBr. at 87; JX-0101C; CX-0691C; CX-0688C; CX-0689C; CX-0687C.). From 2015-2020, Ventria incurred a total of [REDACTED] in R&D expenditures. (See Tr. (LaMotta) at 683:17-22; JX-0101C; CX-0691C; CX-0688C; CX-0689C; CX-0687C.).

As shown in Table 4 below, applying Ventria's sales-based allocation results in

[REDACTED] of these R&D investments attributable to the DI Products.

³⁵ Nothing precludes consideration of R&D investments that predate issuance of the Asserted Patent. (See *Certain Video Game Sys. and Controllers*, Inv. No. 337-TA-743, Comm'n Op. at 6-8 (Apr. 14, 2011)).

Table 4: Investments in R&D Allocated to DI Products

(See CBr. at 87; CDX-0002C at 36; JX-0101C; CX-0691C; CX-0688C; CX-0689C; CX-0687C.).

In addition, the nexus requirement under subsection (C) is satisfied because the relevant R&D expenditures were all incurred in the United States and are attributable to the DI Products, which embody the inventions of the '951 patent. As discussed, *supra*, in Section IX.B, the DI Products practice claim 1 of the '951 patent. Thus, the nexus requirement is satisfied because Ventria's investments are in R&D activities that directly go toward developing DI Products that practice a claim of the Asserted Patent. See *Certain Gas Spring Nailer Prods. and Components Thereof*, Inv. No. 337-TA-1082, Comm'n Opinion at 80 (Apr. 28, 2020) ("The requisite nexus between Kyocera's exploitation activities and the '718 patent is met here because the activities here go toward developing DI products that embody and practice the asserted claims."); *Certain High-Density Fiber Optic Equipment and Components Thereof*, Inv. No. 337-TA-1194, Comm'n Opinion at 71 (Aug. 23, 2021) ("There is also no dispute that the asserted patents relate to the fundamental technology embedded in the DI products.").

Moreover, Ventria's investments are significant and substantial. Notably, all of its investments and activities occurred within the United States. (See Tr. (Deeter) at 181:3-5, 181:17-19, 184:3-5, 185:3-7, 187:7-8, 193:5-10, 194:3-197:15; Tr. (Curl) at 599:25-600:20; Tr. (LaMotta) at 657:16-660:7, 666:16-667:9, 681:10-15.). This weighs heavily in favor of a finding

that Ventria's investments are significant and substantial. For example, in *Certain Carburetors and Products Containing Such Carburetors*, the Commission found that the complainant failed to provide evidence substantiating the nature and significance of its domestic activities with respect to the domestic industry products. *See Certain Carburetors and Products Containing Such Carburetors* Inv. No. 337-TA-1123, Comm'n Opinion at 18-19 (Oct. 28, 2019) ("The Commission has also assessed the relative domestic contribution to the protected article by comparing complainant's product-related domestic activities to its product-related foreign activities.").

In contrast, all of Ventria's investments in its DI Products occurred in the U.S. and thus, the significance and substantiality of its domestic expenditures is apparent when viewed in comparison to its nonexistent foreign expenditures. *See id.*; *see also Certain Wearable Monitoring Devices, Sys., and Components Thereof*, Inv. No. 337-TA-1190, Order No. 34 at 30-31, (Oct. 1, 2020), *aff'd in relevant part by* Comm'n Op. at 39 (May 5, 2021). Specifically, because all of Ventria's investments in the DI Products were made in the United States, all the value for the DI Products is derived from U.S. activities and investments. (*See* Tr. (LaMotta) at 700:21-23.). *Certain Bone Cements, Components Thereof and Prods. Containing the Same*, Inv. No. 337-TA-1153, Comm'n Op. at 26-27 (Jan. 25, 2021) (internal citations omitted). In other words, the DI Products would not exist without the domestic investments described above.

In addition, Ventria's domestic investments are significant and substantial in comparison to its revenues from the DI Products. For example, the evidence shows that for the time period 2015-2020, Ventria earned [REDACTED] in sales from the DI Products. (*See* CX-0768C.). As discussed above, for that same time period, Ventria incurred [REDACTED] in expenditures under subsection (A), [REDACTED] in expenditures under subsection (B), and [REDACTED] in expenditures

under subsection (C). Therefore, Ventria's investments under subsections (A), (B), and (C) amount to about [REDACTED], respectively, of its revenue from the DI Products. This further demonstrates the significance and substantiality of these investments. In addition, by comparison to other biotech companies, Ventria demonstrates that its investments are significant and substantial. For example, Mr. LaMotta explained that two (2) companies – Repligen and Biolife Solutions – incurred R&D expenditures from 2015-2020 that accounted for about 7% and 13% of their revenue, respectively, whereas Ventria's R&D expenditures were [REDACTED] of its DI Product revenues in some years for that same time period.³⁶ (*See* Tr. (LaMotta) at 688:3-689:15.). While this is not a direct comparison to a competitor in the same market, it nonetheless provides context for the significance and substantiality of Ventria's investments.

Accordingly, Ventria's investments satisfy the economic prong under subsections (A), (B), and (C).

E. Ventria Has Satisfied the Economic Prong of the Domestic Industry Requirement Even if Investments Only in Optibumin® are Considered

As discussed, *supra* in Section IX.B, all six DI Products – Cellastim® S, Exbumin®, Optibumin®, OptiPEAK®, OptiVERO®, and ITSETM+A – practice claim 1 of the '951 patent. Thus, as determined above, Ventria's investments in all six DI Products qualify toward a domestic industry. However, while Healthgen maintained that five of the DI Products do not

³⁶ Ventria is not asserting that these companies are direct competitors for the sake of comparison. Rather, Mr. LaMotta chose to analyze Repligen and Biolife because they are publicly-traded companies and thus, he had access to their publicly-available data. (*See* Tr. (LaMotta) at 688:16-19). In addition, he talked to Mr. Deeter to identify Repligen and Biolife as two companies that were in the biotech space and were classified similar to Ventria to make sure he "had an appropriate match-up." (*Id.* at 688:21-25). Thus, even though they were not competitors, they are biotech companies and thus, it is at least informative what their R&D investments were as a percentage of their revenues. (*Id.* at 689:1-15).

practice the '951 patent, it conceded that Optibumin® does practice the '951 patent. (See RRB. at 65; CBr. at 93.). Thus, as an alternative, this initial determination finds that Ventria's domestic investments in Optibumin® alone also satisfy the economic prong of the domestic industry requirement.

As previously mentioned, Ventria does not allocate expenditures on a product-by-product basis. Thus, using the above-described sales-based allocation method, Ventria invested [REDACTED] in plant and equipment costs under subsection (A), [REDACTED] in labor costs under subsection (B), and [REDACTED] in R&D costs under subsection (C)³⁷ attributable to Optibumin®. (See CDX-0002C at 25, 31, 36; CX-0975C; CX-0776C; CX-0786C; CX-0794C; CX-0797C; CX-0867C; CX-0766C; JX-0101C; CX-0691C; CX-0688C; CX-0689C; CX-0687C). Healthgen does not dispute the amount of these investments. (See RRB. at 67; RDX-0003C at 8; RX-0304C; Tr. (Reed) at 1316:23-1318:12.).

Yet again, these investments, when considered in context, are significant and substantial. As mentioned above, it is notable that 100% of Ventria's investments in Optibumin® occur in the United States. (See Tr. (Deeter) at 181:3-5, 181:17-19, 184:3-5, 185:3-7, 187:7-8, 193:5-10, 194:3-197:15; Tr. (Curl) at 599:25-600:20; Tr. (LaMotta) at 657:16-660:7, 666:16-667:9, 681:10-15, 694:21-25.). Again, this weighs heavily in favor of finding that Ventria's

³⁷ Ventria contended that "[b]ecause these R&D expenditures were made in Optibumin, a product that indisputably embodies the patented invention, the R&D expenditures satisfy the nexus requirement." (CBr. at 94 n.9.). As previously discussed, the nexus requirement under subsection (C) is satisfied because the relevant R&D expenditures were all incurred in the United States and are attributable to Optibumin®, which embodies the inventions of the '951 patent. As discussed, *supra*, in Section IX.B, the Optibumin® practices claim 1 of the '951 patent. Thus, the nexus requirement is satisfied because Ventria's investments are in R&D activities that directly go toward developing Optibumin® that practices a claim of the Asserted Patent. In addition, as previously noted, Healthgen conceded that Optibumin® practices the '951 patent. (See RRB. at 65.).

investments are significant and substantial. Similar to the analysis above, because all of Ventria's investments in Optibumin® occur in the United States, Optibumin® derives all of its value from activities occurring in the United States. (*See* Tr. (Reed) at 1342:15-1343:5.).

In addition, these investments are significant and substantial when viewed in comparison to Ventria's revenues from Optibumin®. Ventria had no sales of Optibumin® before 2018, but from 2018-2020, Ventria's sales of Optibumin® amounted to [REDACTED]. (CX-0768C.). Thus, Ventria's allocated investments in Optibumin® were [REDACTED] of its sales under subsection (A), [REDACTED] of its sales under subsection (B), and [REDACTED] of its sales under subsection (C). These proportions further demonstrate the significance and substantiality of the investments.³⁸

However, Healthgen took issue with Ventria's argument about Optibumin®, arguing that the Optibumin® sales were actually meager, which makes those investments, as a percentage of sales, seem more significant than they actually are. (*See* RRB. at 68-69.). For example, Healthgen argued that "Ventria's sales of Optibumin comprise only [REDACTED] of Ventria's total sales from 2018 (when sales of Optibumin began) through the December 2020 filing of the complaint." (*Id.* at 66 (citing Tr. (Reed) at 1323:19-1324:18; RDX-0003C at 6; CX-0975C; CDX-0002C at 20).). But the evidence reflects that Optibumin® is [REDACTED] [REDACTED]. For example, Mr. Curl explained that [REDACTED] [REDACTED]. (*See* Tr. (Curl) at 602:10-

³⁸ And again, Ventria's investments are significant and substantial in comparison to similar companies. As previously discussed, Mr. LaMotta explained that Repligen and Biolife Solutions incurred R&D expenditures from 2015-2020 that accounted for about 7% and 13% of their revenue, respectively, whereas Ventria's allocated R&D expenditures for Optibumin® were [REDACTED] of its Optibumin® sales. (Tr. (LaMotta) at 688:3-689:15).

603-14 [REDACTED]
[REDACTED]
[REDACTED]; *see also* Tr. (Deeter) at 189:16-22 [REDACTED]
[REDACTED]). Mr. LaMotta confirmed this by
explaining that [REDACTED]
[REDACTED] (Tr. (LaMotta) at 670:18-671:13, 692:8-693:17; *see also* Tr. (Reed) at 1345:6-1346:7
(agreeing that it is not uncommon [REDACTED]
[REDACTED])). Thus, it is not surprising that Optibumin®
[REDACTED].

In addition, the sales-based approach, as applied to Optibumin®, also undervalues
Ventria's investments because it does not account for any investments prior to 2018. Yet the
evidence is that Ventria [REDACTED]

[REDACTED]
[REDACTED] (*See* CX-0463C at 2.). [REDACTED]
[REDACTED]
[REDACTED]

[REDACTED]

(*Id.* at 4 [REDACTED]).

Similarly, a [REDACTED]

[REDACTED]

(*See* CX-0464C at 5). [REDACTED]

[REDACTED]

[REDACTED] (*See* Tr. (Curl) at

595:10-24.). Moreover, [REDACTED]

[REDACTED]

[REDACTED] (*See* CX-0655C at 7.). Thus, the sales-based methodology, as applied to Optibumin®, is a somewhat conservative estimate of Ventria’s investments.

Accordingly, even if investments only in Optibumin® are considered, Ventria’s investments satisfy the economic prong under subsections (A), (B), and (C).

XII. RECOMMENDATION ON REMEDY AND BOND

In the event of a finding of violation of Section 337, Ventria has requested that the Commission issue a general exclusion order (“GEO”) and cease and desist orders (“CDOs”).

(CPBr. at 141; CBr. at 101.). Ventria has requested that the Commission impose a bond of at least 100%. (CPBr. at 145; CBr. at 105.).

This decision recommends: (1) Limited Exclusion Orders with a certification provision; (2) Cease and Desist Orders; and (3) that a 100% bond of the entered value be imposed during the Presidential Review Period.

A. Legal Standard

Pursuant to Commission Rule 210.42, an ALJ must issue a recommended determination on: (i) an appropriate remedy if the Commission finds a violation of Section 337, and (ii) an amount, if any, of the bond to be posted. 19 C.F.R. § 210.42(a)(1)(ii). When a Section 337 violation has been found, as here, “the Commission has the authority to enter an exclusion order, a cease and desist order, or both.” *Certain Flash Memory Circuits and Prods. Containing the Same*, Inv. No. 337-TA-382, Comm’n Opinion on the Issues Under Review and on Remedy, the Public Interest and Bonding, at 26 (June 9, 1997). The Commission has broad discretion in selecting the form, scope, and extent of the remedy in a section 337 proceeding. *Viscofan, S.A. v. U.S. Int ’l Trade Comm’n*, 787 F.2d 544, 548 (Fed. Cir. 1986).

When a violation of Section 337 is found, the Commission may issue either a limited exclusion order (“LEO”), directed against products manufactured by or on behalf of named parties found in violation, or a GEO, directed against all infringing products. *See* 19 U.S.C. § 1337(d).

Additionally, a CDO is appropriate where the evidence demonstrates the presence of commercially significant inventory in the United States. 19 U.S.C. § 1337(f); *see also Certain Crystalline Cefadroxil Monohydrate*, Inv. No. 337-TA-293, Comm’n Opinion, USITC Pub. No. 2391, 1991 WL 790061 at *30-32 (June 1991).

Infringing articles may enter upon the payment of a bond during the sixty-day Presidential Review Period. 19 U.S.C. § 1337(j)(3). The bond is to be set at a level sufficient to “offset any competitive advantage resulting from the unfair method of competition or unfair act enjoyed by persons benefiting from the importation.” *Certain Dynamic Random Access Memories, Components Thereof and Prods. Containing Same*, Inv. No. 337- TA-242, Comm’n Opinion, 1987 WL 450856 at 37 (Sept. 21, 1987).

B. A General Exclusion Order Is Not Warranted

Pursuant to Section 337(d)(2), the Commission may issue a GEO that applies to all infringing products, regardless of source, instead of an LEO directed only to persons determined to be in violation of Section 337, when:

- (A) a general exclusion from entry of articles is necessary to prevent circumvention of an exclusion order limited to products of named persons; or
- (B) there is a pattern of violation of this section and it is difficult to identify the source of infringing products.

19 U.S.C. § 1337(d)(2); *accord* 19 C.F.R. § 210.50(c).

The Commission may issue a GEO when either one of the statutory provisions, Section 337(d)(2)(A) or (B), is met. *See Certain Cigarettes & Packaging Thereof*, Inv. No. 337-TA-643, Comm’n Op. at 24 (Oct. 1, 2009). Under either statutory provision, the Commission may consider the activities of third parties, active and defaulting respondents, and respondents that have been terminated. *See Certain Ink Cartridges & Components Thereof*, Inv. No. 337-TA-946, Comm’n Op., at 5-6 (June 29, 2016); *Certain Coaxial Cable Connectors & Components Thereof*, Inv. No. 337-TA-650, Comm’n Op. at 59 (Apr. 14, 2010) (“*Coaxial Cable Connectors*”). “Because of its considerable impact on international trade, potentially extending beyond the parties and articles involved in the investigation, more than just the interests of the

parties is involved. Therefore, the Commission exercises caution in issuing general exclusion orders....” See *Coaxial Cable Connectors* at 56 (quoting *Certain Agricultural Tractors Under 50 Power Takeoff Horsepower*, Inv. No. 337-TA-380, Comm’n Op. at 21 (Mar. 12, 1997)).

1. A GEO Is Not Warranted Under 19 U.S.C. § 1337(d)(2)(A)

Under Section 337(d)(2)(A), the Commission considers “(1) whether conditions are ripe for circumvention, and (2) the appearance of circumvention.” *Certain Lighting Control Devices Including Dimmer Switches & Parts Thereof (IV)*, Inv. No. 337-TA-776, Comm’n Op., 2012 WL 13171646 at *7 (Nov. 8, 2012). In determining whether conditions are “ripe” for circumvention, the Commission has considered factors such as (1) significant and increasing demand for the infringing products; (2) widespread U.S. marketing and distribution networks with multiple intermediaries; (3) a large number of non-respondent foreign manufacturers and/or distributors; (4) frequent name changes for foreign manufacturers and/or distributors; (5) a low barrier to enter the U.S. market through high profit margins and low retail costs in the United States for foreign infringing products, indicative of low foreign manufacturing costs; (6) large online marketplaces have emerged which provide both foreign manufacturers and domestic retailers a dedicated, flexible way to sell to consumers; (7) it is difficult to identify the sources of infringing products because of the ability to package infringing products in unmarked, generic packaging; (8) manufacturers can easily evade a limited exclusion order by establishing shell offshore distribution companies with unclear ties to the original manufacturer; and (9) previous attempts to address infringement have been unsuccessful. *Id.* at *13; *Certain Inkjet Ink Supplies & Components Thereof*, Inv. No. 337-TA-730, Comm’n Op. at 4-5 (Feb. 24, 2012); *Certain Water Filters and Components Thereof*, Inv. No. 337-TA-1126, Initial Determination at 66 (Aug. 7, 2019).

As an initial matter, there appears to be little, if any, evidence in the record of actual circumvention. (SBr. at 10.). The evidence indicates that some U.S. distributors of the Accused Products change the labels on the products to obscure both the manufacturer (i.e., Healthgen) and the country of origin (i.e., China). (RX-0009 (Shore Dep. Tr.)³⁹ at 30:22-31:21, 67:7-25; CX-0080C; SBr. at 10-11.). As Staff noted, this re-labeling appears to occur post-importation, and thus is not evidence of actual circumvention of an exclusion order. (SBr. at 11.).

With respect to whether conditions are ripe for circumvention, the evidence indicates that Ventria and Healthgen are the only manufacturers of the products within the scope of the Investigation. (*See* Tr. (Deeter) at 276:22-277:9 (confirming that Healthgen and Ventria are the only manufacturers of rice-derived rHSA products); Tr. (Curl) at 639:2-10 (“I believe I’ve seen Orybio in the past as a potential manufacturer, but today, you know, based on my research, Wuhan Healthgen, Oryzogen, is the only rice-derived recombinant human serum albumin manufacturer other than Ventria Bioscience”); Tr. (LaMotta) at 769:25-770:7 (“I’m only aware of Ventria and Healthgen that manufacture a rice-derived rHSA at all”).). This evidence strongly suggests that an LEO that covers Healthgen will be sufficient to exclude infringing goods from the U.S. In other words, there is only a single foreign manufacturer, Healthgen, which demonstrates that conditions are not ripe for circumvention.

Similarly, there was no evidence of a widespread U.S. marketing and distribution network with multiple intermediaries. Rather, the evidence indicates that the Accused Products are generally sold for importation into the U.S. by Healthgen and imported into the U.S. by its U.S. distributors. Specifically, the evidence showed that other than for two customers,

³⁹ At the time of his deposition on February 25, 2021, Mr. Warren Shore was the founder, President, and CEO of United States Biological (“US Bio”). (RX-0009 (Shore Dep. Tr.) at 12:4-13:7.).

Healthgen ships its products [REDACTED]

[REDACTED] (See CX-1080C (Cao Depo. Tr.) at 49:18-50:9, 53:3-16.). For the other two customers, eEnzyme and ScienCell, the products are [REDACTED]

[REDACTED] (*Id.* at 54:10-55:1.). In either case, the chain of distribution into the U.S. appears relatively clear, which suggests that it would be difficult for Healthgen to circumvent an LEO.

Moreover, there appears to be little evidence of an increase in demand for the Accused Products steep enough to suggest that a GEO is necessary. Healthgen's sales data shows that Healthgen had approximately [REDACTED] total for 2017-2021, and on the order of [REDACTED]. (CX-0019C; CX-0033C.). The data does not show any rapid increase in demand for Healthgen's Accused Products.

Additionally, there do not appear to be low barriers to entry into the market. The evidence, as discussed below, is to the contrary. Neither do the infringing products appear to be extremely profitable. The Complainant's expert, Mr. LaMotta, testified that if Ventria sold its products at the same price that Healthgen sold its products, Ventria would incur a loss because of the large investment necessary to develop rice-derived rHSA products.⁴⁰ (Tr. (LaMotta) at 773:4-20.). Mr. LaMotta also testified that developing rice-derived rHSA products requires a long lead time and substantial investments in time, employees, equipment, and land. (*Id.* at 773:21-774:1.). This evidence demonstrates that the barriers to entry into this market are quite

⁴⁰ Mr. LaMotta confirmed that Healthgen did not produce profitability information for the Accused Products, so his opinions were based on his review of Ventria's revenues and cost structure. (Tr. (LaMotta), at 772:24-773:3.).

high. This is also consistent with the fact that there are only two (2) sources of the products within the scope of this Investigation: if the barriers were lower, it would be reasonable to expect that more than two companies would be making and selling the products (i.e., more than just Ventria and Healthgen). Thus, the evidence weighs against finding that conditions are ripe for circumvention.

Furthermore, the evidence does not show that it will be difficult for CBP to identify infringing goods. Healthgen's corporate witness, Ms. Cao, testified that it is standard practice for Healthgen to [REDACTED]

[REDACTED]. (See CX-1080C (Cao Depo. Tr.) at 186:14-187:7; JX-0034C.). [REDACTED]

[REDACTED]

[REDACTED]

(JX-0034C.0009 (annotated, copied from SBr. at 14); *see also* JX-0033C-JX-0038C; CX-0008C; RX-0009 (Shore Dep. Tr.) at 47:12-20 (testifying that Accused Products shipped to US Bio identified the source of the product as Healthgen on the label), 66:12-16 (same).).

As shown on the label in Figure 20, the [REDACTED]
[REDACTED] (*Id.*). Hearing testimony confirmed that the brand name “OsrHSA” is unique to Healthgen, which further identifies that the source of the goods in the package are from Healthgen. (Tr. (Deeter) at 279:18-280:1 (testifying that Healthgen is the only company that sells rice-derived rHSA products branded as OsrHSA); Tr. (Curl) at 639:2-10 (same); Tr. (LaMotta) at 769:25-770:7 (same).). Thus, the evidence does not show that conditions are ripe for circumvention.

2. A GEO Is Not Warranted Under 19 U.S.C. § 1337(d)(2)(B)

The evidence adduced in this Investigation does not show a pattern of violation or difficulty in identifying the source of Accused Products for the following reasons.

First, there is only a single source of the Accused Products: Healthgen. (*See* Tr. (Deeter) at 276:22-277:9 (confirming that Healthgen and Ventria are the only manufacturers of rice-derived rHSA products); Tr. (Curl) at 639:2-10 (“I believe I’ve seen Orybio in the past as a potential manufacturer, but today, you know, based on my research, Wuhan Healthgen, Oryzogen, is the only rice-derived recombinant human serum albumin manufacturer other than Ventria Bioscience”); Tr. (LaMotta) at 769:25-770:7 (“I’m only aware of Ventria and Healthgen that manufacture a rice-derived rHSA at all”).). The evidence indicates that *all* the companies identified as buying or importing the Accused Products are buying and importing those products from Healthgen.

The Commission has previously explained that there is no pattern of violation to support a GEO where the “Respondents accounted for all of the infringing imported products” and the

“Complainants have failed to identify a single act of importation that is unrelated to one of the Respondents.” *Certain Self-Cleaning Litter Boxes and Components Thereof*, Inv. No. 337-TA-625, Comm’n Op., at 56 (Apr. 28, 2009) (“Certain Self-Cleaning Litter Boxes”). Here, like *Certain Self-Cleaning Litter Boxes*, every act of importation (but one)⁴¹ is related to one of the Respondents, i.e., Healthgen.

Moreover, Ventria has proven a violation by substantial, probative, and reliable evidence for a single Respondent: Healthgen. In similar circumstances, the Commission has declined to issue a GEO. *See Certain Ground Fault Circuit Interrupters & Products Containing Same*, Inv. No. 337-TA-615, Comm’n Op. at 26 (Mar. 26, 2009) (“[W]e do not regard infringement by four respondents to establish a ‘pattern of violation’ of the type to be sufficient to justify the imposition of a general exclusion order when a limited exclusion order is available instead.”). In *Certain Self-Anchoring Beverage Containers*, Inv. No. 337-TA-1092, Comm’n Op. (Jul. 25, 2019), the Commission found a pattern of violation where only a single respondent was found in violation and the ID identified numerous infringing products available online from non-respondents. *Id.* at 16. However, unlike the present Investigation, in *Self-Anchoring Beverage Containers*, the ID found that the infringing products available online reflected numerous “sources” of infringing goods, i.e., there was no indication that the infringing products all came from a single source, as is the case here. *See Certain Self-Anchoring Beverage Containers*, Inv. No. 337-TA-1092, Initial Det. at 26 (Sep. 7, 2018).

Second, according to the evidence presented, it is not difficult to identify the source of

⁴¹ Ventria presented evidence demonstrating that foreign non-party [REDACTED] imported or sold for importation a limited amount of the Accused Products to U.S. non-party [REDACTED]. (CBr. at 102; CX-0217C; CX-1080C (Cao Dep. Tr.) at 23:16-24:9). However, even in that instance, the ultimate source of the Accused Products was Healthgen. (Tr. (LaMotta) at 772:16-23.).

the Accused Products because there is only one (1) source of the Accused Products: Healthgen. *Certain Cast Steel Railway Wheels, Certain Processes for Manufacturing or Relating to Same and Certain Products Containing Same*, Inv. No. 337-TA-655, Recommended Det. on Remedy and Bonding at 6, n.4 (Mar. 9, 2010), *adopted in relevant part on review* (noting that complainant had not attempted to show that there would difficulty identifying the source of infringing goods, and explaining that “one would not expect it to be difficult to identify the source of a finished product such as a railway wheel in view of the relatively small number of manufacturers that complainant has referred to in the record”). That is also why Ventria’s assertion that “even Ventria’s customers occasionally struggle[] to distinguish between Ventria and Healthgen” does not support their argument with respect to identification of the source. (CBr. at 104.). The only sources for the products at issue are Ventria and Healthgen, and Ventria manufactures its products in the U.S. (Tr. (LaMotta) at 657:6-658:9 (testifying that all Ventria’s operations are in the U.S., including manufacturing).). Thus, any imported rice-derived rHSA products logically must be coming from Healthgen.

Moreover, the evidence demonstrates that the Accused Products are shipped in packages that identify Healthgen, if not by company name, then at least by brand name, i.e., OsrHSA. (See JX-0033C-JX-0038C; CX-0008C (shipping labels and invoices); RX-0009 (Shore Dep. Tr.) at 47:12-20 (testifying that Accused Products shipped to US Bio identified the source of the product as Healthgen on the label), 66:12-16 (same).). The same evidence also reflects that the source of infringing goods is identifiable. *See Certain Self-Cleaning Litter Boxes* at 56-57 (explaining that “the ‘source’ of the infringing products” was not difficult to identify because it was “undisputed that all of the[] imported products are the Respondents” and “each Respondent is clearly identified on its products and the products’ packaging”). Accordingly, the evidence

does not show that it would be difficult to identify the source of infringing goods.

C. Limited Exclusion Orders Are Warranted

As explained above in Section XII.B, the record evidence does not support the issuance of a GEO. However, since this decision finds a violation based on infringement of the '951 patent by Healthgen, the issuance of a LEO against Healthgen is warranted. *See* 19 U.S.C. § 1337(d) (“If the Commission determines, as a result of an investigation under this section, that there is a violation of this section, it shall direct that the articles concerned, imported by any person violating the provision of this section, be excluded from entry into the United States...”).

Additionally, a LEO against each of the Defaulting Respondents is warranted. *See* 19 U.S.C. § 1337(g)(1) (where a respondent is found in default and the complainant seeks relief only against that party, “the Commission shall presume the facts alleged in the complaint to be true and shall, upon request, issue an exclusion from entry or a cease and desist order, or both, limited to that person ...”); *Laerdal Med. Corp. v. Int’l Trade Comm’n*, 910 F.3d 1207, 1215 (Fed. Cir. 2018) (“After the respondents were found in default, the Commission was required to issue relief upon [complainant]’s request, unless precluded by public interest concerns”).

This decision also recommends including a certification provision. The Commission now generally includes a certification provision in every exclusion order because it is something that “CBP typically requests.” *Certain Road Construction Machines & Components Thereof*, Inv. No. 337-TA-1088, Comm’n Op., 2019 WL 6003332, at *27 (July 15, 2019); *Certain Composite Aerogel Insulation Materials and Methods for Manufacturing the Same*, Inv. No. 337-1003, Comm’n Op., at 62 (Feb. 22, 2018) (explaining that “the Commission’s standard practice for the past several years [is] to include certification provisions in exclusion orders to aid CBP”). The Commission’s typical certification provision gives CBP discretion to require “persons seeking to

import covered articles that are potentially subject to [the] Order” to “certify that they are familiar with the terms of [the] Order, that they have made appropriate inquiry, and thereupon state that, to the best of their knowledge and belief, the products being imported are not excluded from entry” under the order. *See e.g., Certain High-Density Fiber Optic Equipment and Components Thereof*, Inv. No. 337-TA-1194, General Exclusion Order, at 3-4 (Aug. 3, 2021).

With respect to the false designation of origin claims, Ventria maintained those claims only against the Defaulting Respondents and not against Healthgen. (*See* CBr. at 6 n. 2.). Thus, it is recommended that a LEO on the false designation of origin claims should issue only against the Defaulting Respondents. *See* 19 U.S.C. § 1337(g)(1); 19 C.F.R. § 210.16(c)(1).

D. Cease and Desist Orders Are Not Warranted

The record evidence does not support issuance of a CDO with respect to Healthgen. Specifically, the evidence indicates that Healthgen does not hold commercially significant inventories in the United States and has no significant domestic operations. Ventria’s expert, Mr. LaMotta,⁴² testified that he was not aware of any Healthgen employees or facilities in the U.S., or any domestic operations beyond selling the products into the U.S. (Tr. (LaMotta), at 767:25-768:11.). Healthgen’s expert, Mr. Reed,⁴³ confirmed that Healthgen has [REDACTED] [REDACTED]. (Tr. (Reed), at 1327:3-8.). Moreover, as Ms. Cao, Healthgen’s

⁴² When he testified on November 8, 2021, Mr. Ryan LaMotta was a Director of ASQ Consulting Group. (CPSt. at Ex. B.). Ventria identified Mr. LaMotta as an expert to testify about “the economic and financial analysis of Ventria’s domestic industry, as well as remedy and bonding.” (*Id.* at 4.).

⁴³ When he testified on November 10, 2021, Mr. Brett Reed was the co-founder and Director of Competition Economics LLC. (RPSt. at Ex. B.). Healthgen identified Mr. Reed as an expert to testify about “Ventria’s failure to satisfy the domestic industry requirement, the lack of harm to Ventria’s domestic industry based on the alleged Lanham Act violation, the appropriate remedy in this investigation, [and] the appropriate amount of bond to be posted during the presidential review period.” (*Id.* at 2.).

corporate representative, corroborated, Healthgen ships most of its products [REDACTED] which demonstrates that Healthgen does not need to maintain inventory in the U.S. [REDACTED] [REDACTED] (CX-1080C (Cao Depo. Tr.) at 49:18-50:9, 53:3-16.).

With regard to the Defaulting Respondents, as Staff noted, CDOs are appropriate with respect to the '951 patent claims and the false designation of origin claims. (SBr. at 33.). Each of the Defaulting Respondents is a domestic entity,⁴⁴ and thus is presumed to hold inventory in the United States. *See, e.g., Certain Stainless Steel Prods., Certain Processes for Mfg. or Relating to Same, and Certain Prods. Containing Same*, Inv. No. 337-TA-933, Comm'n Op., 2016 WL 8809133, at *22 (June 9, 2016) ("In investigations in which a domestic respondent is found in default, the Commission presumes the presence of commercially significant inventories in the United States to warrant a cease and desist order.").

E. Bond During the Presidential Review Period Is Warranted

Ventria requested a recommendation that the Commission impose a bond during the Presidential Review Period of 100%. (CPBr. at 145; CBr. at 105.). For the reasons discussed below, the value of the bond entered during the Presidential review period should be set at 100%.

The Commission frequently sets the bond based on the difference in sales prices between the patented domestic product and the infringing product. *See, e.g., Certain Microsphere Adhesives, Process for Making Same, and Prods. Containing Same, Including Self-Stick Repositionable Notes*, Inv. No. 337-TA-366, USITC Pub. No. 3949, Comm'n Opinion at 24 (Jan. 1996). In other instances where a direct comparison between a patentee's product and the

⁴⁴ *See* Section II.B.3 (regarding the Defaulting Parties).

accused product is not possible, the Commission has set the bond at a reasonable royalty rate. *See, e.g., Certain Integrated Circuit Telecommunication Chips and Prods. Containing Same, Including Dialing Apparatus*, Inv. No. 337-TA-337, Comm. Opinion at 41-43 (Aug. 3, 1993). Commission precedent allows for a 100 percent bond when it is not practical or possible to set the bond based on price differential. *Certain Voltage Regulators, Components Thereof and Prods. Containing Same*, Inv. No. 337-TA-564, Comm’n Opinion at 79 (Public Version Oct. 19, 2007). The purpose of the bond is to protect the complainant from any injury. 19 U.S.C. § 1337(j)(3); 19 C.F.R. §§ 210.42(a)(1)(ii), 210.50(a)(3).

Complainants bear the burden of establishing the need for a bond, including the amount of bond. *See, e.g., Certain Rubber Antidegradants, Components Thereof & Prods. Containing Same*, USITC Pub. No. 3975, Inv. No. 337-TA-533, Comm’n Opinion at 40 (April 2008); *Certain Coenzyme Q10 Products and Methods of Making Same*, Inv. No. 337-TA-790, Initial and Recommended Determination (Sept. 27, 2012) (recommending Commission not impose a bond because complainant failed in its burden to demonstrate the appropriate bond amount); *Certain Mobile Telephones and Wireless Communication Devices Featuring Digital Cameras, and Components Thereof*, Inv. No. 337-TA-703, Recommended Determination (Jan. 24, 2011) (recommending no bond because complainant did not meet its burden in providing evidence on the necessity of a bond); *Certain Liquid Crystal Display Devices and Prods. Containing the Same*, Inv. No. 337-TA-631, Comm’n Opinion at 27-28 (July 14, 2009) (setting zero bond because complainant “simply claimed that it was impossible to conduct a price differential analysis” and “should not benefit from a lack of any effort to identify” relevant pricing information, particularly that which is in its possession).

Healthgen asserted that if a violation is found, the amount of the bond should be zero.

(RRBr. at 79-83.). Specifically, Healthgen argued that “if Ventria’s domestic industry is limited only to Optibumin and/or only Healthgen’s clinical grade product is found to infringe,” then Ventria failed to present evidence comparing the prices of only the “clinical grade (liquid) products.” (*Id.* at 80-81.). Healthgen also argued that the price differential analysis performed by its expert Mr. Brent Reed supports only a bond amount between [REDACTED] (*Id.* at 81-81.). Healthgen’s arguments are mistaken for the following two (2) reasons. First, there is evidence in the record of the price difference between the liquid forms of the Accused Product and the DI Products, respectively, and that evidence supports a bond amount of at least 100%. Second, Mr. Reed’s price differential analysis is flawed and unreliable and is given little to no weight.

With regard to the first reason, Ms. Cao’s deposition testimony confirms that [REDACTED] [REDACTED]. (CX-1080C (Cao Dep. Tr.) at 83:1-14 (identifying [REDACTED])). Ventria presented evidence that the liquid form of Healthgen’s products is packaged in a 50 ml bottle with a 20% concentration. (CX-0050.0002 (Healthgen webpage describing the liquid formulation of the Accused Products)). Healthgen’s sales data also reflect sales in [REDACTED] [REDACTED]. (CX-0019C / CPX-0019C (summary of Healthgen sales from 2017-2020); CX-1080C (Cao Dep. Tr.) at 99:8-100:12, 102:1-5, 14-16 (testifying that [REDACTED] [REDACTED])). According to Mr. Reed’s price analysis, the price per gram for the sales [REDACTED] [REDACTED]. (RX-0300C.).

Additionally, Ventria proffered evidence that the sales price of Ventria’s liquid-form DI

Product (i.e., Optibumin) is approximately [REDACTED]. (CX-0888C.0011-12.). As Staff noted, a comparison of the respective price per gram of the liquid forms of the Accused Product and the DI Product shows that the DI Products are between [REDACTED], which suggests that a bond amount between approximately [REDACTED] would be appropriate. (SRBr. at 4.).

With respect to the second reason, Mr. Reed's price differential analysis has been given little, if any, weight. Healthgen and Mr. Reed do not dispute the accuracy of the Complainant's or Mr. LaMotta's calculations regarding the bond. Rather, they criticize Mr. LaMotta's analysis as being skewed for including Healthgen's sales to [REDACTED]. (See RRB. at 81-82; Tr. (Reed) at 1328:8-1329:9, 1332:2-11; RX-0300C (Mr. Reed's summary of Healthgen's U.S. sales data).). Mr. Reed testified that it is inappropriate to include [REDACTED] in the price differential analysis because [REDACTED] [REDACTED] (Tr. (Reed) at 1328:18-1329:9.). By excluding sales to [REDACTED], Mr. Reed identified a price differential of [REDACTED] [REDACTED] (See *id.* at 1330:17-1332:1; RDX-0003C.0014.). Based on Mr. Reed's analysis, Healthgen concluded that "an appropriate bond rate during presidential review of any remedial orders issued by the Commission is, at best, [REDACTED] [REDACTED]" (RRBr. at 82.).

As Staff noted, Mr. Reed's analysis is unreliable and his opinion that Healthgen's sales to [REDACTED] should be excluded from a price differential analysis is mistaken. (SRBr. at 5.). That [REDACTED] [REDACTED]

[REDACTED]

[REDACTED]. Mr. Reed confirmed that if the price for the lowest-cost DI Products [REDACTED] is compared to the average sale price given to [REDACTED], the Accused Products are almost [REDACTED] less expensive than the DI Products. (Tr. (Reed) at 1357:25-1358:9.). Mr. Reed also confirmed that he was not aware of any evidence that [REDACTED] purchases from Healthgen would change during the Presidential review period. (Tr. (Reed), at 1352:12-18.). This indicates that a bond of only [REDACTED] would clearly not “protect the complainant from any injury” because any sales from Healthgen to [REDACTED] would be undercutting the price of the DI Products by a substantial amount. 19 U.S.C. § 1337(j)(3); *see also* 19 C.F.R. §210.50(a)(3). Thus, because Mr. Reed’s exclusion of the Respondent’s sales to [REDACTED] from his price differential analysis leads to a flawed and unreliable conclusion regarding the bone amount, his opinion has been given little, if any, weight.

XIII. WAIVER OR WITHDRAWAL OF RESPONDENT’S DEFENSES

Healthgen did not raise in its Pre-Hearing Brief or offer any evidence during the Hearing to support its Fourth and Fifth Affirmative Defenses of Unenforceability Based on Equitable Doctrines and Relief Not in the Public Interest, respectively. (Resp. at 33-34.).

Consequently, it is a finding of this decision that Healthgen has withdrawn, waived and/or abandoned its Fourth and Fifth Affirmative Defenses consistent with Ground Rules 7.2 and 10.1. *Kinik Co. v. Int’l Trade Comm’n*, 362 F.3d 1359, 1367 (Fed. Cir. 2004).

XIV. CONCLUSIONS OF FACT OR LAW: THIS INITIAL DETERMINATION FINDS A SECTION 337 VIOLATION BASED UPON INFRINGEMENT OF U.S. PATENT NO. 10,618,951

1. Ventria has satisfied jurisdiction and standing requirements.
2. Importation has been satisfied.

3. Claims 1 and 11-13 of U.S. Patent No. 10,618,951 are valid and have been found to be practiced by the Accused Products.
4. At least one of Ventria's DI Products practices one or more claims of U.S. Patent No. 10,618,951.
5. Ventria's domestic R&D activities with respect to its DI Products have been found to satisfy the economic prong of the domestic industry requirement under 19 U.S.C. § 337(a)(3)(A), (B), and (C).
6. Healthgen has violated Section 337 of the Tariff Act of 1930, as amended, by importing into the United States, selling for importation, or selling within the United States after importation certain plant-derived recombinant human serum albumins that infringe claims 1 and 11-13 of U.S. Patent No. 10,618,951.
7. Each of the Defaulting Respondents has violated Section 337 of the Tariff Act of 1930, as amended, by importing into the United States, selling for importation, or selling within the United States after importation certain plant-derived recombinant human serum albumins that infringe claims 1 and 11-13 of U.S. Patent No. 10,618,951.
8. Each of the Defaulting Respondents has violated the Lanham Act under 15 U.S.C. § 1125 by advertising, promoting and/or selling imported plant-derived rHSA without identifying the foreign country of origin of such products. Violations of the Lanham Act, 15 U.S.C. §§ 1051 et seq., are actionable under Section 337.
9. Limited Exclusion Orders against Healthgen and the Defaulting Parties, Cease and Desist Orders against the Defaulting Parties, and a 100% Bond during the Presidential Review Period are recommended.

The lack of discussion of any matter raised by the Parties, or any portion of the record, does not indicate that it has not been considered. Rather, any such matter(s) or portion(s) of the record has/have been determined to be irrelevant, immaterial or meritless. Arguments made on briefs, which were otherwise unsupported by record evidence or legal precedent, have been accorded no weight.

XV. CONCLUSION AND ORDER

This Initial Determination on Violation of Section 337 of the Tariff Act of 1930 is certified to the Commission. All orders and documents, filed with the Secretary, including the exhibit lists enumerating the exhibits received into evidence in this Investigation, that are part of the record, as defined in 19 C.F.R. § 210.38(a), are not certified, since they are already in the Commission's possession in accordance with Commission Rules. *See* 19 C.F.R. § 210.38(a). In accordance with 19 C.F.R. § 210.39(c), all material found to be confidential under 19 C.F.R. § 210.5 is to be given *in camera* treatment.

After the Parties have provided proposed redactions of confidential business information ("CBI") that have been evaluated and accepted, the Secretary shall serve a public version of this ID upon all parties of record. The Secretary shall serve a confidential version upon counsel who are signatories to the Protective Order (Order No. 1) issued in this Investigation.

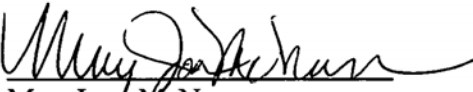
Pursuant to 19 C.F.R. § 210.42(h), this Initial Determination shall become the determination of the Commission unless a party files a petition for review pursuant to 19 C.F.R. § 210.43(a) or the Commission, pursuant to 19 C.F.R. § 210.44, orders on its own motion a review of the Initial Determination or certain issues therein.

Within fourteen (14) business days of the date of this document, the Parties shall jointly submit to the Office of the Administrative Law Judges through McNamara337@usitc.gov a statement whether they seek to have any confidential portion of this document. That is the courtesy copy pursuant to Ground Rule 1.3.2. Any party seeking redactions to the public version must submit to this office through McNamara337@usitc.gov a copy of a proposed public version of this document pursuant to Ground Rule 1.10 with colored highlighting clearly indicating any portion asserted to contain confidential business information. The Parties' submission shall also

include an index identifying the pages of this document where proposed redactions are located.

The Parties' submission concerning the public version of this document need not be filed with the Commission Secretary.

SO ORDERED.



MaryJoan McNamara
Administrative Law Judge