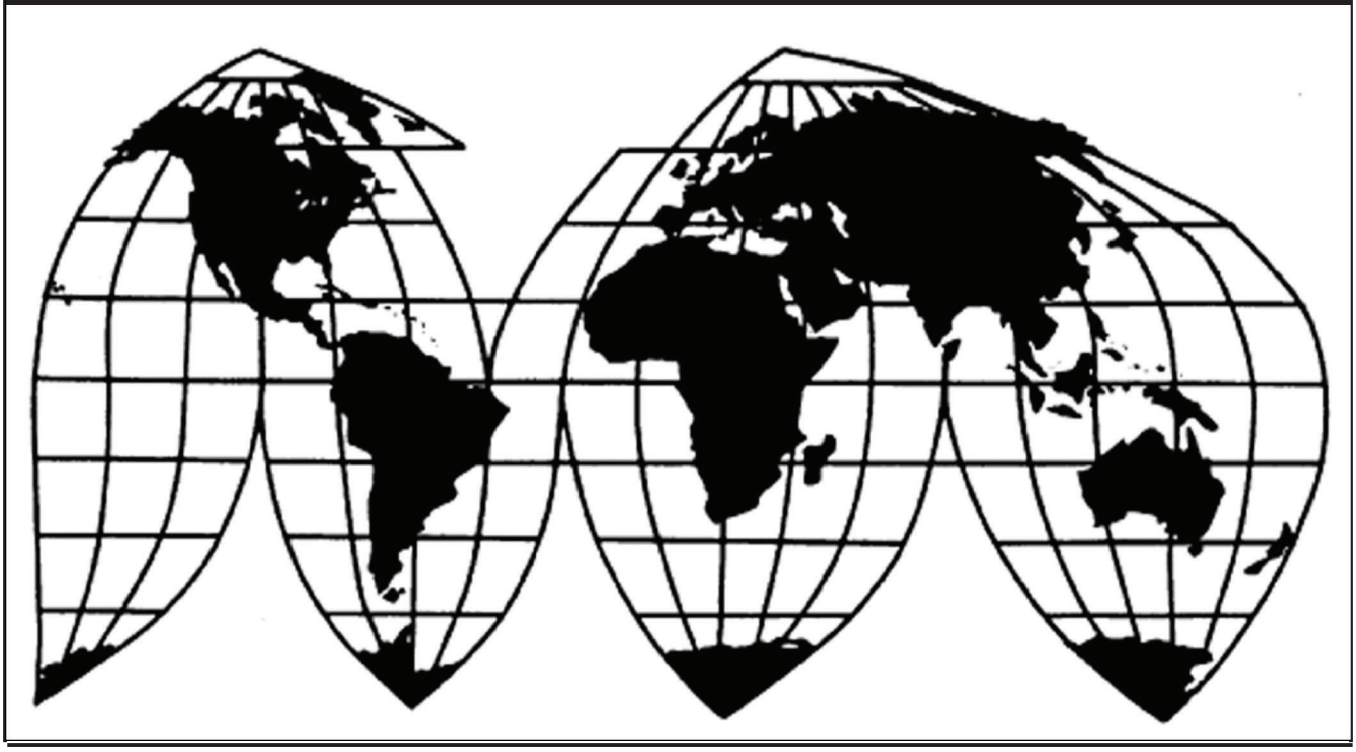
In the Matter of

CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME

337-TA-1120

Publication 5254 **February 2022**

U.S. International Trade Commission



Washington, DC 20436

U.S. International Trade Commission

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In the Matter of

CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME

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UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C.

In the Matter of	
CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME	**Inv. No. 337-TA-1120**

COMMISSION ORDER

On May 19, 2020, the Commission issued a final determination finding a violation of section 337 of the Tariff Act of 1930, as amended (19 U.S.C. § 1337) ("section 337"), based on the importation into the United States, the sale for importation, and the sale within the United States after importation of certain bacterial strains and 2'-fucosyllactose oligosaccharides produced therefrom that infringe certain claims of U.S. Patent No. 9,970,018 ("the '018 patent"). *See* 85 Fed. Reg. 31549 (May 26, 2020); *see also* 83 Fed. Reg. 28865 (June 21, 2018) (defining the scope of the investigation as "2'-fucosyllactose oligosaccharides"). The Commission also adjudicated infringement with respect to a TTFL12 bacterial strain imported by the named respondent and determined that it does not infringe the '018 patent. *See id.* The Commission issued a limited exclusion order ("LEO") barring entry of 2'-fucosyllactose ("2'-FL") oligosaccharides that infringe the asserted patent claims but also including an explicit carve-out for 2'-fucosyllactose oligosaccharides made with the non-infringing TTFL12 bacterial strain.

On June 2, 2020, complainant Glycosyn LLC ("Glycosyn") filed a petition for Commission reconsideration of part III(B) of the Commission Opinion (*i.e.*, "Adjudication of Infringement with Respect to the TTFL12 Strain"). Having considered Glycosyn's petition, the responses thereto, and the record in this investigation, the Commission has determined to deny Glycosyn's petition for reconsideration.

I. BACKGROUND

A. Procedural Background

The Commission instituted this investigation on June 21, 2018, based on a complaint, as amended and supplemented, filed by Glycosyn of Waltham, Massachusetts. *See* 83 Fed. Reg. 28865 (June 21, 2018). The complaint alleged violations of section 337 based upon the importation into the United States, the sale for importation, and the sale within the United States after importation of certain human milk oligosaccharides, by reason of infringement of certain claims of U.S. Patent No. 9,453,230 ("the '230 patent") and the '018 patent. *See id.* The notice of investigation named Jennewein of Rheinbreitbach, Germany as respondent in this investigation. *See id.* The Office of Unfair Import Investigations was also a party to this investigation. *See id.*

The Commission partially terminated the investigation as to certain claims of the '018 patent and all asserted claims of the '230 patent based on the withdrawal of the allegations pertaining to those patent claims. *See* Order No. 5 (Aug. 9, 2018), *unreviewed*, Comm'n Notice (Aug. 29, 2018); Order No. 15 (Oct. 30, 2018), *unreviewed*, Comm'n Notice (Nov. 29, 2018); Order No. 17 (Nov. 19, 2018), *unreviewed*, Comm'n Notice (Dec. 12, 2018); Order No. 25 (Feb. 8, 2019), *unreviewed*, Comm'n Notice (Feb. 28, 2019). Claims 1-3, 5, 8, 10, 12, 18, and 23-28 of the '018 patent remained pending in this investigation.

On September 9, 2019, the administrative law judge ("ALJ") issued a final initial determination ("FID") finding a violation of section 337 based on the infringement of claims 1-3, 5, 8, 10, 12, 18, and 24-28, but not claim 23 of the '018 patent based on non-infringement of that claim. *See* FID at 35. On May 19, 2020, the Commission affirmed the FID's finding of infringement and issued a final determination finding a violation by certain bacterial strains.

See 85 Fed. Reg. 31549 (May 26, 2020). In particular, the Commission reversed the FID's decision not to adjudicate the TTFL12 bacterial strain and determined that it does not infringe any of the asserted claims. *See id.* The Commission issued an LEO barring entry of 2'-FL oligosaccharides that infringe the Asserted Claims but also including an explicit carve-out for 2'-FL oligosaccharides made with the non-infringing TTFL12 bacterial strain.[1] The Commission also set a bond in the amount of five (5) percent of the entered value of Jennewein's 2'-FL product during the period of Presidential review.

On June 2, 2020, pursuant to Commission Rule 210.47 (19 C.F.R. § 210.47), Glycosyn petitioned for reconsideration of part III(B) of the Commission Opinion (*i.e.*, "Adjudication of Infringement with Respect to the TTFL12 Strain").[2] On June 8 and 9, 2020, respectively, Jennewein and the Commission's Investigative Attorney opposed Glycosyn's petition.[3]

II. STANDARD FOR RECONSIDERATION

Commission Rule 210.47 governs petitions for reconsideration and provides that:

> Within 14 days after service of a Commission determination, any party may file with the Commission a petition for reconsideration of such determination or any action ordered to be taken thereunder, setting forth the relief desired and the grounds in support thereof. Any petition filed under this section must be confined to new questions raised by the determination or action ordered to be taken thereunder and upon which the petitioner had no opportunity to submit arguments. . . .

See 19 C.F.R. § 210.47.

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[1] Complainant did not request, and the Commission did not issue, a cease and desist order.

[2] *See* Complainant Glycosyn LLC's Petition for Reconsideration of Part III(B) of the Commission Opinion (June 2, 2020).

[3] *See* Respondent Jennewein Biotechnologie GmbH's Opposition to Complainant Glycosyn LLC's Petition for Reconsideration of Part III(B) of the Commission Opinion (June 8, 2020); Response of the Office of Unfair Import Investigations to Complainant's Petition for Reconsideration of Part III(B) of the Commission Opinion (June 9, 2020).

III. DISCUSSION

Glycosyn's petition for reconsideration does not identify new questions raised by the ALJ's FID or the Commission's final determination or present arguments that Glycosyn did not have the opportunity to address in previous filings before either the ALJ or the Commission. As such, the Commission has determined that Glycosyn's petition for reconsideration does not satisfy the requirements of Commission Rule 210.47.[4]

IV. CONCLUSION

Accordingly, upon consideration of the record and the submissions in this matter, the Commission hereby ORDERS that:

1. Glycosyn's petition for reconsideration is DENIED.

2. The Secretary will serve this Order on all parties to the investigation.

By order of the Commission.

Lisa R. Barton
Secretary to the Commission

Issued: October 1, 2020

[4] Commissioner Schmidtlein respectfully dissents. In light of the particular facts (including the new evidence cited by Glycosyn in its petition for reconsideration) and the procedural history of this investigation, and given the rationale provided in her dissent, in her view, Glycosyn's petition should be granted and Part III(B) of the majority's opinion should be reconsidered.

CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME **Inv. No. 337-TA-1120**

PUBLIC CERTIFICATE OF SERVICE

I, Lisa R. Barton, hereby certify that the attached **COMMISSION ORDER** has been served via EDIS upon the Commission Investigative Attorney, **Lisa Murray, Esq.**, and the following parties as indicated, on **October 1, 2020**

Lisa R. Barton, Secretary
U.S. International Trade Commission
500 E Street, SW, Room 112
Washington, DC 20436

On Behalf of Complainant Glycosyn LLC:

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UNITED STATES INTERNATIONAL TRADE COMMISSION

Washington, D.C.

In the Matter of	
CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME	**Investigation No. 337-TA-1120**

NOTICE OF COMMISSION FINAL DETERMINATION FINDING A VIOLATION OF SECTION 337; ISSUANCE OF A LIMITED EXCLUSION ORDER; TERMINATION OF THE INVESTIGATION

AGENCY: U.S. International Trade Commission.

ACTION: Notice.

SUMMARY: Notice is hereby given that the U.S. International Trade Commission has found a violation of section 337 of the Tariff Act of 1930 ("section 337"), as amended, in this investigation. The Commission has issued a limited exclusion order ("LEO") prohibiting the importation by respondent Jennewein Biotechnologie GmbH ("Jennewein") of Rheinbreitbach, Germany of certain human milk oligosaccharides that infringe complainant's asserted claims. The investigation is terminated.

FOR FURTHER INFORMATION CONTACT: Houda Morad, Office of the General Counsel, U.S. International Trade Commission, 500 E Street SW., Washington, DC 20436, telephone (202) 708-4716. Copies of non-confidential documents filed in connection with this investigation are or will be available for inspection during official business hours (8:45 a.m. to 5:15 p.m.) in the Office of the Secretary, U.S. International Trade Commission, 500 E Street SW., Washington, D.C. 20436, telephone (202) 205-2000. General information concerning the Commission may also be obtained by accessing its Internet server at *https://www.usitc.gov*. The public record for this investigation may be viewed on the Commission's electronic docket (EDIS) at *https://edis.usitc.gov*. Hearing-impaired persons are advised that information on this matter can be obtained by contacting the Commission's TDD terminal on (202) 205-1810.

SUPPLEMENTARY INFORMATION: The Commission instituted this investigation on June 21, 2018, based on a complaint, as amended and supplemented, filed on behalf of Glycosyn LLC of Waltham, Massachusetts ("Glycosyn"). *See* 83 Fed. Reg. 28865 (June 21, 2018). The complaint, as amended and supplemented, alleges violations of section 337 of the Tariff Act of 1930, as amended, 19 U.S.C. 1337 ("section 337"), based upon the importation into the United States, the sale for importation, and the sale within the United States after importation of certain human milk oligosaccharides by reason of infringement of claims 1-40 of U.S. Patent No. 9,453,230 ("the '230 patent") and claims 1-28 of U.S. Patent No. 9,970,018 ("the '018 patent").

See id. The notice of investigation named Jennewein as a respondent in this investigation. *See id.* The Office of Unfair Import Investigations ("OUII") is also named as a party to the investigation. *See id.*

The ALJ conducted an evidentiary hearing on May 14-17, 2019, and on September 9, 2019, issued the FID finding a violation of section 337 based on the infringement of claims 1-3, 5, 8, 10, 12, 18, and 24-28 of the '018 patent (hereinafter, the "Asserted Claims"). In addition, the FID finds that the Asserted Claims are neither invalid under 35 U.S.C. §§ 103 and 112, nor unenforceable for inequitable conduct. Furthermore, the FID finds that the domestic industry requirement is satisfied. All asserted claims in the '230 patent were withdrawn during the investigation. The FID also contains a recommended determination ("RD") recommending that the Commission issue an LEO barring entry of articles that infringe the '018 patent. The RD also recommends that the Commission impose a 5 percent bond during the period of Presidential review. Furthermore, as directed by the Commission, the RD provides findings with respect to the public interest and recommends that the Commission determine that the public interest factors do not preclude entry of the proposed LEO. Glycosyn does not seek and the RD does not recommend issuance of a cease and desist order.

On October 9 and 10, 2019, respectively, Glycosyn and Jennewein filed statements on the public interest pursuant to Commission Rule 210.50. On October 23, 2019, non-party DuPont Nutrition & Health filed a public interest submission pursuant to the Commission's notice requesting public interest comments. *See* 84 Fed. Reg. 49335 (Sept. 19, 2019).

On January 30, 2020, the Commission issued a notice determining to review the FID in part. *See* 85 Fed. Reg. 6573 (Feb. 5, 2020). The Commission's notice requested written submissions in response to certain questions relating to issues under review and on issues of remedy, the public interest, and bonding. On February 18, 2020, the parties, including OUII, filed written submissions in response to the notice, and on February 25, 2020, the parties filed responses to each other's submissions. On February 18, 2020, non-party Abbott Laboratories filed a written submission concerning the public interest.

Having examined the record of this investigation, including the FID, the RD, and the parties' and non-parties' submissions, the Commission has determined to affirm with modification the FID's determination of a violation of section 337 with respect to claims 1-3, 5, 8, 10, 12, 18, and 24-28 of the '018 patent. Specifically, as explained in the Commission Opinion filed concurrently herewith, the Commission has determined to affirm with modification the FID's findings with respect to infringement by the accused Jennewein bacterial strains and to reverse the FID's decision not to adjudicate infringement with respect to Jennewein's TTFL12 bacterial strain. As to the TTFL12 strain, the Commission has determined that it does not infringe the Asserted Claims. All findings in the FID that are not inconsistent with the Commission's determination are affirmed.

The Commission has determined that the appropriate remedy is an LEO against Jennewein's infringing products. The Commission has also determined that the public interest factors enumerated in subsection 337(d)(1) (19 U.S.C. 1337(d)(1)) do not preclude the issuance of the LEO. The Commission has further determined to set a bond during the period of

Presidential review at five (5) percent of the entered value of Jennewein's infringing products (19 U.S.C. 1337(j)).

The Commission's order and opinion were delivered to the President and to the United States Trade Representative on the day of their issuance.

The Commission's vote for these determinations took place on May 19, 2020.

The authority for the Commission's determination is contained in section 337 of the Tariff Act of 1930, as amended (19 U.S.C. 1337), and in part 210 of the Commission's Rules of Practice and Procedure (19 CFR part 210).

By order of the Commission.

Lisa R. Barton
Secretary to the Commission

Issued: May 19, 2020

CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME **Inv. No. 337-TA-1120**

PUBLIC CERTIFICATE OF SERVICE

I, Lisa R. Barton, hereby certify that the attached **NOTICE** has been served via EDIS upon the Commission Investigative Attorney, **Lisa Murray, Esq.**, and the following parties as indicated, on **May 19, 2020**.

Lisa R. Barton, Secretary
U.S. International Trade Commission
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Washington, DC 20436

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UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C.

In the Matter of **CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME**	**Investigation No. 337-TA-1120**

LIMITED EXCLUSION ORDER

The United States International Trade Commission ("Commission") has determined that there is a violation of Section 337 of the Tariff Act of 1930, as amended (19 U.S.C. § 1337), in the unlawful importation, sale for importation, or sale within the United States after importation by Jennewein Biotechnologie GmbH ("Jennewein" or "Respondent") of certain 2'-fucosyllactose oligosaccharides that infringe one or more of claims 1-3, 5, 8, 10, 12, 18, and 24-28 ("the Asserted Claims") of U.S. Patent No. 9,970,018 ("the '018 patent").

Having reviewed the record of this investigation, including the written submissions of the parties, the Commission has made its determination on the issues of remedy, public interest, and bonding. The Commission has determined that the appropriate form of relief includes a limited exclusion order prohibiting the unlicensed entry into the United States of 2'-fucosyllactose oligosaccharides manufactured abroad by or on behalf of, or imported by or on behalf of, Respondent or any of its affiliated companies, parents, subsidiaries, or other related business entities, or its successors or assigns. The exclusion order does not apply to Respondent's TTFL12 bacterial strain and 2'-fucosyllactose oligosaccharides produced by that strain, which, as the Commission determined, do not infringe the Asserted Claims.

The Commission has also determined that the public interest factors enumerated in 19 U.S.C. § 1337(d) do not preclude the issuance of the limited exclusion order, and that the bond

during the period of Presidential review shall be in the amount of five (5) percent of the entered value of the covered articles.

Accordingly, the Commission hereby ORDERS that:

1. 2'-fucosyllactose oligosaccharides that infringe one or more of the Asserted Claims that are manufactured abroad by or on behalf of, or imported by or on behalf of, Respondent, or its affiliated companies, parents, subsidiaries, or other related business entities, or its successors or assigns ("covered articles"), are excluded from entry for consumption into the United States, entry for consumption from a foreign-trade zone, or withdrawal from a warehouse for consumption, for the remaining term of the '018 patent, except under license of the patent owner or as provided by law.

2. This Order does not apply to Respondent's TTFL12 bacterial strain and 2'-fucosyllactose oligosaccharides produced by that strain, which, as the Commission determined, do not infringe the Asserted Claims.

3. Notwithstanding paragraph 1 of this Order, covered articles are entitled to entry into the United States for consumption, entry for consumption from a foreign trade zone, or withdrawal from a warehouse for consumption, under bond in the amount of five (5) percent of the entered value of the infringing products pursuant to subsection (j) of section 337 of the Tariff Act of 1930, as amended (19 U.S.C. § 1337(j)), and the Presidential Memorandum for the United States Trade Representative of July 21, 2005, (70 FR 43251), from the day after this Order is received by the United States Trade Representative, and until such time as the United States Trade representative notifies the Commission that this Order is approved or disapproved but, in any event, not later than sixty (60) days after the date of receipt of this Order. All entries of

covered articles made pursuant to this paragraph are to be reported to U.S. Customs and Border Protection ("CBP"), in advance of the date of the entry, pursuant to procedures CBP establishes.

4. At the discretion of CBP and pursuant to the procedures it establishes, persons seeking to import 2'-fucosyllactose oligosaccharides, that are potentially subject to this Order may be required to certify that they are familiar with the terms of this 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 paragraph 1 of this Order. At its discretion, CBP may require persons who have provided the certification described in this paragraph to furnish such records or analyses as are necessary to substantiate this certification.

5. In accordance with 19 U.S.C. § 1337(l), the provisions of this Order shall not apply to 2'-fucosyllactose oligosaccharides that are imported by or for the use of the United States, or imported for and to be used for, the United States with the authorization or consent of the Government.

6. The Commission may modify this Order in accordance with the procedures described in Rule 210.76 of the Commission's Rules of Practice and Procedure (19 C.F.R. § 210.76).

7. The Secretary shall serve copies of this Order upon each party of record in this Investigation and upon CBP.

8. Notice of this Order shall be published in the Federal Register.

By order of the Commission.

Lisa R. Barton
Secretary to the Commission

Issued: May 19, 2020

CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME **Inv. No. 337-TA-1120**

PUBLIC CERTIFICATE OF SERVICE

I, Lisa R. Barton, hereby certify that the attached **ORDER, COMMISION** has been served via EDIS upon the Commission Investigative Attorney, **Lisa Murray, Esq.**, and the following parties as indicated, on **May 19, 2020**.

Lisa R. Barton, Secretary
U.S. International Trade Commission
500 E Street, SW, Room 112
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PUBLIC VERSION

UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C.

In the Matter of **CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME**	**Inv. No. 337-TA-1120**

COMMISSION OPINION

The Commission has determined that there has been a violation of section 337 of the Tariff Act of 1930, as amended, 19 U.S.C. § 1337 ("section 337"), on review of the final initial determination ("FID") of the presiding administrative law judge ("ALJ"), based on the infringement of U.S. Patent No. 9,970,018 by respondent's accused bacterial strains. The Commission has also determined to reverse the FID's decision declining to adjudicate respondent's alternative TTFL12 strain and finds no infringement as to that strain. This opinion sets forth the Commission's reasoning in support of that determination. In addition, the Commission adopts the findings in the FID that are not inconsistent with this opinion.

I. BACKGROUND

A. Procedural Background

The Commission instituted this investigation on June 21, 2018, based on a complaint, as amended and supplemented, filed by Glycosyn LLC ("Glycosyn") of Waltham, Massachusetts. *See* 83 Fed. Reg. 28865-66 (June 21, 2018). The complaint alleged violations of section 337 based upon the importation into the United States, the sale for importation, and the sale within the United States after importation of certain human milk oligosaccharides, by reason of infringement of certain claims of U.S. Patent Nos. 9,453,230 ("the '230 patent") and 9,970,018 ("the '018 patent"). *See id.* The complaint also alleges the existence of a domestic industry.

The notice of investigation named Jennewein Biotechnologie GmbH of Rheinbreitbach, Germany ("Jennewein") as respondent in this investigation. *See id.* The Office of Unfair Import Investigations ("OUII") is also a party to this investigation. *See id.*

The Commission later terminated the investigation as to all asserted claims of the '230 patent and certain asserted claims of the '018 patent based on the withdrawal of the allegations pertaining to those claims. *See* Order No. 5 (Aug. 9, 2018), *unreviewed*, Comm'n Notice (Aug. 29, 2018); Order No. 15 (Oct. 30, 2018), *unreviewed*, Comm'n Notice (Nov. 29, 2018); Order No. 17 (Nov. 19, 2018), *unreviewed*, Comm'n Notice (Dec. 12, 2018); Order No. 25 (Feb. 8, 2019), *unreviewed*, Comm'n Notice (Feb. 28, 2019). Claims 1-3, 5, 8, 10, 12, 18, and 23-28 of the '018 patent remain pending in this investigation.

The ALJ conducted an evidentiary hearing on May 14-17, 2019. On September 9, 2019, the ALJ issued the FID finding a violation of section 337 based on the infringement of claims 1-3, 5, 8, 10, 12, 18, and 24-28 (hereinafter, "the Asserted Claims") but not claim 23 of the '018 patent, based on non-infringement of that claim.[1] *See* FID at 35. Furthermore, the FID finds that the domestic industry requirement is satisfied.

The FID also contains a Recommended Determination ("RD") recommending, should a violation of section 337 be found, that the Commission issue a limited exclusion order ("LEO") barring entry of articles that infringe the Asserted Claims.[2] The RD also recommends that the Commission impose a bond in the amount of five (5) percent of the entered value of the infringing articles during the period of Presidential review. Furthermore, as directed by the

[1] Glycosyn did not petition for review of the FID's finding that Jennewein does not infringe claim 23.

[2] Glycosyn did not request, and the RD does not recommend, a cease and desist order against Jennewein.

Commission (*see* 83 Fed. Reg. at 28865), the RD provides findings with respect to the public interest and recommends that the Commission determine that the public interest factors do not preclude entry of the proposed LEO.

On September 23, 2019, Jennewein and the Commission's Investigative Attorney ("IA") filed petitions for review of the FID.[3] Jennewein petitioned for review of the FID's findings with respect to claim construction and infringement, and both Jennewein and the IA petitioned for review of the FID's decision not to adjudicate infringement with respect to Jennewein's TTFL12 bacterial strain, which Glycosyn did not accuse in its complaint. On October 1, 2019, Glycosyn and the IA filed responses to the various petitions.[4]

On October 9 and 10, 2019, respectively, Glycosyn and Jennewein filed statements on the public interest pursuant to Commission Rule 210.50(a)(4), 19 C.F.R. 210.50(a)(4).[5] On October 23, 2019, non-party DuPont Nutrition & Health ("DuPont") filed a public interest submission pursuant to the Commission's notice requesting public interest comments, *see* 84 Fed. Reg. 49335 (Sept. 19, 2019), supporting the ALJ's recommended LEO and asserting that it has the capacity to replace the excluded products in a commercially reasonable time.[6]

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[3] *See* Respondent Jennewein Biotechnologie GmbH's Petition for Commission Review (Sep. 23, 2019) (hereinafter, "Jennewein's Pet."); OUII Petition for Review (Sep. 23, 2019) (hereinafter, "IA's Pet.").

[4] *See* Complainant Glycosyn LLC's Consolidated Response to Respondent Jennewein Biotechnologie GmbH's and Office of Unfair Import Investigations' Petitions for Commission Review (Oct. 1, 2019) (hereinafter, "Glycosyn's Pet. Resp."); Office of Unfair Import Investigations' Response to Respondent's Petition for Review (Oct. 1, 2019) (hereinafter, "IA's Pet. Resp.").

[5] *See* Complainant Glycosyn LLC's Statement of Information Relating to the Public Interest (Oct. 9, 2019) (hereinafter, "Glycosyn's PI Br."); Public Interest Statement of Respondent Jennewein Biotechnologie GmbH (Oct. 10, 2019) (hereinafter, "Jennewein's PI Br.").

[6] *See* Public Interest Submission of DuPont Nutrition & Health (hereinafter, "DuPont PI Br.").

On January 30, 2020, the Commission issued a notice determining to review the FID in part. *See* 85 Fed. Reg. 6573-75 (Feb. 5, 2020) ("the WTR/Remedy Notice"). Specifically, the Commission determined to review: (1) the FID's infringement findings with respect to Jennewein's bacterial strains adjudicated in this investigation; and (2) the FID's decision not to adjudicate infringement as to Jennewein's alternative bacterial strain, *i.e.*, the TTFL12 strain. *See id.* The Commission determined not to review the remainder of the FID. *See id.* The notice invited written submissions from the parties on issues under review, and from the parties, interested government agencies, and any other interested parties on issues of remedy, the public interest, and bonding. *See id.*

On February 18, 2020, the parties, including OUII, filed written submissions in response to the WTR/Remedy Notice,[7] and on February 25, 2020, the parties filed responses to each other's submissions.[8] Also on February 18, 2020, non-party Abbott Laboratories ("Abbott") filed a written submission concerning the public interest in response to the WTR/Remedy Notice,

[7] *See* Complainant Glycosyn LLC's Response to Questions in the Commission's Notice of Commission Decision to Review in Part a Final Initial Determination Finding a Violation of Section 337 (Feb. 18, 2020) (hereinafter, "Glycosyn's Resp."); Complainant Glycosyn LLC's Initial Submission on the Form of Remedy, the Public Interest, and Bonding Pursuant to the Commission's Notice of Commission Decision to Review in Part a Final Initial Determination Finding a Violation of Section 337 (Feb. 18, 2020) (hereinafter, "Glycosyn's Remedy Br."); Respondent Jennewein Biotechnologie GmbH's Responses to Questions Raised by the Commission (Feb. 18, 2020) (hereinafter, "Jennewein's Resp."); Brief of the Office of Unfair Import Investigations on Issues under Review and on Remedy, the Public Interest, and Bonding (Feb. 18, 2020) (hereinafter, "IA's Resp.").

[8] *See* Complainant Glycosyn LLC's Reply to Respondent's and OUII's Responses to the Commission's Questions regarding Final Initial Determination Finding a Violation of Section 337 (Feb. 25, 2020) (hereinafter, "Glycosyn's Reply"); Respondent Jennewein Biotechnologie GmbH's Reply to Responses by Glycosyn LLC and the Office of Unfair Import Investigations to Questions Raised by the Commission and Responses to Glycosyn's and OUII's Submissions on Remedy, the Public Interest, and Bonding (Feb. 25, 2020) (hereinafter, "Respondents' Reply"); Reply Brief of the Office of Unfair Import Investigations on Issues under Review and on Remedy, the Public Interest, and Bonding (Feb. 25, 2020) (hereinafter, "IA's Reply").

and alleged that "Jennewein is the only supplier whose product has been fully qualified through Abbott's quality and regulatory processes, raising public interest concerns from remedial relief."[9]

B. The Asserted Patent

The '018 patent issued on May 15, 2018. *See* JX-3, '018 Patent. The '018 patent, titled "Biosynthesis of Human Milk Oligosaccharides in Engineered Bacteria," relates to "compositions and methods for producing fucosylated oligosaccharides" which are "typically found in human milk" and which "serve critical roles in the establishment of a healthy gut microbiome, in the prevention of disease and in immune function." *See id.* at 1:27-39. The specification of the '018 patent states that "the invention . . . makes use of an engineered bacterium *E. coli* or other bacteria engineered to produce" fucosylated oligosaccharides. *See id.* at 15:66-16:4.

The '018 patent specification explains that "[b]iosynthesis of fucosylated HMOS[10] requires the generation of an enhanced cellular pool of both lactose and GDP[11]-fucose." *See id.* at 16:27-29; *see also id.* at Figure 3 (requiring both lactose and GDP-fucose for the synthesis of 2'-fucosyllactose). For example, the specification discloses that "[t]he ability of the *E. coli* host strain to accumulate lactose was . . . engineered by simultaneous deletion of the endogenous β-galactosidase gene (lacZ) and the lactose operon repressor gene (lacI)" while "the lacIq promoter was placed immediately upstream of the lactose permease gene, lacY." *See id.* at 16:37-43 (Example 1). The specification states that "[t]he modified strain thus maintains its

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[9] *See* Public Interest Submission of Abbott Laboratories (Feb. 18, 2020) (hereinafter "Abbott's PI Br.").

[10] "HMOS" refers to Human Milk Oligosaccharides.

[11] "GDP" refers to guanosine diphosphate. *See* JX-3, '018 Patent at 1:61-63.

ability to transport lactose from the culture medium via LacY" but the lacZ (β-galactosidase) gene responsible for lactose catabolism (*i.e.*, breakdown) is deleted. *See id.* at 16:43-47 (Example 1). Therefore, the specification continues, "[a]n intracellular lactose pool is . . . created when the modified strain is cultured in the presence of exogenous lactose." *See id.* at 16:47-49 (Example 1).

The specification also describes "bacterial host cells with the ability to accumulate a[n] intracellular lactose pool while simultaneously possessing low, functional levels of cytoplasmic β-galactosidase activity for example as provided by the introduction of a functional recombinant *E. coli* lacZ gene or by a β-galactosidase gene from any of a number of other organisms." *See id.* at 7:22-28. The specification explains that "low level of cytoplasmic β-galactosidase activity while not high enough to significantly diminish the intracellular lactose pool is nevertheless very useful for tasks such as phenotypic marking of desirable genetic loci during construction of host cell backgrounds, for detection of cell lysis due to undesired bacteriophage contaminations in fermentation processes, or for the facile removal of undesired residual lactose at the end of fermentations." *See id.* at 7:37-45.

With regard to GDP-fucose production, the specification of the '018 patent further states that "[o]ne strategy for GDP-fucose production is to enhance the bacterial cell's natural synthesis capacity," *e.g.*, "by inactivating enzymes involved in GDP-fucose consumption, and/or by overexpressing a positive regulator protein, RcsA, in the colanic acid (a fucose containing exopolysaccharide) synthesis pathway." *See id.* at 17:4-10. The specification explains that "this metabolic engineering strategy redirects the flux of GDP-fucose destined for colanic acid synthesis to oligosaccharide synthesis." *See id.* at 17:10-12.

Still further, the specification of the '018 patent describes a "bacterium [that] possesses fucosyl transferase activity," *e.g.*, "an exogenous fucosyltransferase gene." *See id.* at 5:28-32. The specification explains that "[a]n exemplary . . . fucosyltransferase gene is the wcfW gene" and that "[p]rior to the present invention, this wcfW gene . . . was not suspected to possess the ability to utilize lactose as an acceptor sugar," *i.e.*, as a substrate for HMOS synthesis. *See id.* at 5:28-38; *see also id.* at Figure 3 (involving α(1,2)FT, *i.e.*, fucosyltransferase, in the synthesis of 2'-fucosyllactose).

Claim 1 of the '018, from which the remaining asserted claims depend, patent recites the following invention (with the disputed claim limitations in bold):

> A method for producing a fucosylated oligosaccharide in a bacterium, comprising
>
> providing an isolated *E. coli* bacterium comprising,
>
> (i) a deletion or functional inactivation of an endogenous β-galactosidase gene;
>
> (ii) ***an exogenous functional β-galactosidase gene*** comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium, wherein ***the level of β-galactosidase activity comprises between 0.05 and 200 units***;
>
> (iii) an inactivating mutation in a colanic acid synthesis gene; and
>
> (iv) an exogenous lactose-accepting fucosyltransferase gene;
>
> culturing said bacterium in the presence of lactose; and
>
> retrieving a fucosylated oligosaccharide from said bacterium or from a culture supernatant of said bacterium.

See id. at 111:41-57 (claim 1).

C. Domestic Industry Product

The FID identifies Glycosyn's E997 bacterial strain and its production of 2'-fucosyllactose (2'-FL) as practicing at least one claim of the '018 patent. *See* FID at 7. The FID also determines that Glycosyn satisfies the domestic industry requirement. *See id.* at 61-67,

96-113. No party petitioned for review of these findings, and the Commission determined not to review these findings.

D. Accused and Redesigned or Alternative Products

The accused product in this investigation is Jennewein's 2'-FL product which was produced using *E. coli* bacterial strains #1540 and a derivative thereof, known as "the #1540 derivative" or "the #2410 strain" (collectively, "Accused Strains"). *See* FID at 7. The FID finds that the Accused Strains infringe the Asserted Claims of the '018 patent.

Jennewein also requested adjudication as to its redesigned or alternative TTFL12 bacterial strain in this investigation. Glycosyn did not accuse that strain in this investigation and the FID declined to adjudicate infringement with respect to that strain. *See id.* at 28-35. The Commission determined to review the FID's decision not to adjudicate infringement with respect to the TTFL12 strain. *See* 85 Fed. Reg. at 6574.

II. LEGAL STANDARDS

A. Standard on Review

Commission Rule 210.45(c) provides that "[o]n review, the Commission may affirm, reverse, modify, set aside or remand for further proceedings, in whole or in part, the initial determination of the administrative law judge" and that "[t]he Commission also may make any findings or conclusions that in its judgment are proper based on the record in the proceeding." *See* 19 C.F.R. § 210.45(c). In addition, as explained in *Certain Polyethylene Terephthalate Yarn and Products Containing Same*, "[o]nce the Commission determines to review an initial determination, the Commission reviews the determination under a *de novo* standard." Inv. No. 337-TA-457, Comm'n Op., 2002 WL 1349938, *5 (June 18, 2002) (citations omitted). This is "consistent with the Administrative Procedure Act which provides that once an initial agency

decision is taken up for review, 'the agency has all the powers which it would have in making the initial decision except as it may limit the issues on notice or by rule.'" *Id.* (citing 5 U.S.C. § 557(b)).

B. Infringement

"An infringement analysis entails two steps. The first step is determining the meaning and scope of the patent claims asserted to be infringed. The second step is comparing the properly construed claims to the device accused of infringing." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996) (citations omitted). Infringement must be proven by a preponderance of the evidence. *See SmithKline Diagnostics, Inc. v. Helena Labs. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988). The preponderance of the evidence standard "requires proving that infringement was more likely than not to have occurred." *Warner-Lambert Co. v. Teva Pharm. USA, Inc.*, 418 F.3d 1326, 1341 n.15 (Fed. Cir. 2005).

Literal infringement requires the patentee to prove that the accused device contains each and every limitation of the asserted claim(s). *See Frank's Casing Crew & Rental Tools, Inc. v. Weatherford Int'l, Inc.*, 389 F.3d 1370, 1378 (Fed. Cir. 2004). Where literal infringement is not found, infringement can still be found under the doctrine of equivalents. *See TIP Sys., LLC v. Phillips & Brooks/Gladwin, Inc.*, 529 F.3d 1364, 1376 (Fed. Cir. 2008) ("Infringement under the doctrine of equivalents may be found when the accused device contains an 'insubstantial' change from the claimed invention.") (citations omitted).

III. DISCUSSION

The Commission determined to review: (1) the FID's infringement findings with respect to Jennewein's bacterial strains adjudicated in this investigation; and (2) the FID's decision not

to adjudicate infringement as to Jennewein's alternative or redesigned bacterial strain, *i.e.*, the TTFL12 strain. *See* 85 *Fed. Reg.* at 6574.

A. Infringement as to the Term Exogenous Functional β-Galactosidase Gene

The previously presiding ALJ[12] construed "functional β-galactosidase gene" to mean "functional sequence of DNA that encodes β-galactosidase." *See* Order No. 22 at 29 (Dec. 18, 2018). No party petitioned for review of that construction. The parties also agreed that "exogenous" is properly construed as "originating outside an organism, tissue, or cell." *See id.* at 12.

The FID finds that the Accused Strains do not literally satisfy the claim term "an exogenous functional β-galactosidase gene," but that the term is satisfied under the doctrine of equivalents. *See* FID at 38-45. The FID reasons that Jennewein's Accused Strains include two distinct DNA sequences, namely, *lacZα* and *lacZ*Ω, which, together, encode for the β-galactosidase enzyme. *See id.* at 38-39. The FID concludes that "Jennewein's Accused Strains do not literally infringe 'an exogenous functional β-galactosidase gene' because they lack a single sequence of DNA which functions to create a β-galactosidase gene." *See id.* at 39. Nevertheless, the FID finds "no difference between the combination of *lacZα* and *lacZ*Ω genes on the one hand, and any particular individual 'functional β-galactosidase gene' on the other." *See id.* at 40.

In addition, the FID recognizes that "*lacZα* in the Accused Strains was not added by Jennewein, but was present in the original BL21 (DE3) strain which Jennewein engineered to achieve the Accused Strains." *See id.* at 44-45. The FID finds, however, that "the exogenous

[12] At the time of Order No. 22, the investigation was assigned to the Chief ALJ. On April 2, 2019, the investigation was transferred to Judge Elliot.

nature of *lacZ*Ω is enough to meet the limitation" at issue. *Id.* The FID explains that "[i]t is the combination of *lacZα* and *lacZ*Ω which is equivalent to the claimed 'β-galactosidase gene,' and this combination does not exist until *lacZ*Ω is inserted into the bacterium's genome from outside the organism." *See id.* at 45. Thus, the FID concludes, "the combination is 'exogenous' and satisfies the claim limitation at least under the doctrine of equivalents." *See id.*

Jennewein petitioned for review of the FID's infringement findings with respect to the claim term "an exogenous functional β-galactosidase gene." Jennewein's Pet. at 30-35. Jennewein did not dispute the FID's findings that the combination of the *lacZα* and *lacZ*Ω genes is equivalent to a functional β-galactosidase gene, but Jennewein argued that the combination is not exogenous because only *lacZ*Ω is exogenous while *lacZα* is endogenous.[13] *See id*. at 31. Jennewein reasoned that the FID "departs from the parties' agreed-upon construction for 'exogenous'" and "incorrectly concludes that '[i]t is the combination of *lacZα* and *lacZ*Ω which is equivalent to the claimed 'β-galactosidase gene,' and this combination *does not exist* until *lacZΩ* is inserted into the bacterium's genome from outside the organism.'" *See id.* (citation omitted) (emphasis in original). Jennewein explained that "[t]he claim language does not encompass a combination of gene fragments that did not 'exist' until one fragment is inserted into the genome" but "[r]ather, it requires that the combination itself originated outside of Jennewein's strain." *See id.* (citation omitted).

The Commission finds that the FID correctly determined that Jennewein's Accused Strains include a combination that is equivalent to the claimed "exogenous functional β-galactosidase gene." *See* FID at 38-45. Jennewein argued that the ID's finding that the

[13] Jennewein explains that "'endogenous' genes are those present in the host strain prior to any genetic engineering." Jennewein's Pet. at 34 (citing Hr'g Tr. (Prather) at 441:25-442:4).

combination "does not exist" in the host strain until *lacZΩ* is inserted into the bacterium's genome, is incorrect because, in Jennewein's view, the construction of "exogenous" (*i.e.*, "originating outside an organism, tissue, or cell") requires that "the combination itself originate[s] outside of Jennewein's strain." *See* Jennewein Pet. at 31. This alleged distinction, however, is unpersuasive. Indeed, as the FID finds, the combination does not exist in the original strain, and therefore the combination itself does not originate from within the organism. *See* FID at 44-45 (citing CX-213 at Figure 2, 5158). Thus, the Commission agrees with the FID that "the exogenous nature of *lacZ*Ω is enough" to make the combination exogenous and any difference between the claim term "an exogenous functional β-galactosidase gene" and the accused products is insubstantial. *See id.* at 45; *accord* Glycosyn's Pet. Resp. at 28; IA's Pet. Resp. at 10.

In addition, the Commission finds that *lacZα*, which is present in the genetically-engineered strain, *i.e.*, BL21[DE3], is also exogenous as compared to the wild-type *E. coli* bacterium. *See* Glycosyn's Pet. Resp. at 30-31. As Glycosyn explains, "[i]t is . . . undisputed that the *lacZα* gene exists in the BL21(DE3) genome only by way of human intervention." *See id.* at 30 (citing CX-213 (Jennewein's GRAS Notice) at CX-213.297 ("Since its isolation in 1818, the *E. coli* B strain has also undergone multiple rounds of genetic manipulation resulting in the strain BL21 (DE3)."); RX-386C (Parschat[14]) at Q/As 68-69). In addition, "it is undisputed that the DE3 is derived from a prophage, or in other words, a virus, that infects *E. coli.* to insert foreign DNA into the *E. coli*." *See id.* at 31 (citing RX-386C (Parschat) at Q/As 133-134 ("We discovered there was actually a lacZ[α] like fragment already present in the DE3 prophage in the

[14] Katja Parschat is Jennewein's Deputy Head of Research and Development.

genome of strain #1540. . . . A prophage is the genome [of] an *E. coli* virus or phage or part of that genome that is integrated into the bacterial chromosome replicate.")).

The language of the Asserted Claims and the specification of the '018 patent make clear that the claimed genetically-engineered bacterium and its "exogenous functional β-galactosidase gene" are to be compared to the native or wild-type *E. coli* bacterium rather than to a genetically-engineered strain, *i.e.*, BL21[DE3]. *See* JX-3, '018 patent at 111:45-49 (claim 1) ("A method for producing a fucosylated oligosaccharide in a bacterium comprising[:] providing an isolated *E. coli* bacterium comprising . . . an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced *compared to that of a wild-type E. coli bacterium*.") (emphasis added); *id.* at 5:1-5 ("The bacteria used herein to produce HMOS are genetically engineered to comprise an increased intracellular guanosine diphosphate (GDP)-fucose pool, an increased intracellular lactose pool (*as compared to wild type*) and to comprise fucosyl transferase activity.") (emphasis added); *id.* at 6:45-53 ("In the case of lactose and GDP-fucose, endogenous *E. coli* metabolic pathways and genes are manipulated in ways that result in the generation of increased cytoplasmic concentrations of lactose and/or GDP-fucose, *as compared to levels found in wild type E. coli*. For example the bacteria contain at least 10%, 20%, 50%, 2x, 5x, 10x or more of the levels in a corresponding wild type bacteria that lacks the genetic modifications described above.") (emphasis added).

There is no dispute that, as compared to the wild-type *E. coli* bacterium, both *lacZα and lacZ*Ω are exogenous, *i.e.*, they "originat[e] outside an organism, tissue, or cell." *See* CX-213 at CX-213.297; RX-386C (Parschat) at Q/As 68-69, 133-34. Thus, the Commission has determined to affirm with modification the FID's finding that the Accused Strains infringe the

Asserted Claims under the doctrine of equivalents, and supplements the FID's analysis as discussed above.

B. Adjudication of Infringement with Respect to the TTFL12 Strain

During the investigation, Jennewein sought adjudication of infringement with respect to its TTFL12 bacterial strain, which Glycosyn did not accuse in its complaint. Jennewein identified the TTFL12 strain on September 14, 2018, in its Ground Rule 7.2 disclosure[15] (CX-226C) and in its interrogatory responses served on November 5, 2018 (CX-237C). Jennewein further provided two documents, RX-320C (a draft article) and RX-382 (European Patent Application No. 14 162 869.3) (both produced on August 21, 2018), to establish the relevant features of the TTFL12 strain.

The FID declines Jennewein's request for adjudication, reasoning that "there can be no dispute that Glycosyn has not accused [the TTFL12 strain] of infringement." *See* FID at 28. The FID states that Commission precedent follows "a four-factor test as to whether a respondent has met its burden to show that infringement of a redesigned product should be adjudicated," namely, whether "[t]he product [is]: (1) within the scope of the investigation, (2) imported, (3) sufficiently fixed in design, and (4) subject to extensive discovery." *See id.* at 29 (citing *Certain Two-Way Radio Equipment and Systems, Related Software, & Components Thereof*, Inv. No. 337-TA-1053, Comm'n Op. at 8, 2018 WL 8648379 (Dec. 18, 2018) ("*Two-Way Radio*")).

"Of these factors, [the FID] finds Respondents have not met their burden as to the fourth factor, subject to extensive discovery." *See id.* Specifically, the FID determines that Jennewein failed to "provide[] 'extensive' or 'sufficient' discovery on the TTFL12 strain." *See*

[15] Ground Rule 7.2 relates to the "Disclosure of Products Within the Scope of the [Notice of Investigation]." *See* Order No. 2 (June 21, 2018).

id. at 32. The FID reasons that "while Jennewein identified TTFL12 as falling under the scope of the investigation in its Ground Rule 7.2 disclosure [(CX-226C)], and identified the 'draft' article, RX-0320C, as evidence of TTFL12's relevant features, it did not identify the patent application [(RX-382)] such that Glycosyn would have been on notice of it," because the patent application "does not refer to TTFL12 by name." *See id.* at 32-33. The FID further finds that "RX-0320C may provide information on the conception of TTFL12, but it does not sufficiently identify and describe a product that could serve as an accused product." *See id.* at 34.

The FID also rejects Jennewein's discovery responses as insufficient because they were served on the last day of discovery, which ended on November 5, 2018. *See id.* The FID determines that Jennewein's failure to identify TTFL12 in response to Glycosyn's request for admission on importation "was more than enough to dissuade Glycosyn from investigating anything other than the #1540 strain during discovery." *See id.* at 34-35. The FID further finds that "Glycosyn [was] on notice of just three things: a strain referred to as TTFL12 exists and was described in an unpublished, undated article as lacking a *lacZ* gene (CX-0226; CX-0320C); at some point the strain was used to create an unspecified amount of 2'-FL (CX-2037C at 1-2); but that 2'-FL had not been imported into the United States (CX-0216C at 5)." *See id.* at 34.

The FID recognizes that "Glycosyn failed to take discovery of its own on [the TTFL12] issue . . . and to respond to Jennewein's own requests for admission on TTFL12," but the FID finds that "it is Jennewein's burden to introduce TTFL12-based 2'-FL into the case." *See id.* at 35 (citing *Two-Way Radio*). Thus, the FID concludes that "adjudication of whether the TTFL12 strain infringes [is not] appropriate at this time because the discovery on TTFL12 was not adequate." *See id.*

Jennewein and the IA petitioned for review of the FID's alleged failure to adjudicate infringement with respect to Jennewein's TTFL12 bacterial strain. Jennewein's Pet. at 35-41; IA's Pet. at 5-22. Jennewein argued that the FID errs in requiring a heightened burden of "extensive discovery" where Commission precedent requires only that the respondent "provid[e] sufficient information to put the complainant on notice that [the TTFL12 strain] may be at issue." *See* Jennewein's Pet. at 37-38 (citing *Certain Television Sets, Television Receivers, Television Tuners, & Components Thereof*, Inv. No. 337-TA-910, Order No. 46 at 23 (Nov. 28, 2014), *unreviewed*, Comm'n Notice (Dec. 3, 2014)); *accord* IA's Pet. at 22 ("[T]he [FID's] conclusion that the disclosure was somehow not 'sufficient' was a clearly erroneous finding of material fact that merits review by the Commission.").

Jennewein also argued that the FID should have adjudicated non-infringement because the "TTFL12 strain lacks a functional β-galactosidase gene, and therefore it is incapable of having any β-galactosidase activity as the claim clearly requires." *See* Jennewein's Pet. at 39. Jennewein asserted that "[its] witnesses explained the structure and capabilities of the TTFL12 strain such that a noninfringement opinion would be straightforward." *See id.* at 39-40 (citing RX-320C (Jennewein draft manuscript produced August 2018) ("[g]enes encoding proteins involved in pathways that compete with 2'-FL biosynthesis were inactivated or deleted"); RX-409C (Stephanopoulos[16] RWS[17]) at Q/A 278 (testifying that the *lacZ* gene has been deleted or inactivated and that TTFL12 was not further engineered to insert a functional exogenous β-galactosidase gene); Hr'g Tr. (Parschat) at 384:10-17 ("The complete *lacZ* gene as occurs in

[16] Gregory Stephanopoulos was Jennewein's technical expert in this investigation.

[17] "RWS" refers to Rebuttal Witness Statement.

the operon is not present in the TTFL-12 strain."); RX-387C (Parkot[18] Witness Statement ("WS")) at Q/A 85 ("The TTFL12 strain is a 2'-FL production strain that has no β-galactosidase (lacZ) gene and does not use lactose to synthesize 2'-FL."); *see also* IA's Pet. at 16-17 ("Unlike in the bacterial strain discussed in the '018 Patent, in the TTFL12 strain the inactivated lacZ gene was not replaced with an exogenous functional β-galactosidase gene.") (citing RX-320C). *Accord* IA's Resp. at 3-7; Jennewein's Resp. at 2-11.

Jennewein further argued that the FID "improperly rewards Glycosyn for its refusal to take discovery on the TTFL12 strain." *See* Jennewein's Pet. at 40. Jennewein reasons that "Glycosyn never tested the TTFL12 strain during its inspection of Jennewein's facilities in Germany, even though it had every chance to do so" and "never asked its expert, Dr. Prather, to opine on TTFL12." *See id.* (citing Hr'g Tr. (Prather[19]) at 558:11-14 ("Q. . . . So you at least never asked, through Dr. Wheeler or otherwise, to test the TTFL-12 strain; correct? A. That's correct. We never asked for it."), 509:17-25); *see also id.* at 530:17-19 ("Q. So you did not analyze the TTFL-12 strain for the purpose of this investigation? A. I did not."); *accord* IA's Pet. at 14-15 ("A complainant cannot willfully ignore evidence of noninfringement presented in discovery and then expect that any remedy imposed will apply to the products that the complainant declined to investigate.") (citing *Certain Electronic Digital Media Devices & Components Thereof*, Inv. No. 337-TA-796, Comm'n Op., 2013 WL 10734395, *71 (Sept. 6, 2013) ("*Electronic Digital Media Devices*") ("When confronted with Samsung's evidence of noninfringement, Apple had an obligation to either present evidence of infringement or withdraw its allegations concerning these products, but it did neither.")).

[18] Julia Parkot is Jennewein's Head of Quality Management.

[19] Kristala L. Jones Prather was Glycosyn's technical expert in this investigation.

Glycosyn argued that Jennewein failed to satisfy its burden under *Two-Way Radio* to establish that the TTFL12 product is fixed in design and that it was imported, and that Jennewein did not provide sufficient discovery on TTFL12. *See* Glycosyn's Pet. Resp. at 33-34. Glycosyn reasoned that "Jennewein failed to produce even the most basic common laboratory documents for any of its strains, including its #1540 production strain." *See id.* at 34. Glycosyn further argued that "Jennewein and Staff are . . . wrong to suggest that Glycosyn should have done more to obtain discovery regarding Jennewein's TTFL12 strain" and that "Glycosyn sought, and Jennewein failed to produce, documents sufficient to describe the nature or use of TTFL12." *See id.* at 41.

The Commission has determined to reverse the FID's decision not to adjudicate the TTFL12 bacterial strain.[20] The Commission previously stated that the test for determining whether a respondent has met its burden for adjudication of a redesigned or alternative product includes four factors: (1) whether the product is within the scope of the investigation; (2) whether it has been imported[21]; (3) whether it is sufficiently fixed in design; and (4) whether it has been sufficiently disclosed by respondent during discovery. *See Two-Way Radio*, 2018 WL 8648379 at *13-14. The Commission also reiterates its policy in favor of adjudicating redesigns to prevent subsequent and potentially burdensome proceedings that could have been resolved in the first instance in the original Commission investigation. *See*, *e.g.*, *Certain*

[20] Commissioner Schmidtlein dissents from Part III(B) of the Commission's decision and has filed a separate opinion concurring in part and dissenting in part.

[21] The Commission notes that while importation may be relevant to the inquiry, actual importation of the redesign is not a mandatory requirement. *See, e.g.*, *Certain Multiple Mode Outdoor Grills and Parts Thereof*, Inv. No. 337-TA-895, Comm'n Op. at 20 (July 23, 2014); *Certain Television Sets, Certain Television Receivers, Television Tuners, and Components Thereof*, Inv. No. 337-TA-910, Order No. 46 (Initial Determination) at 29 (Nov. 28, 2014) (Lord, J.) (not reviewed).

Television Sets, Television Receivers, Television Tuners, & Components Thereof, Inv. No. 337-TA-910, Order No. 46 at 23-24 (Nov. 3, 2014), *unreviewed*, Comm'n Notice (Dec. 3, 2014) ("As a policy matter, 'consideration of design around products during the course of the proceedings before the ALJ provides predictability in enforcement of the order by U.S. Customs and Border Protection.") (quoting *Certain Multiple Mode Outdoor Grills & Parts Thereof*, Inv. No. 337-TA-895, Comm'n Op., 2014 WL 12890485, *10 (July 23, 2014)). However, redesigned products are still within the scope of remedial orders that are issued upon the termination of the investigation even if such products were not adjudicated for infringement in the original investigation. *See Certain Optical Disk Controller Chips & Chipsets & Prods. Containing Same, Including DVD Players & PC Optical Storage Devices*, Inv. No. 337-TA-506, Comm'n Op., 2007 WL 4713920, *64 (Sept. 28, 2005) ("[W]hile individual models may be evaluated to determine importation and infringement, the Commission's jurisdiction extends to all models of infringing products that are imported at the time of the Commission's determination and to all such products that will be imported during the life of the remedial orders.") (internal quotation omitted); *cf.* IA's Pet. at 8 ("[A]lthough it refused to identify TTFL12-based 2'-FL as an accused product, Complainant argued that the product should nevertheless be covered by any exclusion order that issues in this investigation."). To the contrary, once a respondent has been determined to be in violation of the Commission's remedial orders, such orders extend to all infringing products (*e.g.*, respondent's redesigned products), whether or not they were adjudicated in the original investigation.

The Commission agrees with the FID that the record evidence establishes that the first three factors specified above are satisfied. *See* FID at 29. With respect to factor (1) (scope of the investigation), there is no dispute that the 2'-FL produced with the TTFL12 strain is within

the scope of the investigation, which is defined in the notice of investigation as "2'-fucosyllactose oligosaccharides." *See* 83 Fed. Reg. at 28865. As to factor (2) (importation), although Jennewein did not identify TTFL12 in its September 20, 2018 response to Glycosyn's request for admission as to importation (because it had not been imported at the time), *see* CX-216C at 5, there is ample evidence that the 2'-FL product from that strain was subsequently imported on October 11, 2018, prior to the close of fact discovery. *See* IA's Pet. at 10-12 (citing FID at 34; RX-278C (Jennewein shipping invoice); RX-279C (Jennewein 2'-FL material safety data sheet); RX-280C (summary of Jennewein 2'-FL importation); RX-385C (Jennewein WS) at Q/As 135 ("180 g of 2'-FL produced by using the TTFL12 strain were imported into the U.S."), 171-72; RX-387C (Parkot WS) Q/As 101-110); Hr'g Tr. at 347:6-22, 348:7-25 (Parkot); *id.* at 215:24-216:7 (Jennewein)).

The record evidence also demonstrates that the TTFL12 strain satisfies factor (3) (sufficiently fixed in design). As Jennewein's witnesses testified, *see* Hr'g Tr. at 197:12-21 (Jennewein), "[t]he strain has been in development since 2012" and "[a] lot of different fermentation runs have been done since then." *See also id.* at 347:6-22 (Parkot) (discussing certain records showing that Jennewein has actually produced 2'-FL using the TTFL12 strain).

Lastly, as to factor (4) (sufficient disclosure in discovery), the Commission disagrees with the FID's conclusion that Jennewein has not met its burden to establish that this factor is satisfied. *See* FID at 29. Jennewein was required to provide sufficient (not extensive)[22] fact and expert discovery to put Glycosyn on notice of that strain and its relevant features. *Cf. Two-*

[22] The FID recites both "sufficient" and "extensive" evidence (*see*, *e.g.*, FID at 29, 32), but as explained herein, the test for adjudicating redesigns does not require extensive discovery. Rather, the test requires discovery that is sufficient for the complainant to assess the features relevant to the asserted patent claims.

Way Radio, 2018 WL 8648379 at *14 ("[T]he principal issues on review are (1) whether [respondent] produced discovery that is sufficient to inform [complainant] with respect to the redesigned product features relevant to the asserted . . . patents . . . ; and (2) whether [complainant's] decision not to assert infringement by the redesigned products with respect to these [asserted] patents constitutes a failure to satisfy its burden to prove infringement.").

The Commission finds that Jennewein presented sufficient documentary evidence as well as fact and expert testimony to put Glycosyn on notice of the relevant features of the TTFL12 strain.[23] Specifically, Jennewein identified the TTFL12 strain on September 14, 2018, in its Ground Rule 7.2 disclosure (CX-226C) and in its interrogatory responses served on November 5, 2018 (CX-237C). Jennewein also produced two key documents, RX-320C and RX-382 (both produced on August 21, 2018, well before November 5, 2018, the close of fact discovery), supported by expert and witness testimony, showing the relevant features of the TTFL12 strain and establishing that the strain does not infringe the asserted patent because it lacks an exogenous functional β-galactosidase gene (*lacZ*). *See* Jennewein's Resp. (citing RX-382 at 24 (Eur. App. No. 14 162 869.3) (showing that the TTFL12 strain was engineered to make lactose inside the cell and to lack or inactivate the β-galactosidase gene because the gene otherwise destroys the lactose feedstock needed to make 2'-FL)); *see also* RX-409C (Stephanopoulos RWS) at Q/As 279-280 ("[RX-382] describes a preferred bacterial host cell lacking expression of *lacZ* in one embodiment."); RX-386C (Parschat WS) at Q/As 161 ("The *lacZ* gene . . . is

[23] The Dissent dismisses witness testimony provided after the close of discovery and/or at the hearing but such testimony is based on expert reports or deposition testimony which must be produced during discovery (generally, such reports are not included in the record evidence). *See* Order No. 24, Ground Rule 11.5.5 ("An expert's testimony at the trial shall be limited in accordance with the scope of his or her expert report(s), deposition testimony, or within the discretion of the Chief Administrative Law Judge. Direct testimony from an expert that is outside this scope will be excluded.").

actually detrimental since it degrades the lactose substrate needed to make 2'-FL. . . . Since no addition of lactose is needed for 2'-FL production using the TTFL12 strain there is no lactose to remove and the *lacZ* gene is unnecessary."); Hr'g Tr. (Jennewein) at 226:25-227:7 (testifying that TTFL12 strain lacked a *lacZ* gene because there is no surplus of lactose which would have required β-galactosidase to eliminate the surplus); RX-385C (Jennewein[24]) at Q/As 166-174.

The FID finds that exhibits RX-320C and RX-382 have low probative value or provide unreliable evidence of an accused product's features. *See* FID at 33-34. However, the testimonial (fact and expert) evidence establishes the relevance of the documents to Jennewein's non-infringement claims. *See*, *e.g.*, RX-409C (Stephanopoulos RWS) at Q/As 272-86 (discussing RX-320C and Jennewein's non-infringement theory, *i.e.*, that the *lacZ* gene has been deleted or inactivated and that TTFL12 was not further engineered to insert a functional exogenous β-galactosidase gene); Hr'g Tr. (Parschat) at 384:10-17 (testifying that "[t]he complete *lacZ* gene as occurs in the operon is not present in the TTFL-12 strain"); RX-387C (Parkot WS) at Q/A 85 ("The TTFL12 strain is a 2'-FL production strain that has no β-galactosidase (lacZ) gene and does not use lactose to synthesize 2'-FL."); *accord* IA's Pet. at 13-14, 16-17, 19-22, 19-20 ("[T]he ALJ appears to have overlooked the hearing testimony of . . . Ms. Parkot . . . [which] is sufficient to supply the missing link between the 2'-FL that was 'actually produced' and the TTFL12 strain described in the draft Jennewein article, RX-320C."), 20 ("RX-382 demonstrates that Respondent had developed a 'total fermentation' strain by no later than early 2014, when the European patent application was filed.").

With regard to the FID's comment that "[a]n earnest effort to force TTFL12 into the investigation would have seen Jennewein prove to Glycosyn the nature of TTFL12, and how it

[24] Stefan Jennewein is the Managing Director of Jennewein.

had been used to produce imported 2'-FL, before the very last day of fact discovery," FID at 35, the Commission notes that the parties do not dispute that Jennewein produced relevant discovery as to TTFL12 within the fact discovery period established by the procedural schedule. If Glycosyn and its expert deemed such evidence to be insufficient, Glycosyn could and should have taken available procedural steps, such as a motion to reopen discovery or to compel further discovery, because the burden of establishing infringement remains with Glycosyn.[25]

The Commission also finds that Glycosyn failed to satisfy its burden of establishing infringement with respect to Jennewein's TTFL12 strain. *See Medtronic, Inc. v. Mirowski Family Ventures, LLC*, 571 U.S. 191, 194 (2014) (holding that the burden of proving infringement remains with the patentee even in a declaratory judgment action to establish non-infringement); *Electronic Digital Media Devices*, 2013 WL 10734395, *71 ("When confronted with Samsung's evidence of noninfringement, Apple had an obligation to either present evidence of infringement or withdraw its allegations concerning these products, but it did neither.").

Unlike the accused #1540 strain and its derivative, there is no evidence that a *lacZΩ* fragment was inserted into the TTFL12 strain or any of its precursors. *See* RX-320C at 17-18

[25] In Glycosyn's submissions to the Commission in response to the notice of review, Glycosyn does not contend that the testimony of fact witnesses or the opinions of Jennewein's expert witness provided in discovery were insufficient to apprise it of information relating to the TTFL12 strain or Jennewein's non-infringement theory. Glycosyn's Resp. at 35-39, Glycosyn's Reply at 13-16. Indeed, the IA points out that "Glycosyn failed to question any witnesses about the product during fact discovery, or to test a sample of the TTFL12 strain or 2'-FL made using the TTFL12 strain during its onsite testing at Jennewein's facility." IA's Resp. at 34; *see also* Jennewein Resp. at 32-33 ("Glycosyn never questioned any of Jennewein's fact witnesses at their depositions about the properties of the TTFL12 strain. SIB at 71. And when it traveled to Jennewein's German facility to conduct testing of Jennewein's other production strains – six weeks after Jennewein had disclosed TTFL12 and its genetic composition – Glycosyn never asked to test it."). Glycosyn does not deny the IA and Jennewein's assertions that it chose not to question witnesses or to test the TTFL12 strain or 2'-FL made using the TTFL12 strain during its on-site testing in Germany. Glycosyn's Reply at 15.

(Table 1); RX-409C (Stephanopoulos RWS) at Q/As 277-278 (testifying that "the *lacZ* gene has been deleted or inactivated" and that "TTFL12 was not further engineered to insert a functional exogenous β-galactosidase gene"); *see also* Hr'g Tr. (Parschat) at 384:10-17 ("The complete *lacZ* gene as occurs in the operon is not present in the TTFL-12 strain."); RX-386C (Parschat WS) at Q/As 159-160 ("[T]here is no β-galactosidase gene so the strain cannot produce β-galactosidase."); RX-387C (Parkot WS) at Q/A 85 ("The TTFL12 strain is a 2'-FL production strain that has no β-galactosidase (lacZ) gene and does not use lactose to synthesize 2'-FL."); RX-385C (Jennewein) at Q/As 160-62, 176-177 (testifying that "[Jennewein] deleted the *lacZ* gene and also did not insert any β-galactosidase gene or complementary β-galactosidase gene fragments so there can be no β-galactosidase activity"); Hr'g Tr. (Jennewein) at 227:8-13 (testifying that he wrote the RX-320 article). Thus, based on the record evidence, the Commission finds that the TTFL12 strain does not contain an "exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity" as required by the Asserted Claims. *Accord* IA's Resp. at 3-7; Jennewein's Resp. at 2-11.

Unlike Jennewein, Glycosyn presented no expert evidence to establish the presence of a *lacZ* gene or *lacZΩ* fragment in the TTFL12 strain, and thereby infringement by that strain, arguing instead that Jennewein presented insufficient discovery. *See* Glycosyn's Resp. at 11; *see also Centricut, LLC v. Esab Group, Inc.*, 390 F.3d 1361, 1370 (Fed. Cir. 2004) (finding no infringement where "a patent law plaintiff who presents complex subject matter without inputs from experts qualified on the relevant points in issue when the accused infringer has negated

infringement with its own expert.").[26] Glycosyn asserts that "TTFL12[] contain[s] a functional *lacZα* β-galactosidase gene," but Glycosyn says nothing about *lacZ*Ω. *See* Glycosyn's Resp. at 11-14. As the FID finds, "[i]t is the combination of *lacZα* and *lacZ*Ω which is equivalent to the claimed 'β-galactosidase gene,' and this combination does not exist until *lacZ*Ω is inserted into the bacterium's genome from outside the organism." *See* FID at 45; *see also* Hr'g Tr. (Prather) at 436:1-6 (agreeing that "the alpha fragment[] . . . cannot make beta-galactosidase on its own"). Nor is there any evidence that the *lacZ*Ω was inserted in the TTFL12 strain. Thus, the Commission finds that Glycosyn failed to establish that the TTFL12 strain contains an "exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity" as required by the Asserted Claims. Accordingly, Glycosyn failed to satisfy its burden to establish infringement by the TTFL12 strain.[27]

Thus, the Commission has determined to reverse the FID's decision not to adjudicate infringement with respect to the TTFL12 strain and provides its reasoning above as to why such adjudication is warranted. The Commission further finds that the TTFL12 strain does not infringe the Asserted Claims as discussed above.

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[26] The ALJ determined that "one of ordinary skill in the art would have (1) a Ph.D in molecular biology, biochemistry, or chemical engineering, or an equivalent field, and 1-2 years of experience working with *E. coli* bacteria or related systems, or (2) a lower level degree (*e.g.*, a M.A.) in a similar field to those listed above, but a greater amount of relevant working experience (*e.g.*, 5-6 years of experience working with *E. coli* bacteria or related systems)." *See* Order No. 22 at 7.

[27] Glycosyn also argues that 35 U.S.C. § 295 creates a presumption that Jennewein's product was made by the patented process, and that Jennewein has the burden to establish that the product was not made by the patented process. *See* Glycosyn's Resp. at 14-18. Glycosyn waived this argument both before the ALJ and the Commission. *See* Order No. 38 at 2-3 (June 14, 2019); 19 C.F.R. § 210.43(b)-(c); *see Finnigan Corp. v. ITC*, 180 F.3d 1354, 1362-63 (Fed. Cir. 1999) ("A party seeking review . . . of a determination by the Commission must specifically assert the error made by the ALJ in its petition for review to the Commission."). In any event, the record in this investigation shows that any presumption under 35 U.S.C. § 295 is overcome by Jennewein as to the TTFL12 strain.

IV. REMEDY, PUBLIC INTEREST, AND BONDING

The RD recommends that the Commission issue an LEO barring entry of Jennewein's articles that infringe the asserted patent claims. *See* RD at 116-18. The RD does not recommend that the Commission issue a CDO against Jennewein.[28] The RD further recommends that the Commission impose a five (5) percent bond during the period of Presidential review. *See id.* at 118-19. Still further, as directed by the Commission, the RD provides findings with respect to the public interest and recommends that the Commission determine that the public interest factors do not preclude entry of the proposed LEO. *See id.* at 119-20.

A. Limited Exclusion Order

The Commission has "broad discretion in selecting the form, scope, and extent of the remedy." *Viscofan, S.A. v. US. Int'l Trade Comm'n*, 787 F.2d 544, 548 (Fed. Cir. 1986).

Section 337(d)(1) provides that "[i]f 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, unless, after considering the [public interest], it finds that such articles should not be excluded from entry." 19 U.S.C. § 1337(d)(1). *See also Spansion, Inc. v. Int'l Trade Comm'n*, 629 F.3d 1331, 1358 (Fed. Cir. 2010) ("[T]he Commission is required to issue an exclusion order upon the finding of a Section 337 violation absent a finding that the effects of one of the statutorily-enumerated public interest factors counsel otherwise.").

The RD recommends that the Commission issue an LEO excluding Jennewein's infringing 2'-FL product. *See* RD at 117. Consistent with its decision not to adjudicate the

[28] Glycosyn does not request a CDO against Jennewein.

TTFL12 strain, the RD recommends against a carve-out for 2'-FL product made with the TTFL12 strains. *See id.* The RD, however, recommends "a certification provision, wherein said certification is required to state with particularity the grounds of non-infringement of the imported oligosaccharide and be accompanied by sufficient corroborating evidence of the type provided in discovery in this investigation." *See id.* at 118.

The Commission has determined to issue an LEO barring importation of 2'-fucosyllactose oligosaccharides that infringe the Asserted Claims. Consistent with its finding that the TTFL12 strain does not infringe the Asserted Claims, the Commission has determined to include an explicit carve-out for 2'-FL product made with the TTFL12 strain. In addition, the Commission has determined that the LEO should include the standard certification provision. The Commission finds that the certification provision is justified because it may not be readily apparent by inspection whether the imported article is covered or exempted by the LEO, *i.e.*, whether the imported 2'-FL product is made by an infringing strain (*e.g.*, bacterial strains #1540 and its derivative) or by a non-infringing strain (*i.e.*, the TTFL12 strain). *See Certain Graphics Sys., Components Thereof, & Consumer Prods. Containing the Same*, Inv. No. 337-TA-1044, Comm'n Op. at 65-66 (Sept. 18, 2018). To be clear, as the Commission has previously held, "[t]he standard certification 'does not apply to redesigns that have not been adjudicated as non-infringing.'" *See Automated Teller Machines, ATM Modules, Components Thereof, & Prods. Containing the Same*, Inv. No. 337-TA-972, Comm'n Op., 2017 WL 11198798, *16-17 (June 12, 2017) (quoting *Certain Marine Sonar Imaging Devices, Including Downscan & Sidescan Devices, Prods. Containing the Same, & Components Thereof*, Inv. No. 337-TA-921, Commn Op., 2016 WL 10987364, *53 (Jan. 6, 2016)).

Thus, the Commission has determined to issue an LEO: (1) covering "2'-fucosyllactose oligosaccharides that infringe the Asserted Claims"; (2) including the standard certification provision in the LEO; and (3) including an explicit carve-out for 2'-FL product made with the TTFL12 strain.

B. The Public Interest

Section 337 requires the Commission, upon finding a violation of section 337, to issue an LEO "unless, after considering the effect of such exclusion upon the public health and welfare, competitive conditions in the United States economy, the production of like or directly competitive articles in the United States, and United States consumers, it finds that such articles should not be excluded from entry." 19 U.S.C. § 1337(d)(l).

The RD "do[es] not find the requested [LEO] would meaningfully impact public health and welfare, competitive conditions, domestic production of articles, or U.S. consumers." *See* RD at 120. The RD finds that "the purpose of providing 2'-FL in infant formula is to improve public health, [but] the evidence shows that the otherwise well-established market has only recently begun including 2'-FL into its products, and with amounts that have unclear efficacy levels." *See id.* The RD concludes that "[t]he U.S. public is therefore not dependent on such products, as of yet." *See id.*

1. Public Health and Welfare

Jennewein argues that "2'-FL has important health benefits, including its use in infant formula," and "at this time, Jennewein is the only company that can supply 2'-FL to the U.S. market in commercial quantities." *See* Jennewein's PI Br. at 1. Jennewein further argues that its product is incorporated as an ingredient in Abbott's Similac® product which is "the number one selling infant formula" in the U.S. *See id.* (citing RX-385C (Jennewein WS) at Q/A 187).

Jennewein faults the RD for stating that the "market has only recently begun including" its 2'-FL product. *See id.* at 2. To the contrary, Jennewein continues, "Abbott has been adding 2'-FL in its infant formula since 2016" and "there is no reason to doubt that Abbott chooses to include 2'-FL in its Similac® because of the health benefits of 2'-FL." *See id.* (citing CX-205); *accord* Abbott's PI Br. at 1-3.

Glycosyn does not dispute that "HMOs provide health benefits." *See* Glycosyn's Remedy Br. at 2. Glycosyn, however, argues that the proposed LEO will not adversely impact the public health or welfare. *See id.* at 2-4. Glycosyn reasons that "only a subsection of infant formulas in the United States contain 2'-FL, and that even in those that do, the amounts 'have unclear efficacy levels.'" *See id.* at 3 (citing RD at 120); *accord* IA's Resp. at 39-40. Glycosyn also explains that there are "many entities that can meet the demand for 2'-FL in the United States." *See* Glycosyn's Remedy Br. at 4; IA's Resp. at 40-42; DuPont PI Br. at 1-2.

The Commission finds no evidence that the LEO would adversely affect the public health and welfare, particularly in view of the Commission's determination that using the TTFL12 strain does not infringe the Asserted Claims. For example, Jennewein can import its 2'-FL product if it certifies that such product was produced using the TFL12 strain.

Thus, the Commission finds that the LEO discussed *supra* section IV(A) would not have an adverse effect on the public health and welfare.

2. Competitive Conditions in the United States Economy

Jennewein argues that "[it] is the only company currently producing 2'-FL for infants in the U.S. market on a commercial scale." *See* Jennewein's PI Br. at 4 (citing Hr'g Tr. (Newburg[29]) at 57:3-4; RX-385C (Jennewein WS) at Q/A 188). According to Jennewein, "there

[29] Howard Newburg is Co-Chief Executive Officer and Chief Financial Officer of Glycosyn.

is no showing that Glycosyn can offer any product at this time or in the near future, let alone produce quantities sufficient to replace Jennewein's production." *See id.* at 4.

Glycosyn disagrees and argues that "[its] licensee, Friesland, and other third-party industry leaders can replace the subject articles in the U.S. in a commercially reasonable time." *See* Glycosyn's Remedy Br. at 4-5; *accord* IA's Resp. at 44; DuPont PI Br. at 1-2.

The Commission finds no evidence that the LEO would adversely affect the competitive conditions in the United States economy, particularly in view of the Commission's determination that using the TTFL12 strain does not infringe the Asserted Claims. For example, Jennewein can import its 2'-FL product if it certifies that such product was produced using the TTFL12 strain. Moreover, the evidence indicates alternative suppliers (including Glycosyn, FrieslandCampina, Glycom, and DuPont) can also replace the excluded products within a commercially reasonable time. *See* IA's Resp. at 41-42 (citing, *inter alia*, RX-385C (Jennewein WS) at Q/A 135; CX-3C (Newburg WS) Q/As 76, 79-80).

Thus, the Commission finds that the LEO discussed *supra* section IV(A) would not have an adverse effect on the competitive conditions in the United States economy.

3. The Production of Like or Directly Competitive Articles

Jennewein does not address this factor specifically, but its arguments as to this factor appear to be the same as discussed above in connection with competitive conditions in the United States economy. *See* Jennewein's PI Br. at 3-4. Both Glycosyn and the IA argue that the proposed LEO will have no effect on this factor because there is no evidence that the 2'-FL product is produced domestically in the United States. *See* Glycosyn's Remedy Br. at 7; *accord* IA's Resp. at 45.

The Commission finds that the presence of alternative suppliers capable of providing alternative non-infringing 2'-FL product (including Glycosyn, DuPont, and Jennewein itself)

negates any evidence that the LEO would adversely affect the production of like or directly competitive articles, particularly in view of the Commission's determination that using the TTFL12 strain does not infringe the Asserted Claims. For example, Jennewein can import its 2'-FL product if it certifies that such product was produced using the TTFL12 strain.

Thus, the Commission finds that the LEO discussed *supra* section IV(A) would not have an adverse effect on the production of like or directly competitive articles.

4. United States Consumers

Jennewein argues that the requested LEO would have a severely negative impact on U.S. consumers. *See* Jennewein's PI Br. at 4-5. Jennewein explains that it is "the only company making GRAS-approved 2'-FL on a commercial scale for the U.S. market." *See id.* Glycosyn asserts that "alternative suppliers of biosynthesized 2'-FL by Glycosyn's licensee Friesland, Glycom, and DuPont can provide ample replacement articles of like or directly competitive products." *See* Glycosyn's Remedy Br. at 8; *accord* IA's Resp. at 46. Glycosyn also notes that "Friesland received GRAS approval from the FDA on April 6, 2018, to manufacture 2'-FL." *See* Glycosyn's Remedy Br. at 4.

The Commission finds that the presence of alternative suppliers capable of providing non-infringing 2'-FL product (including DuPont and Jennewein itself) negates any evidence that the LEO would adversely affect U.S. consumers, particularly in view of the Commission's determination that using the TTFL12 strain does not infringe the Asserted Claims. For example, Jennewein can import its 2'-FL product if it certifies that such product was produced using the TTFL12 strain.

Thus, the Commission finds that the LEO discussed *supra* section IV(A) would not have an adverse effect on U.S. consumers.

5. Conclusion

Based on the record evidence, the Commission finds that an LEO directed against Jennewein's infringing articles, and including a standard certification provision and an explicit carve-out for articles produced using Jennewein's non-infringing TTFL12 strain, would cause little to no harm to the public health and welfare, the competitive conditions in the United States economy, the production of like or directly competitive products in the United States, and United States consumers. Thus, after considering the parties' submissions and the effect that remedial orders would have on the public interest, the Commission has determined to issue a limited exclusion order.

C. Bonding

If the Commission enters an exclusion order or a cease and desist order, a respondent may continue to import and sell its products during the 60-day period of Presidential review under a bond in an amount determined by the Commission to be "sufficient to protect the complainant from any injury." 19 U.S.C. § 1337(j)(3); *see also* 19 C.F.R. § 210.50(a)(3).

When reliable price information is available in the record, the Commission has often set the bond in an amount that would eliminate the price differential between the domestic product and the imported, infringing product. *See Certain Microsphere Adhesives, Processes for Making Same, & Prods. Containing Same, Including Self-stick Repositionable Notes*, Inv. No. 337-TA-366, USITC Pub. No. 2949, Comm'n Op. at 24 (Jan. 16, 1996). The Commission also has used a reasonable royalty rate to set the bond amount where a reasonable royalty rate could be ascertained from the evidence in the record. *See, e.g., Certain Audio Digital-to-Analog Converters & Prods. Containing Same*, Inv. No. 337-TA-499, Comm'n Op. at 25 (Mar. 3, 2005). Where the record establishes that the calculation of a price differential is impractical or there is insufficient evidence in the record to determine a reasonable royalty, the Commission has

imposed a 100 percent bond. *See, e.g., Certain Liquid Crystal Display Modules, Prods. Containing Same, & Methods Using the Same*, Inv. No. 337-TA-634, Comm'n Op. at 6-7 (Nov. 24, 2009). The complainant, however, bears the burden of establishing the need for a bond. *Certain Rubber Antidegradants, Components Thereof & Prods. Containing Same*, Inv. No. 337-TA-533, USITC Pub. No. 3975, Comm'n Op. at 40 (July 21, 2006).

As stipulated by the parties, the RD recommends a bond of five (5) percent of the entered value of Jennewein's 2'-FL product during the period of Presidential review. *See* RD at 114-115 (citing JX-7 (stipulation regarding bond)). Consistent with the parties' agreement and the RD's recommendation, the Commission has determined that a bond in the amount of five (5) percent of the entered value of the imported products is appropriate for subject imports entered during the period of Presidential review.

V. CONCLUSION

For the reasons set forth herein, the Commission determines that complainant Glycosyn has established a violation of section 337 by respondent Jennewein based on the infringement of the Asserted Claims of the '018 patent. Accordingly, the investigation is terminated with a finding of a violation of section 337. The Commission determines that the appropriate remedy is an LEO directed against Jennewein's infringing human milk oligosaccharides, that the public interest factors do not weigh against issuing that remedy, and that the bond during the Presidential review period is set in the amount of five (5) percent of the entered value of the infringing articles.

By order of the Commission.

Lisa R. Barton

Secretary to the Commission

Issued: June 8, 2020

CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME **Inv. No. 337-TA-1120**

PUBLIC CERTIFICATE OF SERVICE

I, Lisa R. Barton, hereby certify that the attached **COMMISSION OPINION** has been served via EDIS upon the Commission Investigative Attorney, **Lisa Murray, Esq.**, and the following parties as indicated, on **June 8, 2020**.

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PUBLIC VERSION

UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C.

In the Matter of **CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME**	**Inv. No. 337-TA-1120**

SEPARATE VIEWS OF COMMISSIONER SCHMIDTLEIN CONCURRING IN PART AND DISSENTING IN PART

I concur with and join Part III(A) of the majority opinion, which affirms the ID's finding that the Accused Strains include an exogenous functional β-galactosidase gene. I respectfully dissent from Part III(B) of the majority opinion, which concludes that the administrative law judge ("ALJ") should have adjudicated whether the TTFL12 strain infringes the asserted method claims. Given the parties' briefing and the evidence and exhibits cited therein, I would affirm the ID's conclusion that the TTFL12 strain was not subject to sufficient discovery and not reach the question of whether using the TTFL12 strain infringes the asserted claims.

In determining whether an alternative or redesigned product identified by a respondent should be adjudicated, the Commission has considered whether there has been sufficient discovery on the product. *See, e.g.*, *Certain Electronic Digital Media Devices and Components Thereof*, Inv. No. 337-TA-796, Comm'n Op. at 103–05 (Sept. 6, 2013) ("*Electronic Digital Media Devices*") (finding that the complainant took substantial discovery on the design-around products, which included product inspections by complainant's expert, source code production, and depositions of respondent's witnesses); *Certain Multiple Mode Outdoor Grills and Parts Thereof*, Inv. No. 337-TA-895, Comm'n Op. at 15–20 (July 23, 2014) ("*Outdoor Grills*")

(finding that the respondent produced photographs and product manuals that were sufficient to show that certain redesigned products did not infringe the asserted claims); *Certain Television Sets, Certain Television Receivers, Television Tuners, and Components Thereof*, Inv. No. 337-TA-910, Order No. 46 (Initial Determination) at 23–29 (Nov. 28, 2014) (Lord, J.) ("*Television Sets*") (not reviewed) (listing 22 facts establishing that respondents had provided sufficient discovery on an alternative product; notably, the respondents identified the alternative product before the investigation was instituted, produced 9,000 pages of technical documents, and submitted an expert report opining on non-infringement). Further, as these decisions show, the Commission's analysis of the "sufficient discovery" question focuses on the documents and contentions produced before the close of fact and expert discovery.

In the present investigation, the majority opinion finds that Jennewein provided sufficient discovery on the TTFL12 strain by combining the limited disclosures and documents produced during discovery with hearing testimony and witness statements provided after the close of discovery. With regard to the information produced during the discovery period, the majority opinion points to (1) the mandatory Ground Rule 7.2 disclosure and interrogatory responses served on the last day of fact discovery that identified the TTFL12 stain and (2) a draft article and patent application that purportedly disclose the TTFL12 strain.[1] Maj. Op. at 21–22. Like

[1] The majority opinion states that a respondent must present "sufficient documentary evidence as well as fact and expert testimony to put [the complainant] ***on notice*** of the relevant features of the [alternative or redesigned product]." Maj. Op. at 21 (emphasis added, footnote omitted). But, as the decisions cited above show, the threshold for demonstrating that the respondent has provided sufficient discovery on a redesigned or alternative product is higher than simply putting the complainant "on notice" of a product or its relevant features. For example, the Commission has considered whether the discovery proffered on the redesigned products was analogous to the information and materials the parties cited in their infringement arguments. *See Outdoor Grills*, Comm'n Op. at 18 ("the parties premised their infringement positions based on photographs or diagrams, thereby demonstrating that this particular limitation was readily ascertainable from the

the ALJ, I find this discovery insufficient.

A review of Jennewein's discovery responses show that Jennewein overwhelmingly focused on the #1540 strain and, importantly, repeatedly disavowed importation of 2'-FL product made by any other strain besides the #1540 strain. For instance, during discovery, Jennewein identified the #1540 strain as its only production strain for the U.S. market[2] and admitted in response to requests for admissions that the "#1540 is the only strain Jennewein uses to produce the 2'-FL that is imported into the United States."[3] In the mandatory ground rule disclosure cited by the majority opinion, Jennewein identified the TTFL12 strain by referencing just one document, the undated, unpublished draft article (RX-320C).[4] Subsequent to this disclosure, on October 20, Jennewein's founder testified in a deposition that the #1540 strain was "the only strain that Jennewein was using to create" the product that was being imported.[5] Four days later, Jennewein provided interrogatory responses stating that Jennewein had imported 2'-FL made with the TTFL12 strain.[6] On the last day of discovery, Jennewein provided supplemental responses stating that Jennewein had imported 2'-FL made with the TTFL12 strain on October

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discovery provided by Respondents at the time the motion was filed."); *Television Sets*, Order No. 46 at 21, 27–28; *see also Certain Coaxial Cable Connectors*, 337-TA-938, Order No. 9 (Initial Determination) at 4 (Aug. 21, 2015) (Lord, J.) ("*Cable Connectors*") (not reviewed) (in finding that respondent's new designs did not infringe, the ALJ noted that the same type of evidence used to show infringement of the legacy designs "applies to all of the new C3 designs, for which [respondent] produced technical drawings and expert [deposition] testimony").

[2] *See* CX-228C (Interrogatory Responses) at 5.

[3] *See* CX-215C (Responses to Requests for Admission) at 4–5.

[4] Because the draft article is undated, it does not show when Jennewein produced 2'-FL with the TTFL12 strain. Thus, the article does not show that the 2'-FL sample Jennewein imported was made with the TTFL12 strain.

[5] *See* Tr. (Jennewein) at 189 (affirming Oct. 20, 2018 deposition testimony).

[6] *See* CX-236C (Interrogatory Responses) at 4–6.

12.[7] In the supplemental responses, Jennewein provided, for the first time, its contentions that using the TTFL12 strain does not infringe the asserted claims.[8]

Given that Jennewein repeatedly disavowed during discovery that it was producing and importing product made with an alternative strain, I do not consider that the initial ground rule disclosure of an undated, unpublished article, along with Jennewein's crafty approach to responding to written discovery, to provide a basis for finding that Jennewein provided "sufficient" discovery.

Moreover, the absence of the type of discovery that typically informs the "sufficient discovery" inquiry also shows that Jennewein did not provide sufficient discovery on the TTFL12 strain. For example, Jennewein points to no expert report in relation to the TTFL12 strain.[9] Indeed, the statement of undisputed material facts from Jennewein's motion for summary determination lacks an allegation that its expert opined on TTFL12.[10] While the majority opinion relies on witness statements provided after the close of discovery and hearing testimony to buttress the documents produced during discovery, this evidence simply is not discovery.[11] As such, that evidence is not germane to the question before the Commission,

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[7] *See* CX-236C (Interrogatory Responses) at 4–6; CX-237C (First Amended Interrogatory Responses) at 2, 9, 18–20; RX-278C (delivery slip dated Oct. 12, 2018, indicating 180g of 2'-FL was imported); RX-280C (production summary indicating 180g of 2'-FL made using the TTFL12 strain had been imported).

[8] *See* CX-237C (First Amended Interrogatory Responses) at 2, 9, 18–20.

[9] *See, e.g.*, *Electronic Digital Media Devices*, *Television Sets*, *Cable Connectors*, *supra*. In these investigations, respondents' experts' opinions were relied on to conclude the alternative products had been subject to sufficient discovery and that they did not infringe.

[10] *See* Jennewein Mem. in Supp. of Mot. for Summary Det. at 8–10 (EDIS Doc. ID No. 663068, filed Nov. 30, 2018).

[11] The majority opinion observes that this opinion "dismisses" witness testimony provided after the close of discovery and finds that the "testimony is based on expert reports or deposition

which concerns what was provided during the discovery period.

Likewise, the total absence of materials similar to what the parties used in their infringement and domestic industry technical prong contentions further shows that the discovery Jennewein provided is insufficient. For instance, Glycosyn's expert relied on lab notebooks, weekly lab meeting presentations, internal databases and bioreactor run spreadsheets, Glycosyn's GRAS notice, and analytical testing in formulating her opinion that Glycosyn practices claim 1 of the asserted patent.[12] In opining on infringement, Glycosyn's expert relied on many sources of evidence, including Jennewein's responses to Glycosyn's requests for admission, Jennewein's interrogatory responses, Jennewein's GRAS notice, photographs of Jennewein's production equipment, and Jennewein's in-house analytical testing.[13] Jennewein's expert, in opining on non-infringement, relied on Jennewein's GRAS notice and analytical testing of the #1540 and #1540 derivative strains.[14] In my view, the absence of *any* of these types of documents further indicates that Jennewein failed to provide sufficient discovery. Accordingly, Glycosyn was not

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testimony which must be produced during discovery (generally, such reports are not included in the record evidence)." Maj. Op. at 21 n.23. The majority opinion, however, points to no portion of an expert report or deposition transcript addressing the TTFL12 strain, but rather just assumes that Jennewein's expert's report and its employees' deposition testimony pertain to the relevant hearing testimony. Further, this aspect of the majority opinion stands apart from Commission precedent that has explicitly credited expert reports and deposition testimony in concluding that the respondent provided sufficient discovery. *See Two-Way Radio*, Comm'n Op. at 26 (noting the respondent "produced discovery (including source code, corporate witness depositions, and expert reports), as well as testimonial evidence at the hearing, regarding its non-infringement contentions"); *Television Sets*, ID at 30 (noting that respondents submitted "an extensive expert report . . . on non-infringement"); *Cable Connectors*, ID at 2 (noting that respondents "submitted a noninfringement expert report"). Ultimately, the sufficient-discovery factor hinges on what the respondent provided in discovery, not on what evidence may have been introduced at a hearing.

[12] *See* CX-4C (Prather WS) at Q/A 107, 112, 124, 125, and 149.

[13] *Id.* at Q/A 434, 435, 437, 440, 486.

[14] *See* RX-409C (Stephanopoulos RWS) at Q/A 13, 43–46.

provided sufficient information regarding the TTFL12 strain prior to the close of discovery to allow it to decide whether to assert infringement.[15]

In sum, while I do not mean to suggest that all or even a substantial number of the types of discovery discussed above must be provided in order to put a redesigned or alternative product at issue, it is my view that the total absence of these types of documents in this case along with Jennewein's repeated assertions that it was not producing and importing 2'-FL made with the TTFL12 strain demonstrates that Jennewein did not provide sufficient discovery on the TTFL12 strain.[16] Consequently, I find no error in the ALJ's decision and therefore respectfully dissent from Part III(B) of the majority opinion.

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[15] The majority opinion finds that Glycosyn "does not contend that" the discovery Jennewein did provide was "insufficient to apprise it of information relating to the TTFL12 strain or Jennewein's non-infringement theory." Maj. Op. at 23 n.25. This approach, however, obligates a complainant to investigate alternative or redesigned products of dubious viability, including products that a respondent has repeatedly represented were not made altogether, intended for, or imported into the U.S. market.

[16] As I find that Jennewein failed to provide sufficient discovery on the TTFL12 strain, I also find that Jennewein failed to show that its process of making 2'-FL with the TTFL12 strain is sufficiently fixed in design. *Compare* Maj. Op. at 20 (finding the TTFL12 strain fixed in design). For this factor, the majority relies on two citations to the hearing transcript. *See id.* In the testimony, Dr. Jennewein averred that Jennewein has been developing the strain since 2012 and that it has conducted "[a] lot of different fermentation runs" since 2012. *See* Tr. (Jennewein) at 197. Dr. Parkot averred that she prepared the TTFL12 sample for importation and that the company could provide "manufacturing documentation" on request. *See* Tr. (Parkot) at 347. During discovery, however, Jennewein repeatedly disavowed that it was producing and importing product made with the TTFL12 strain. Similarly, although Jennewein apparently can provide manufacturing documents that might substantiate its argument, it did not produce them during discovery. Taken together, this testimony does not establish that the TTFL12 strain and its attendant production process is sufficiently fixed in design. *See Certain GPS Chips, Associated Software and Systems, and Prods. Containing Same*, Inv. No. 337-TA-596, USITC Pub. No. 4133, Initial Determination at 51–55 (June 13, 2008) (Luckern, J.) (unreviewed) (declining to adjudicate a new product, where, amongst other things, the product was subject to modification in light of subsequent testing); *see also* Tr. (Jennewein) at 205–206 (describing a lengthy document-finalization process and the need for additional analysis of the TTFL12 strain).

UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C.

In the Matter of **CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME**	**Investigation No. 337-TA-1120**

NOTICE OF COMMISSION DECISION TO REVIEW IN PART A FINAL INITIAL DETERMINATION FINDING A VIOLATION OF SECTION 337; SCHEDULE FOR FILING WRITTEN SUBMISSIONS ON THE ISSUES UNDER REVIEW AND ON REMEDY, THE PUBLIC INTEREST, AND BONDING

AGENCY: U.S. International Trade Commission.

ACTION: Notice.

SUMMARY: Notice is hereby given that the U.S. International Trade Commission has determined to review in part a final initial determination ("FID") of the presiding administrative law judge ("ALJ") finding a violation of section 337 of the Tariff Act of 1930, as amended. The Commission requests briefing from the parties on certain issues under review, as set forth in this notice. The Commission also requests briefing from the parties, interested persons, and government agencies on the issues of remedy, the public interest, and bonding.

FOR FURTHER INFORMATION CONTACT: Houda Morad, Office of the General Counsel, U.S. International Trade Commission, 500 E Street SW., Washington, DC 20436, telephone (202) 708-4716. Copies of non-confidential documents filed in connection with this investigation are or will be available for inspection during official business hours (8:45 a.m. to 5:15 p.m.) in the Office of the Secretary, U.S. International Trade Commission, 500 E Street SW., Washington, D.C. 20436, telephone (202) 205-2000. General information concerning the Commission may also be obtained by accessing its Internet server at *https://www.usitc.gov*. The public record for this investigation may be viewed on the Commission's electronic docket (EDIS) at *https://edis.usitc.gov*. Hearing-impaired persons are advised that information on this matter can be obtained by contacting the Commission's TDD terminal on (202) 205-1810.

SUPPLEMENTARY INFORMATION: The Commission instituted this investigation on June 21, 2018, based on a complaint, as amended and supplemented, filed on behalf of Glycosyn LLC of Waltham, Massachusetts ("Glycosyn"). *See* 83 Fed. Reg. 28865 (June 21, 2018). The complaint, as amended and supplemented, alleges violations of section 337 of the Tariff Act of 1930, as amended, 19 U.S.C. 1337 ("section 337"), based upon the importation into the United States, the sale for importation, and the sale within the United States after importation of certain human milk oligosaccharides by reason of infringement of claims 1-40 of U.S. Patent No. 9,453,230 ("the '230 patent") and claims 1-28 of U.S. Patent No. 9,970,018 ("the '018 patent").

See id. The notice of investigation named Jennewein Biotechnologie GmbH ("Jennewein") of Rheinbreitbach, Germany as a respondent in this investigation. *See id.* The Office of Unfair Import Investigations ("OUII") is also named as a party to the investigation. *See id.*

On August 9, 2018, the ALJ partially terminated the investigation as to claims 4-7, 9-12, 14, 23-26, 28-31, 33, and 39-40 of the '230 patent and claims 6, 7, 9, 11, 13-17, 19, and 22 of the '018 patent based on the withdrawal of the allegations pertaining to those claims. *See* Order No. 5 (Aug. 9, 2018), *unreviewed*, Comm'n Notice (Aug. 29, 2018). On October 30, 2018, the ALJ partially terminated the investigation as to claims 1-3, 8, 13, and 15-20 of the '230 patent based on the withdrawal of the allegations pertaining to those claims. *See* Order No. 15 (Oct. 30, 2018), *unreviewed*, Comm'n Notice (Nov. 29, 2018). On November 19, 2018, the ALJ partially terminated the investigation as to claim 27 of the '230 patent and claims 4, 20, and 21 of the '018 patent based on the withdrawal of the allegations pertaining to those claims. *See* Order No. 17 (Nov. 19, 2018), *unreviewed*, Comm'n Notice (Dec. 12, 2018). On February 8, 2018, the ALJ partially terminated the investigation as to claims 21, 22, 32, and 34-38 of the '230 patent based on the withdrawal of the allegations pertaining to those claims. *See* Order No. 25 (Feb. 8, 2019), *unreviewed*, Comm'n Notice (Feb. 28, 2019). Claims 1-3, 5, 8, 10, 12, 18, and 23-28 of the '018 patent remain pending in this investigation.

The ALJ conducted an evidentiary hearing on May 14-17, 2019, and on September 9, 2019, issued the FID finding a violation of section 337 based on the infringement of claims 1-3, 5, 8, 10, 12, 18, and 24-28 of the '018 patent. In addition, the FID finds that the asserted claims are neither invalid under 35 U.S.C. §§ 103 and 112, nor unenforceable for inequitable conduct. Furthermore, the FID finds that the domestic industry requirement is satisfied. The FID also contains a recommended determination ("RD") recommending that the Commission issue a limited exclusion order ("LEO") barring entry of articles that infringe the '018 patent. The RD also recommends that the Commission impose a 5% bond during the period of Presidential review. Furthermore, as directed by the Commission, the RD provides findings with respect to the public interest and recommends that the Commission determine that the public interest factors do not preclude entry of the LEO.

On September 23, 2019, Jennewein and OUII filed petitions for review of the FID. On October 1, 2019, Glycosyn and OUII filed responses to Jennewein's and the IA's petitions.

Having examined the record of this investigation, including the FID, the RD, and the parties' submissions, the Commission has determined to review the FID in part. Specifically, the Commission has determined to review the FID's infringement findings with respect to Jennewein's bacterial strains adjudicated in this investigation. In addition, the Commission has determined to review the FID's decision not to adjudicate infringement as to Jennewein's alternative bacterial strain, the TTFL12 strain. The Commission has determined not to review the remainder of the FID.

In connection with its review, the Commission requests written responses regarding the following inquiries:

1. Assuming that the Commission determines to adjudicate infringement with respect to Jennewein's TTFL12 bacterial strain, please provide your position, with support from the evidentiary record, as to whether the TTFL12 strain infringes or does not infringe the asserted patent claims.

2. Should the Commission adjudicate infringement with respect to Jennwein's alternative strain? Is the Commission's determination of whether to adjudicate an alternative or redesigned product a legal question, a factual question, a mixed question of law or fact, an exercise of discretion, or something else?

3. Is the TTFL12 strain within the scope of the investigation? What criteria and evidence normally informs this analysis?

4. Does a respondent need to import an alternative or redesigned product for the product to be adjudicated?

5. What evidence corroborates Jennewein's assertion that the products listed in the shipping documents (RX-278C and RX-280C) were produced with the TTFL12 strain? Please provide your answers in a table with citations in one column and a brief explanation in a second column.

6. What is the effect of Jennewein's responses to Glycosyn's request for admission? Why has Jennewein failed to amend its responses if they are incorrect or misleading?

7. Is the TTFL12 strain sufficiently fixed in design? What criteria and evidence normally informs this analysis? Is there any declaratory judgment precedent that is relevant? Which party bears the burden of showing that an alternative or redesigned product is fixed in design?

8. Has the TTFL12 strain been subject to sufficient discovery? What criteria and evidence normally informs the "sufficient discovery" analysis?

9. Should the Commission issue remedial orders that are directed to the adjudicated strains (the #1540 and #1540 derivative) at this juncture?

Responses to the above questions should not exceed 40 pages, and replies should not exceed 20 pages.

In addition, in connection with the final disposition of this investigation, the statute authorizes issuance of (1) an order that could result in the exclusion of the subject articles from

entry into the United States, and/or (2) a cease and desist order that could result in the respondent being required to cease and desist from engaging in unfair acts in the importation and sale of such articles. Accordingly, the Commission is interested in receiving written submissions that address the form of remedy, if any, that should be ordered. If a party seeks exclusion of an article from entry into the United States for purposes other than entry for consumption, the party should so indicate and provide information establishing that activities involving other types of entry either are adversely affecting it or likely to do so. For background, *see Certain Devices for Connecting Computers via Telephone Lines*, Inv. No. 337-TA-360, USITC Pub. No. 2843, Comm'n Op. at 7-10 (Dec. 1994).

The statute requires the Commission to consider the effects of any remedy upon the public interest. The public interest factors the Commission will consider include the effect that an exclusion order and/or cease and desist orders would have on (1) the public health and welfare, (2) competitive conditions in the U.S. economy, (3) U.S. production of articles that are like or directly competitive with those that are subject to investigation, and (4) U.S. consumers. The Commission is therefore interested in receiving written submissions that address the aforementioned public interest factors in the context of this investigation.

If the Commission orders some form of remedy, the U.S. Trade Representative, as delegated by the President, has 60 days to approve, disapprove, or take no action on the Commission's determination. *See* Presidential Memorandum of July 21, 2005, 70 FR 43251 (July 26, 2005). During this period, the subject articles would be entitled to enter the United States under bond, in an amount determined by the Commission and prescribed by the Secretary of the Treasury. The Commission is therefore interested in receiving submissions concerning the amount of the bond that should be imposed if a remedy is ordered.

WRITTEN SUBMISSIONS: The parties to the investigation are requested to file written submissions limited to the briefing questions above. Parties to the investigation, interested government agencies, and any other interested parties are encouraged to file written submissions on the issues of remedy, the public interest, and bonding. Such initial written submissions should include views on the recommended determination by the ALJ on remedy, the public interest, and bonding. Complainant and the Commission Investigative Attorney are also requested to identify the form of remedy sought and to submit proposed remedial orders for the Commission's consideration in their initial written submissions. Complainant is further requested to state the date that the asserted patent expires and the HTSUS numbers under which the accused products are imported, and to supply the names of known importers of the products at issue in this investigation.

Initial written submissions and proposed remedial orders must be filed no later than close of business on **February 18, 2020**. Reply submissions must be filed no later than the close of business on **February 25, 2020** and must be limited to issues raised in the initial written submissions. No further submissions on any of these issues will be permitted unless otherwise ordered by the Commission.

Persons filing written submissions must file the original document electronically on or before the deadlines stated above and submit eight (8) true paper copies to the Office of the

Secretary by noon the next day pursuant to section 210.4(f) of the Commission's Rules of Practice and Procedure (19 CFR 210.4(f)). Submissions should refer to the investigation number ("Inv. No. 337-TA-1120") in a prominent place on the cover page and/or the first page. (*See* Handbook for Electronic Filing Procedures, https://www.usitc.gov/documents/handbook_on_filing_procedures.pdf). Persons with questions regarding filing should contact the Secretary (202-205-2000).

Any person desiring to submit a document to the Commission in confidence must request confidential treatment. All such requests should be directed to the Secretary to the Commission and must include a full statement of the reasons why the Commission should grant such treatment. *See* 19 CFR 201.6. Documents for which confidential treatment by the Commission is properly sought will be treated accordingly. All information, including confidential business information and documents for which confidential treatment is properly sought, submitted to the Commission for purposes of this Investigation may be disclosed to and used: (i) by the Commission, its employees and Offices, and contract personnel (a) for developing or maintaining the records of this or a related proceeding, or (b) in internal investigations, audits, reviews, and evaluations relating to the programs, personnel, and operations of the Commission including under 5 U.S.C. Appendix 3; or (ii) by U.S. government employees and contract personnel[1], solely for cybersecurity purposes. All non-confidential written submissions will be available for public inspection at the Office of the Secretary and on EDIS.

The authority for the Commission's determination is contained in section 337 of the Tariff Act of 1930, as amended (19 U.S.C. 1337), and in part 210 of the Commission's Rules of Practice and Procedure (19 CFR part 210).

By order of the Commission.

Lisa R. Barton
Secretary to the Commission

Issued: January 30, 2020

[1] All contract personnel will sign appropriate nondisclosure agreements.

CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME **Inv. No. 337-TA-1120**

PUBLIC CERTIFICATE OF SERVICE

I, Lisa R. Barton, hereby certify that the attached **NOTICE** has been served by hand upon the Commission Investigative Attorney, **Lisa Murray, Esq.**, and the following parties as indicated, on **January 30, 2020**.

Lisa R. Barton, Secretary
U.S. International Trade Commission
500 E Street, SW, Room 112
Washington, DC 20436

On Behalf of Complainants Glycosyn LLC:

Michael C. Newman, Esq.
MINTZ LEVIN COHN FERRIS GLOVSKY AND POPEO, PC
1 Financial Center
Boston, MA 02111

☐ Via Hand Delivery
☐ Via Express Delivery
☒ Via First Class Mail
☐ Other:_____

On Behalf of Respondent Jennewein Biotechnologie GmbH:

Gary M. Hnath
MAYER BROWN LLP
1999 K Street, NW
Washington, DC 20006

☐ Via Hand Delivery
☐ Via Express Delivery
☒ Via First Class Mail
☐ Other:_____

[redacted]

UNITED STATES INTERNATIONAL TRADE COMMISSION

Washington, D.C.

In the Matter of **CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME**	**Inv. No. 337-TA-1120**

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

Administrative Law Judge Cameron Elliot

(September 9, 2019)

Pursuant to the Notice of Investigation and Rule 210.42(a) of the Rules of Practice and Procedure of the United States International Trade Commission, this is my Initial Determination in the matter of *Certain Human Milk Oligosaccharides and Methods of Producing the Same*, Investigation No. 337-TA-1120.

[redacted]

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TABLE OF ABBREVIATIONS

CDX	Complainant's Demonstrative Exhibit
CIB	Complainant's Revised Initial Post-Hearing Brief
CPB	Complainant's Pre-Hearing Brief
CPX	Complainant's Physical Exhibit
CRB	Complainant's Reply Post-Hearing Brief
CX	Complainant's Exhibit
Dep. Tr.	Deposition Transcript
Hr'g Tr.	Hearing Transcript
JX	Joint Exhibit
RDX	Respondents' Demonstrative Exhibit
RIB	Respondents' Initial Post-Hearing Brief
RPB	Respondents' Pre-Hearing Brief
RPX	Respondents' Physical Exhibit
RRB	Respondents' Reply Post-Hearing Brief
RX	Respondents' Exhibit
SDX	Staff's Demonstrative Exhibit
SIB	Staff's Initial Post-Hearing Brief
SPB	Staff's Pre-Hearing Brief
SPX	Staff's Physical Exhibit
SRB	Staff's Reply Post-Hearing Brief
SX	Staff's Exhibit

[redacted]

I. INTRODUCTION

A. Procedural Background

Complainant Glycosyn LLC ("Glycosyn" or "Complainant") filed the complaint underlying this Investigation on April 2, 2018, and then filed an amended complaint on May 16, 2018. The complaint alleged respondent Jennewein Biotechnologie GmbH ("Jennewein" or "Respondent") imports certain products that infringe one or more claims of U.S. Patent Nos. 9,453,230 (the "'230 patent") and 9,970,018 (the "'018 patent" also referred to as JX-0003).

By publication of a notice in the *Federal Register* on June 21, 2018, the U.S. International Trade Commission ordered that:

> Pursuant to subsection (b) of section 337 of the Tariff Act of 1930, as amended, an investigation be instituted to determine whether there is a violation of subsection (a)(1)(B) of section 337 in the importation into the United States, the sale for importation, or the sale within the United States after importation of products identified in paragraph (2) by reason of infringement of one or more of claims 1–40 of the '230 patent; and claims 1–28 of the '018 patent; and whether an industry in the United States exists as required by subsection (a)(2) of section 337[.]

83 Fed. Reg. 28,865 (June 21, 2018). On July 16, 2018, the presiding administrative law judge set a target date of October 21, 2019 for completion of this investigation and set the evidentiary hearing for February 22, 2019. (Order No. 4.) On August 20, 2018, the administrative law judge issued the procedural schedule. (Order No. 6.) On September 4, 2018, and due to the retirement of the presiding administrative law judge, the investigation was reassigned to the Chief Administrative Law Judge. (EDIS Doc. ID 654642.)

In accordance with the issued procedural schedule, on October 16, 2018, the Chief Administrative Law Judge held a technology tutorial and *Markman* hearing, and on December 18, 2018, issued Order No. 22, construing certain terms of the asserted patents.

[redacted]

At times throughout the investigation, Glycosyn moved for the termination of certain asserted claims from those identified in the complaint. Specifically, on July 27, 2018, Glycosyn moved to terminate claims 4-7, 9-12, 14, 23-26, 28-31, 33, and 30-40 of the '230 patent and claims 6, 7, 9, 11, 13-17, 19, and 22 of the '018 patent. The presiding administrative law judge at the time granted Glycosyn's motion on August 9, 2018 with Order No. 5. The Commission determined not to review Order No. 5 on August 29, 2018. (EDIS Doc. ID 654274.) On October 18, 2018, Glycosyn moved to terminate claims 1-3, 8, 13, and 15-20 of the '230 patent. The Chief Administrative Law Judge granted Glycosyn's motion on October 30, 2018 with Order No. 15. The Commission determined not to review Order No. 15 on November 29, 2018. (EDIS Doc. ID 662881.) On November 9, 2018, Glycosyn moved to terminate claim 27 of the '230 patent and claims 4, 20, and 21 of the '018 patent. The Chief Administrative Law Judge granted Glycosyn's motion on November 19, 2018 with Order No. 17. The Commission determined not to review Order No. 17 on December 12, 2018. (EDIS Doc. ID 663942.) Lastly, on January 30, 2019, Glycosyn moved to terminate claims 21, 22, 32, and 34-38 of the '230 patent. The Chief Administrative Law Judge granted Glycosyn's motion on February 8, 2019 with Order No. 25. The Commission determined not to review Order No. 25 on February 28, 2019. (EDIS Doc. ID 668665.) Importantly, Order No. 25 terminated the last remaining asserted claims of the '230 patent, thereby terminating that patent in its entirety from the investigation. Thus, the sole remaining patent in this investigation is the '018 patent.

Also during the investigation, Jennewein filed two summary determination motions of non-infringement with respect to certain of their processes for the manufacture of its accused product. The Chief Administrative Law Judge denied both motions on March 8, 2019 with Order Nos. 27 and 28.

[redacted]

With respect to the procedural schedule, the government shutdown occurring between December of 2018 and January of 2019 necessitated an extension of all deadlines and the target date in this investigation. At the completion of the shutdown, on January, 29, 2019, the Chief Administrative Law Judge issued Order No. 23 which moved the start of the evidentiary hearing to May 13, 2019. Accordingly, the Chief Administrative Law Judge set a new procedural schedule for all remaining deadlines on February 7, 2019 with Order No. 24 and also extended the target date of the investigation approximately eleven weeks to January 9, 2020 with Order No. 26, issuing on February 21, 2019. The Commission determined not to review Order No. 26 on March 14, 2019. (EDIS Doc. ID 670060.)

Finally, on April 2, 2019 the investigation was reassigned a second time from the Chief Administrative Law Judge to me. (EDIS Doc. ID 671950.) I then conducted an evidentiary hearing between May 14, 2019 and May 17, 2019.

Following the evidentiary hearing, and pursuant to the procedural schedule, the parties submitted initial and reply post-hearing briefs on June 3, 2019 and June 17, 2019 respectively. Further, on June 10, 2019, Jennewein moved to strike certain portions of Glycosyn's initial post-hearing brief—a motion which I granted-in-part on June 14, 2019 with Order No. 38. On June 17, 2019, Glycosyn submitted a revised initial post-hearing brief in accordance with that order.

As of the date of this initial determination, no motions remain pending.

B. The Parties

Complainant Glycosyn LLC is organized and exists under the laws of Massachusetts. (SIB at 2.) It was founded in 2002 to pursue research and development "of commercially-viable methods for synthesizing and producing human milk oligosaccharides, commonly known as HMOs. (CIB at 7.) While Glycosyn conducts its research and development in the United States,

[redacted]

it is currently linked with a Dutch production partner, Royal FrieslandCampina N.V., to manufacture and distribute the 2'-FL HMO for the infant formula market. (*Id.* at 7-8; *see* RIB at 3 (citing RX-0056).)

Respondent Jennewein Biotechnologie GmbH is based in Germany, and founded in 2005 for the similar purpose of researching means of manufacture for HMOs. (CIB at 8.) Jennewein claims it "is the true innovator and market leader for 2'-FL in the United States" as "[n]o other company, including Glycosyn or its partner, is supplying 2'-FL to American consumers." (RIB at 4 (citing Hr'g Tr. at 57:3-4; RX-0385C at Q188); *see* SIB at 3.) In this investigation, and as described further below, Glycosyn has alleged Jennewein's methods of producing 2'-FL imported into the United States infringe the '018 patent. (*Id.*)

C. The Asserted Patent and Claims

The asserted patent relates to compositions and methods for providing engineered bacteria to produce certain HMOs. The following claims remain at issue in this investigation:

Patent Number	**Infringement Claims**	**Domestic Industry Claims**
'018 patent	1-3, 5, 8, 10, 12, 18, 23-28	1-3, 5, 8-14, 18, 22-28

(*See* CIB at 15-16.)

The '018 patent is entitled, "Biosynthesis of Human Milk Oligosaccharides in Engineered Bacteria." (JX-0003.) It was filed on September 21, 2017, and claims priority as a continuation application of an application filed on February 24, 2017, itself a continuation of an application filed on September 23, 2013, which was a division of an application filed on February 16, 2012.

[redacted]

(*Id.*) Through these applications, the '018 patent also claims further priority to a provisional application filed on February 16, 2011. (*Id.*)[1] The '018 patent issued on May 15, 2018.

The '018 patent generally describes "compositions and methods for engineering bacteria to produce fucosylated oligosaccharides, and the use thereof in the prevention or treatment of infection." (*See id.* at Abstract.) The patent explains:

> Human milk contains a diverse and abundant set of neutral and acidic oligosaccharides (human milk oligosaccharides, HMOS). Many of these molecules are not utilized directly by infants for nutrition, but they nevertheless serve critical roles in the establishment of a healthy gut microbiome, in the prevention of disease, and in immune function. Prior to the invention described herein, the ability to produce HMOS inexpensively at large scale was problematic. For example, HMOS production through chemical synthesis was limited by stereo-specificity issues, precursor availability, product impurities, and high overall cost. As such, there is a pressing need for new strategies to inexpensively manufacture large quantities of HMOS for a variety of commercial applications.

(*Id.* at 1:34-47.) In some methods disclosed in the patent, an *E. coli* bacterium is used. The bacterium is engineered in several ways that assist the production and collection of the desired oligosaccharide. For example, the bacterium may be engineered by the addition, deletion, or inactivation of genes to: create the desired oligosaccharide from first and second basic sugar building blocks (*e.g.*, fucosyltransferase gene, GDP-fucose synthesis pathway); improve the ability to intake the sugar building block(s) from an outside medium (*e.g.*, lactose permease gene); inactivate certain pathways that compete with oligosaccharide production (*e.g.*, colonic acid synthesis gene); and produce certain enzymes which compete with oligosaccharide production but otherwise assist later steps of purification and retrieval of the oligosaccharide (*e.g.*, functional β-galactosidase gene). (*See id.* at 1:51-60, 3:44-50.)

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[1] The effective date of the asserted patents pre-dates the America Invents Act ("AIA") enacted by Congress on September 16, 2011.

[redacted]

This last purpose, involving β-galactosidase activity, is pointedly in dispute in this investigation. The '018 patent describes one particularly relevant example of *E. coli* engineering and culturing:

> Also described herein are bacterial host cells with the ability to accumulate a[n] intracellular lactose pool while simultaneously possessing low, functional levels of cytoplasmic β-galactosidase activity, for example as provided by the introduction of a functional recombinant *E. coli* lacZ gene, or by a β-galactosidase gene from any of a number of other organisms . . .. Low, functional levels of cytoplasmic β-galactosidase include β-galactosidase activity levels, of between 0.05 and 200 units, e.g., between 0.05 and 5 units, between 0.05 and 4 units, between 0.05 and 3 units, or between 0.05 and 2 units (for unit definition see: Miller J H, Laboratory CSH. Experiments in molecular genetics. Cold Spring Harbor Laboratory Cold Spring Harbor, N.Y.; 1972; incorporated herein by reference). This low level of cytoplasmic β-galactosidase activity, while not high enough to significantly diminish the intracellular lactose pool, is nevertheless very useful for tasks such as . . . the facile removal of undesired residual lactose at the end of fermentations.

('018 patent at 7:22-45.) In this art, and as used throughout this initial determination, genes are normally identified with a starting lower-case letter and in italics (*e.g.*, *lacZ*), and the peptide created from that gene starts in upper case with no italics (*e.g.*, LacZ). (RX-0384C at Q152; CX-0004C at Q61.)[2]

Glycosyn contends it owns the '018 patent, which is reflected in the assignment filed with its prosecution history (CIB at 31 (citing JX-0006 at -4790; '018 patent)) and neither Jennewein nor the Staff disputes ownership (*see* SIB at 3; *see generally* RIB; RRB).

D. Products at Issue

1. Domestic Industry Products

The domestic industry products in this investigation consist of certain non commercial-level amounts of 2'-FL produced by Glycosyn within the United States as part of its research and

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[2] The '018 patent does not itself necessarily follow the italics scheme for genes. (*See, e.g.*, '018 patent at 7:26.)

[redacted]

development efforts. (CIB at 92 (citing CX-0059C; CX-0131C; CX-0064C); CX-0004C at Q124-125.) Glycosyn identifies its E997 bacterial strain as practicing at least one claim of the '018 patent, and contends many other strains are fairly represented by E997 with respect to this issue. (CIB at 15-16 (citing CX-0004 at Q99, 123), 126 n.8, 9.) Glycosyn claims the following strains, developed since 2015, are represented by its E997 strain as patent practicing:

Products at Issue	**Representative Product**
[redacted]	E997

(CIB at 126 n.9 (citing CX-0002C at Q107-108; CX-0060C; CX-0058C; CX-0059C; CX-0130C).)

2. Accused Product

The accused product in this case is 2'-FL which Jennewein has imported or sold for importation into the United States ("Accused Product") using methods claimed in the '018 patent. In this investigation, Glycosyn has accused Jennewein's 2'-FL production methods based on an *E. coli* #1540 bacterial strain, [redacted] The #1540 [redacted] Jennewein seeks adjudication of [redacted] known as TTFL12. For reasons discussed below, I do not find adjudication of TTFL12 is warranted at this time.

II. STANDARDS OF LAW

A. Claim Construction

"The construction of claims is simply a way of elaborating the normally terse claim language in order to understand and explain, but not to change, the scope of the claims." *Embrex, Inc. v. Serv. Eng'g Corp.*, 216 F.3d 1343, 1347 (Fed. Cir. 2000). Although most of the disputed

claim terms were construed in an earlier order, some of the issues presented below are only resolvable with additional claim construction. (*See* Order No. 22.)

Claim construction focuses on the intrinsic evidence, which consists of the claims themselves, the specification, and the prosecution history. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (en banc); *see also Markman v. Westview Instr., Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995) (en banc). As the Federal Circuit in *Phillips* explained, courts must analyze each of these components to determine the "ordinary and customary meaning of a claim term" as understood by a person of ordinary skill in art at the time of the invention. 415 F.3d at 1313. "Such intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." *Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc.*, 262 F.3d 1258, 1267 (Fed. Cir. 2001).

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude.'" *Phillips*, 415 F.3d at 1312 (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). "Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of particular claims terms." *Id.* at 1314; *see Interactive Gift Express, Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001) ("In construing claims, the analytical focus must begin and remain centered on the language of the claims themselves, for it is that language that the patentee chose to use to 'particularly point [ ] out and distinctly claim [ ] the subject matter which the patentee regards as his invention."). The context in which a term is used in an asserted claim can be "highly instructive." *Phillips*, 415 F.3d at 1314. Additionally, other claims in the same patent, asserted or unasserted, may also provide guidance as to the meaning of a claim term. *Id.* "Courts do not rewrite claims; instead, we give

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effect to the terms chosen by the patentee." *K-2 Corp. v. Salomon S.A.*, 191 F.3d 1356, 1364 (Fed. Cir. 1999).

"[T]he specification 'is always highly relevant to the claim construction analysis. Usually it is dispositive; it is the single best guide to the meaning of a disputed term.'" *Phillips*, 415 F.3d at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). "[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Id.* at 1316. "In other cases, the specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor." *Id.* As a general rule, however, the particular examples or embodiments discussed in the specification are not to be read into the claims as limitations. *Id.* at 1323. In the end, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be ... the correct construction." *Id.* at 1316 (quoting *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998)).

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

When the intrinsic evidence does not establish the meaning of a claim, then extrinsic evidence (*i.e.*, all evidence external to the patent and the prosecution history, including

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

The construction of a claim term is generally guided by its ordinary meaning. However, courts may deviate from the ordinary meaning when: (1) "the intrinsic evidence shows that the patentee distinguished that term from prior art on the basis of a particular embodiment, expressly disclaimed subject matter, or described a particular embodiment as important to the invention;" or (2) "the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in either the specification or prosecution history." *Edwards Lifesciences LLC v. Cook Inc.*, 582 F.3d 1322, 1329 (Fed. Cir. 2009); *see GE Lighting Sols., LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1309 (Fed. Cir. 2014) ("the specification and prosecution history only compel departure from the plain meaning in two instances: lexicography and disavowal."); *Omega Eng'g, Inc, v. Raytek Corp.*, 334 F.3d 1314, 1324 (Fed. Cir. 2003) ("[W]here the patentee has unequivocally disavowed a certain meaning to obtain his patent, the doctrine of prosecution disclaimer attaches and narrows the ordinary meaning of the claim congruent with the scope of the surrender."); *Rheox, Inc. v. Entact, Inc.*, 276 F.3d 1319, 1325 (Fed. Cir. 2002) ("The prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution."). Nevertheless, there is a "heavy presumption that a claim term carries its ordinary and customary meaning." *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir.

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2002) (citations omitted). The standard for deviating from the plain and ordinary meaning is "exacting" and requires "a clear and unmistakable disclaimer." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1366-67 (Fed. Cir. 2012); *see Epistar Corp. v. Int'l Trade Comm'n*, 566 F.3d 1321, 1334 (Fed. Cir. 2009) (requiring "expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope" to deviate from the ordinary meaning) (citation omitted).

B. Infringement

"An infringement analysis entails two steps. The first step is determining the meaning and scope of the patent claims asserted to be infringed. The second step is comparing the properly construed claims to the device accused of infringing." *Markman*, 52 F.3d at 976.

A patentee may prove infringement either literally or under the doctrine of equivalents. Infringement of either sort must be proven by a preponderance of the evidence. *SmithKline Diagnostics, Inc. v. Helena Labs. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988). A preponderance of the evidence standard "requires proving that infringement was more likely than not to have occurred." *Warner-Lambert Co. v. Teva Pharm. USA, Inc.*, 418 F.3d 1326, 1341 n.15 (Fed. Cir. 2005).

Literal infringement, a form of direct infringement, is a question of fact. *Finisar Corp. v. DirecTV Group, Inc.*, 523 F.3d 1323, 1332 (Fed. Cir. 2008). "To establish literal infringement, every limitation set forth in a claim must be found in an accused product, exactly." *Microsoft Corp. v. GeoTag, Inc.*, 817 F.3d 1305, 1313 (Fed. Cir. 2016) (quoting *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1575 (Fed. Cir. 1995). 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).

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Doctrine of equivalents is also a form of direct infringement. One rubric for evaluating if a claimed feature is not literally, but nonetheless equivalent to, a claimed feature is known as the function-way-result test. Under this test, the accused feature is equivalent to the claim limitation when "it performs substantially the same function in substantially the same way to obtain the same result." *Duncan Parking Techs., Inc. v. IPS Grp., Inc.*, 914 F.3d 1347, 1362 (Fed. Cir. 2019) (quoting *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 608 (1950)). Another test is known as in the insubstantial differences test, where "[a]n element in the accused device is equivalent to a claim limitation if the only differences between the two are insubstantial." *Voda v. Gordia Corp.*, 536 F.3d 1311, 1139 (Fed. Cir. 2008). The Supreme Court has further instructed, "the proper time for evaluating equivalency . . . is at the time of infringement, not at the time the patent was issued." *Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 37 (1997).

C. Domestic Industry

In an investigation based on a claim of patent infringement, Section 337 requires that an industry in the United States, relating to the articles protected by the patent, exist or be in the process of being established. 19 U.S.C. § 1337(a)(2). Under Commission precedent, the domestic industry requirement has been divided into (i) a "technical prong" " (which requires articles covered by the asserted patent) and (ii) an "economic prong" (which requires certain levels of activity with respect to the protected articles or patent itself). *See Certain Video Game Systems and Controllers*, Inv. No. 337-TA-743, Comm'n Op. at 6-7 (April 14, 2011) ("*Video Game Systems*").

1. Technical Prong

The technical prong of the domestic industry requirement is satisfied when the complainant in a patent-based section 337 investigation establishes that it is practicing or exploiting the patents

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at issue. *See* 19 U.S.C. §§ 1337 (a)(2), (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 (U.S.I.T.C. Jan. 16, 1996). "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*, Inv. No. 337-TA-477, Comm'n Op. at 55 (U.S.I.T.C. Aug. 28, 2003).

The test for claim coverage for the purposes of the technical prong of the domestic industry requirement is the same as that for infringement. *See Certain Doxorubicin and Preparations Containing Same*, Inv. No. 337-TA-300, Initial Determination at 109 (U.S.I.T.C. May 21, 1990), *aff'd*, Views of the Commission at 22 (U.S.I.T.C. Oct. 31, 1990); *Alloc, Inc. v. Int'l Trade Comm'n*, 342 F.3d 1361, 1375 (Fed. Cir. 2003). "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." *Certain Doxorubicin and Preparations Containing Same*, Inv. No. 337-TA-300, Initial Determination at 109. As with infringement, 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, ID at 44, Pub. No. 2575 (U.S.I.T.C. May 15, 1992). In short, the patentee must establish by a preponderance of the evidence that the domestic product practices one or more claims of the patent.

2. Economic Prong

The "economic prong" of the domestic industry requirement is satisfied when there exists in the United States, in connection with products practicing at least one claim of the patent at issue: (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, and licensing. 19 U.S.C. § 1337(a)(3). Establishment of the "economic prong" is not dependent

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on any "minimum monetary expenditure" and there is no need for 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 significance of its activities with respect to the articles protected by the patent. *Certain Printing and Imaging Devices and Components Thereof*, Inv. No. 337-TA-690, Comm'n Op. at 30 (Feb. 17, 2011) ("*Imaging Devices*"). Further, a complainant can show that its activities are significant by showing how those activities are important to the articles protected by the patent in the context of the company's operations, the marketplace, or the industry in question. *Id.* at 27-28. That significance, however, must be shown in a quantitative context. *Lelo Inc. v. Int'l Trade Comm'n*, 786 F.3d 879, 886 (Fed. Cir. 2015). The Federal Circuit noted that when the ITC first addressed this requirement, it found the word "'significant' denoted 'an assessment of the *relative* importance of the domestic activities.'" *Id.* at 883-4 (internal citation omitted) (emphasis added). In general, "[t]he purpose of the domestic industry requirement is to prevent the ITC from becoming a forum for resolving disputes brought by foreign complainants whose only connection with the United States is ownership of a U.S. patent." *Certain Battery-Powered Ride-On Toy Vehicles*, Inv. No. 337-TA-314, USITC Pub. No. 2420, Initial Determination at 21 (Aug. 1991).

The Commission "has long recognized that the 'its' in the phrase 'investment in its exploitation' in subparagraph (C) refers to the asserted patent or other intellectual-property right being asserted. That conclusion is supported by the clear text of the statute." *Certain Integrated Circuit Chips and Products Containing the Same*, Inv. No. 337-TA-859, Comm'n Op. at 36 (Aug. 11, 2014) ("*Integrated Circuit Chips*"). This connection between the investment and the patent is known as the "nexus" requirement. *Id.* at 38. "To the extent that the patented technology arises

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from endeavors in the United States, such a nexus would ordinarily exist." *Id.* at 39. "'Exploitation' is a generally broad term that encompasses activities such as efforts to improve, develop, or otherwise take advantage of the asserted patent." *Id.* Similarly, investments in plant and equipment, labor, and capital that may fairly be considered investments in research and development are eligible for consideration under subsections (A) and (B), in addition to subsection (C). *See Certain Solid State Storage Drives, Stacked Electronics Components, and Products Containing Same*, Inv. No. 337-TA-1097, Comm'n Op. at 14 (June 29, 2018) ("*Solid State Storage Drives*").

D. Invalidity

1. 35 U.S.C. § 102

Pursuant to 35 U.S.C. § 102, a patent claim is invalid as anticipated if:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant;
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States;
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent;"
>
> (g)(2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it.

35 U.S.C. § 102 (pre-AIA). "A patent is invalid for anticipation if a single prior art reference discloses each and every limitation of the claimed invention. Moreover, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is

necessarily present, or inherent, in the single anticipating reference." *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (citations omitted).

2. 35 U.S.C. § 103

Section 103 of the Patent Act states:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

35 U.S.C. § 103(a) (pre-AIA). "Obviousness is a question of law based on underlying questions of fact." *Scanner Techs. Corp. v. ICOS Vision Sys. Corp. N.V.*, 528 F.3d 1365, 1379 (Fed. Cir. 2008). The underlying factual determinations include: "(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) objective indicia of non-obviousness." *Id.* (citing *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966)). These factual determinations are often referred to as the "Graham factors."

The critical inquiry in determining the differences between the claimed invention and the prior art is whether there is a reason to combine the prior art references. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418-21 (2007). In *KSR*, the Supreme Court rejected the Federal Circuit's rigid application of the teaching-suggestion-motivation test. While the Court stated that "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does," it described a more flexible analysis:

> 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 . . . . As our precedents make clear, however, the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.

Id. at 418. Since *KSR*, the Federal Circuit has announced that, where a patent challenger contends that a patent is invalid for obviousness based on a combination of 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 . . . 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); *see KSR*, 550 U.S. at 399 ("The proper question was whether a pedal designer of ordinary skill in the art, facing the wide range of needs created by developments in the field, would have seen an obvious benefit to upgrading Asano with a sensor.").

In addition to demonstrating that a reason exists to combine prior art references, the challenger must demonstrate that the combination of prior art references discloses all of the limitations of the claims. *Hearing Components, Inc. v. Shure Inc.*, 600 F.3d 1357, 1373-4 (Fed. Cir. 2010) (abrogated on other grounds by *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S.Ct. 2120 (2014)) (upholding finding of non-obviousness based on the fact that there was substantial evidence that the asserted combination of references failed to disclose a claim limitation); *Velander v. Garner*, 348 F.3d 1359, 1363 (Fed. Cir. 2003) (explaining that a requirement for a finding of obviousness is that "all the elements of an invention are found in a combination of prior art references").

"A reference qualifies as prior art for a determination under § 103 when it is analogous to the claimed invention." *Innovention Toys, LLC v. MGA Entm't, Inc.*, 637 F.3d 1314, 1321 (Fed.

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Cir. 2011) (citing *In re Clay*, 966 F.2d 656, 658 (Fed. Cir. 1992)). "Two separate tests define the scope of analogous prior art: (1) whether the art is from the same field of endeavor, regardless of the problem addressed and, (2) if the reference is not within the field of the inventor's endeavor, whether the reference still is reasonably pertinent to the particular problem with which the inventor is involved." *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004) (citing *In re Deminski,* 796 F.2d 436, 442 (Fed. Cir. 1986)). One way of evaluating whether a reference is reasonably pertinent is to consider if, "logically [it] would have commended itself to an inventor's attention in considering his problem." *K-TEC, Inc. v. Vita-Mix Corp.*, 696 F.3d 1364, 1375 (Fed. Cir. 2012) (citing *Innovention*, 637 F.3d at 1321)). The requirement for prior art to be analogous is "meant to defend against hindsight." *In re Khan*, 441 F.3d 977, 986-987 (Fed. Cir. 2006).

An obviousness determination should also include a consideration of "secondary considerations" such as "commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *Graham*, 338 U.S. at 17-18. "For [such] objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995); *see Merck & Cie v. Gnosis S.P.A.*, 808 F.3d 829, 837 (Fed. Cir. 2015). "Where the offered secondary consideration actually results from something other than what is both claimed and novel in the claim, there is no nexus to the merits of the claimed invention." *In re Huai-Hung Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011).

3. 35 U.S.C. § 112

Pursuant to 35 U.S.C. § 112, a patent claim is invalid for lack of written description if the patent's specification fails to "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharm., Inc. v. Eli Lilly &*

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Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skilled in the art," *id.*, and "the level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology," *id.* (citing *Capon v. Eshar*, 418 F.3d 1349, 1357-58 (Fed. Cir. 2005)).

Additionally, under 35 U.S.C. § 112, a patent claim is invalid for indefiniteness if "its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments, Inc.,* 134 S. Ct. 2120, 2124 (2014). Indefiniteness can result from a single claim covering both an apparatus and a method of use of that apparatus, as "a manufacturer or seller of the claimed apparatus would not know from the claim whether it might also be liable for contributory infringement because a buyer or user of the apparatus later performs the claimed method using the apparatus." *IPXL Holdings v. Amazon.com*, 430 F.3d 1377, 1384 (Fed. Cir. 2005); *see UltimatePointer, L.L.C. v. Nintendo Co.*, 816 F.3d 816, 826 (Fed. Cir. 2016) (holding these types of claims may make it "unclear whether infringement . . . occurs when one creates an infringing system, or whether infringement occurs when the user actually uses the system in an infringing manner") (citation omitted). "[A]pparatus claims are not necessarily indefinite for using functional language," however, as in, for example, means-plus-function formatted claims. *MasterMine Software, Inc. v. Microsoft Corp.*, 874 F.3d 1307, 1313 (Fed. Cir. 2017) (citing *Microprocessor Enhancement Corp. v. Tex. Instruments Inc.*, 520 F.3d 1367, 1375 (Fed. Cir. 2008)). Another example may be when the claim merely recites "that the system 'possesses the recited structure which is capable of performing the recited functions.'" *Id.* at 1315-16 (quoting *Microprocessor Enhancement*, 520 F.3d at 1375).

[redacted]

Further, under 35 U.S.C. § 112, a patent specification must contain a description "of the manner and process of making and using" the invention. 35 U.S.C. § 112. This is referred to as the enablement requirement, and a patent claim is sufficiently enabled only when the specification teaches "those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). To determine whether the specification leaves a person of ordinary skill to perform undue experimentation, the Federal Circuit has identified the following factors to consider: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. *In re Wands*, 585 F.2d 731, 737 (Fed. Cir. 1988). "[I]t is not necessary that a court review all the *Wands* factors to find a disclosure enabling. They are illustrative, not mandatory." *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991).

E. Unenforceability

"Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section." 37 C.F.R. § 1.56(a). Thus, a patent may become unenforceable if "the applicant misrepresented or omitted material information with the specific intent to deceive the PTO." *Therasense, Inc. v. Becton, Dickinson and Co.*, 649 F.3d 1276, 1287 (Fed. Cir. 2011) (en banc). "Unlike validity defenses, which are claim specific, *see* 35 U.S.C. § 288, inequitable conduct

[redacted]

regarding any single claim renders the entire patent unenforceable." *Id.* at 1288 (citing *Kingsdown Med. Consultants, Ltd. v. Hollister Inc.*, 863 F.2d 867, 877 (Fed. Cir. 1988)).

"Intent and materiality are separate requirements." *Id.* at 1290 (citing *Hoffman-La Roche, Inc. v. Promega Corp.*, 323 F.3d 1354, 1359 (Fed. Cir. 2003)). With respect to materiality:

> [T]he materiality required to establish inequitable conduct is but-for materiality. When an applicant fails to disclose prior art to the PTO, that prior art is but-for material if the PTO would not have allowed a claim had it been aware of the undisclosed prior art. Hence, in assessing the materiality of a withheld reference, the court must determine whether the PTO would have allowed the claim if it had been aware of the undisclosed reference.

Id. at 1291. With respect to intent:

> A finding that the misrepresentation or omission amounts to gross negligence or negligence under a "should have known" standard does not satisfy this intent requirement. *Kingsdown,* 863 F.2d at 876. "In a case involving nondisclosure of information, clear and convincing evidence must show that the applicant *made a deliberate decision* to withhold a *known* material reference." *Molins,* 48 F.3d at 1181 (emphases added). In other words, the accused infringer must prove by clear and convincing evidence that the applicant knew of the reference, knew that it was material, and made a deliberate decision to withhold it.

Id. at 1290. Further, the evidence of specific intent must "*require* a finding of deceitful intent in the light of all the circumstances" such that "when there are multiple reasonable inferences that may be drawn, intent to deceive cannot be found." *Id.* at 1290-91 (citations omitted). In the context of withheld prior art, "[p]artial disclosure of material information about the prior art to the PTO cannot absolve a patentee of intent if the disclosure is intentionally selective." *Am. Calcar, Inc. v. Am. Honda Motor Co.*, 768 F.3d 1185, 1190 (Fed. Cir. 2014) (citing *Aventis Pharma S.A. v. Hospira, Inc.*, 675 F.3d 1324, 1335-36 (Fed. Cir. 2012)); *Semiconductory Energy Lab. Co. v. Samsung Elecs. Co.*, 204 F.3d 1368, 1376 (Fed. Cir. 2000)). It is also true that "[a]n inference of intent to deceive is appropriate where the applicant engages in 'a pattern of lack of candor,' including where the applicant repeatedly makes factual representations 'contrary to the true

[redacted]

information he had in his possession.'" *Regeneron Pharm., Inc. v. Merus N.V.*, 864 F.3d 1343, 1351 (Fed. Cir. 2017) (citing *Apotex Inc. v. UCB, Inc.*, 763 F.3d 1354, 1362 (Fed. Cir. 2014)). Nevertheless, "the specific intent to deceive must be 'the single most reasonable inference able to be drawn from the evidence.'" *Therasense*, 649 F.3d at 1290 (citation omitted).

III. JURISDICTION AND IMPORTATION

Jennewein has stipulated to importation, as noted in its own briefing. (*See* RIB at 10 (citing JX-0008C; JX-0009C).) I therefore find the importation requirement under 19 U.S.C. § 1337(a)(1)(B) satisfied, and find the Commission has *in rem* jurisdiction over the Accused Product. *See Sealed Air Corp. v. Int'l Trade Comm'n*, 645 F.2d 976, 985 (C.C.P.A. 1981).

[redacted] One of Jennewein's fact witnesses, Dr. Stefan Jennewein, testified that an exhibit, RX-0280C, "is a summary of the 2'-FL we produced and imported into the U.S. according to strain." (RX-0385C at Q132-133.) He explained the information came from Jennewein's CFO, who "prepared it from our accounting system in response to one of Glycosyn's discovery requests." (*Id.* at Q134.) Based on this document, he concluded that [redacted] TTFL12 [redacted] (*Id.* at Q135.)

The importation record, RX-0280C, is brief and shows the following:

[redacted]

[redacted]

[redacted]

(RX-0280C at -284583.) [redacted] Dr. Jennewein's testimony confirms it (RX-0385C at Q135) as does Jennewein's final response to Glycosyn's request for admission on this issue:

> REQUEST FOR ADMISSION 7:
>
> Admit that Jennewein's strain #1540 is the only strain Jennewein uses to produce the 2'-FL that is imported into the United States.
>
> AMENDED RESPONSE TO REQUEST NO. 7
>
> Jennewein objects to this Request as vague and ambiguous with respect to the terms "uses" and "produce." Subject to its objections, Jennewein responds as follows:
>
> [redacted]

(CX-0216C at 5).

[redacted]

IV. U.S. PATENT NO. 9,970,018

A. Level of Ordinary Skill in the Art

In Order No. 22, the Chief Administrative Law Judge found a person of ordinary skill in the art for the asserted patent at the time of the invention would have (1) a Ph.D in molecular biology, biochemistry, or chemical engineering, or an equivalent field, and 1-2 years of experience working with *E. coli* bacteria or related systems, or (2) a lower level degree (*e.g.*, a M.A.) in a similar field to those listed above, but a greater amount of relevant working experience (*e.g.*, 5-6 years of experience working with *E. coli* bacteria or related systems). (Order No. 22 at 7.) I find no reason to diverge from this definition and apply it throughout this initial determination.

B. Claims-at-Issue

Claims 1-3, 5, 8-14, 18, and 22-28 of the '018 patent are at issue in this investigation, either through allegations of infringement or of the domestic industry technical prong:

> 1. A method for producing a fucosylated oligosaccharide in a bacterium, comprising
>
> providing an isolated *E. coli* bacterium comprising,
>
> (i) a deletion or functional inactivation of an endogenous β-galactosidase gene;
>
> (ii) an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium, wherein the level of β-galactosidase activity comprises between 0.05 and 200 units;
>
> (iii) an inactivating mutation in a colanic acid synthesis gene; and
>
> (iv) an exogenous lactose-accepting fucosyltransferase gene;
>
> culturing said bacterium in the presence of lactose; and
>
> retrieving a fucosylated oligosaccharide from said bacterium or from a culture supernatant of said bacterium.
>
> 2. The method of claim 1, wherein said colanic acid synthesis gene comprises an *E. coli* wcaJ, wzxC, wcaD, wza, wzb, or wzc gene.

3. The method of claim 2, wherein said colanic acid synthesis gene comprises a wcaJ gene.

. . . .

5. The method of claim 1, wherein said exogenous lactose-accepting fucosyltransferase gene encodes α(1,2) fucosyltransferase and/or α(1,3) fucosyltransferase.

. . . .

8. The method of claim 1, wherein said exogenous functional β-galactosidase gene comprises an *E. coli lacZ* gene.

9. The method of claim 8, wherein the *lacZ* gene is inserted into an endogenous lon gene.

10. The method of claim 1, wherein said bacterium further comprises a functional lactose permease gene.

11. The method of claim 10, wherein said lactose permease gene is an endogenous lactose permease gene.

12. The method of claim 10, wherein said lactose permease gene comprises an *E. coli* lacY gene.

13. The method of claim 1, wherein said bacterium further comprises an exogenous *E. coli* rcsA or *E. coli* rcsB gene.

14. The method of claim 1, wherein said bacterium further comprises an inactivating mutation in a lacA gene.

. . . .

18. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 5 units.

. . . .

22. The method of claim 1, wherein said bacterium comprises the genotype of

(a) ampC::(PtrpBλcI+), PlacI q (ΔlacI-lacZ)lacY+, ΔwcaJ, thyA::Tn10, Δlon::(kan, lacZ+); or

(b) ampC::(PtrpBλcI+), PlacI q (ΔlacI-lacZ)lacY+, ΔwcaJ, thyA::Tn10, Δlon::(kan, lacZ+), ΔlacA.

[redacted]

23. The method of claim 1, wherein said exogenous functional β-galactosidase gene is inserted into an endogenous gene.

24. The method of claim 1, wherein said exogenous functional β-galactosidase gene comprises a recombinant β-galactosidase gene engineered to produce a detectable level of β-galactosidase activity that is reduced compared to the level of β-galactosidase activity in a wild-type *E. coli* bacterium.

25. The method of claim 24, wherein the level of β-galactosidase activity comprises between 0.05 and 5 units.

26. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 4 units.

27. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 3 units.

28. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 2 units.

(CIB at 15-16.)

C. Claim Construction

As part of the *Markman* process, the following terms of the '018 patent were construed, either as-agreed between the parties or determined by Order No. 22:

Claim Term	**Construction**
"providing"	plain and ordinary meaning, *i.e.*, furnishing, supplying, making available, or preparing.
"in the presence of lactose"	plain and ordinary meaning, *i.e.*, lactose is available to the bacterium
"exogenous"	plain and ordinary meaning, *i.e.*, originating outside an organism, tissue, or cell
"colonic acid synthesis gene"	"By 'colanic acid synthesis gene' is meant a gene involved in a sequence of reactions, usually controlled and catalyzed by enzymes that result in the synthesis of colanic acid."
"*E. coli lacZ* gene"	plain and ordinary meaning, *i.e.*, a structural gene that encodes the β-galactosidase protein and is part of the lac operon in the DNA of *E. coli*

[redacted]

"β-galactosidase activity comprises between 0.05 and [200 units / 5 units / 4 units / 3 units / 2 units]"	Not indefinite; "β-galactosidase activity is measurable at between exactly 0.05 and exactly [200/5/4/3/2] Miller Units, as defined in Miller, J.H., Experiments in Molecular Genetics (Cold Spring Harbor Lab. 1972) at 352-355"
"functional . . . β-galactosidase gene"	"a functional sequence of DNA that encodes B-galactosidase"
"wild type"	"the type most commonly found in nature"

(*See* Order No. 22 at 12-13, 22-35.) None of Glycosyn, Jennewein, or the Staff specifically identify any remaining claim construction issues for this initial determination. (*See* CIB at 32-33; RIB at 16-17; SIB at 29-30.)

D. Infringement

According to Glycosyn's post-hearing briefing, and not contested by Jennewein or the Staff, the following products are within the scope of the Investigation and accused of infringing the following claims of the '018 patent:

Product	**Claims**
Jennewein #1540 and [redacted]	1-3, 5, 8, 10, 12, 18, 23-28

(CIB at 15.) As referred to above, Jennewein and the Staff each argue that another of Jennewein's *E. coli* strains is properly within the scope of the investigation and subject to a determination of infringement—a strain designated TTFL12. Glycosyn disputes that an infringement determination on TTFL12 is appropriate given the circumstances.

[redacted]

1. Regarding the Jennewein TTFL12 Strain

With respect to Jennewein's 2'-FL produced by the TTFL12 Strain, there can be no dispute that Glycosyn has not accused it of infringement such that it is an "accused product." (CPB at 27 ("E. The Accused Process. At the hearing, Glycosyn will demonstrate that [] Jennewein's method of making 2'-FL using Jennewein's #1540 and [redacted]) infringes the asserted claims of the '018 Patent."); SIB at 61 ("Glycosyn has not alleged that 2'-FL made using Jennewein's TTFL12 strain infringes any claim of the asserted patents, either literally or under the doctrine of equivalents.").) Nevertheless, Jennewein contends it placed this strain into the scope of the investigation such that an infringement determination is warranted. (RIB at 66 ("Despite being aware of Jennewein's TTFL12 strain since August 21, 2018, Glycosyn failed to accuse 2'-FL made using this strain of infringing any claim of the '018 patent.").) The Staff concurs. (SIB at 63.) As noted, Glycosyn disputes that such a determination should be made. (CIB at 67.)

The Commission has recently addressed the circumstances under which non-accused products nonetheless fall within the scope of an investigation. In *Certain Two-Way Radio Equipment and Systems, Related Software, and Components Thereof* ("*Two-Way Radio*"), the Commission had determined to review "(5) the [final] ID's finding that insufficient record evidence exists to make a conclusive determination as to whether any redesigned products infringe the '701 patent and the ID's lack of an express finding on this issue with respect to the '869 or '991 patent[s]." Inv. No. 337-TA-1053, Comm'n Op. at 8 (Dec. 18, 2018) (public version). Contrary to that ID's finding, the Commission held "[respondent] has met its burden to show that the redesigned products are fixed in design, have been imported, and have been sufficiently disclosed by respondents during discovery." *Id.* at 23 (citations omitted). The Commission also noted that in a prior opinion, it had affirmed an ID which found that "redesigned products should be

[redacted]

adjudicated where 'the design around products are within the scope of the investigation, have been imported into the United States or sold in the United States, [and] were the subject of extensive discovery as well as testimony during the evidentiary hearing in this investigation.'" *Id.* at 24 (citation omitted); *see id.* at 27 ("sufficiently fixed, have been subject to extensive discovery, and have been imported").

From these discussions in *Two-Way Radio*, I divine a four-factor test as to whether a respondent has met its burden to show the infringement of a redesigned product should be adjudicated. The product must be: (1) within the scope of the investigation, (2) imported, (3) sufficiently fixed in design, and (4) subject to extensive discovery. Of these factors, I find Respondents have not met their burden as to the fourth factor, subject to extensive discovery.

Technically, the issue of whether TTFL12 was subject to extensive discovery is not actually disputed, given that when Glycosyn first attempted to argue this in their initial post-hearing brief, it was struck upon motion by Order No. 38. (*See* Order No. 38 at 3-4.) I understand from the parties' reply briefing that Glycosyn has resurrected this line of argument in its reply brief (CRB at 35-37 (Section II.B.2)), but I disregard this content and do not depend on it in reaching the present finding.

Both Jennewein and the Staff contend that Glycosyn either was aware or should have been aware of the TTFL12 strain on August 21, 2018. (RIB at 66; SIB at 61.) Jennewein cites no evidence to explain why this is (*see* RIB at 66), but the Staff states this date is "when Jennewein produced documents describing that product, including the TTFL12 strain's genotype and construction." (SIB at 61.) To support its assertion, the Staff cites two documents, RX-0320C and RX-0382, which I infer to mean these documents were produced on or before that day. (*See* SIB at 61.)

[redacted]

The first, RX-0320C, is an article authored by certain Jennewein personnel, characterized by Jennewein as a "draft article" (RIB at 67), and which Dr. Jennewein testified was submitted for publication but then withdrawn to protect the information disclosed in it (RX-0385C at Q160-165). The article bears Bates numbers of JENNITC1120_0020176-210. The document discusses Jennewein's strain engineering activities which resulted in [redacted] (RX-0320C at -20177.) [redacted] (*id.* at -20192, -20207).

The second document, RX-0382, is described as a European patent application (RIB at 9 n.2), although it is unclear if the particular copy is the EPO publication of that application or a copy of a Jennewein submission as part of that application process; Dr. Jennewein offered a third explanation, that RX-0382 is the issued patent itself (RX-0385C at Q166-167). In any event, the document bears Bates numbers of JENNITC1120_00006729-85 and discloses a "present invention relat[ing] to a method for producing oligosaccharides comprising a terminal galactose-91->4)-glucose disaccharide." (RX-0382 at -6729.) Importantly, it discloses bacterial strains that intentionally lack β-galactosidase activity as well as bacteria including that activity. (*Id.* at [0084]-[0088]). The document does not appear to refer to any of its embodiments or strains as TTFL12.

In any event, on September 14, 2018, Jennewein complied with its Ground Rule 7.2 obligation to identify those of its products it understood to be within the scope of the Investigation. (*See* RIB at 9 n.2; SIB at 70.) In this mandatory disclosure, CX-0226C, Jennewein provided, in relevant part:

> Pursuant to Ground Rule 7.2.1(2), Jennewein identifies the following processes that are within the scope of the investigation:

[redacted]

. . . .

[redacted]
TTFL12. *See, e.g.*, JENNEITC1120_0020176-JENNITC1120_0020210.

(CX-0226C at 2.) Notably, the production numbers listed here correspond only to the draft article, which is RX-0320C, and not RX-0382.

Six days later, on September 20, 2018, Jennewein amended a response to one of Glycosyn's requests for admission regarding importation (SIB at 33-34). On that day, Jennewein provided the following:

> REQUEST FOR ADMISSION 7:
>
> Admit that Jennewein's strain #1540 is the only strain Jennewein uses to produce the 2'-FL that is imported into the United States.
>
> AMENDED RESPONSE TO REQUEST NO. 7
>
> Jennewein objects to this Request as vague and ambiguous with respect to the terms "uses" and "produce." Subject to its objections, Jennewein responds as follows:
>
> [redacted]

(CX-0216C at 5.) Notably, this response does not mention TTFL12 at all.

The last important discovery date is November 5, 2018, the close of fact discovery, which saw Jennewein provide a final round of discovery responses, CX-0237C. (RRB at 7; SIB at 70.) According to Jennewein, it "plainly disclosed the TTFL12 strain to Glycosyn during discovery, first in its [Ground Rule 7.2 disclosure] and again in its discovery responses on November 5, 2018." (RRB at 7.) The Staff also characterizes that day as when "Jennewein amended its

[redacted]

interrogatory responses to clearly identify the TTFL12 strain." (SIB at 70.) In both of their descriptions, Jennewein and the Staff reference page 2 of CX-0237C, where Jennewein provided the following:

> INTERROGATORY NO. 2:
>
> For each version, commercial name, and internal code name or other unique identifier of Jennewein 2'-FL identified in response to Interrogatory No. 1, identify all corresponding bacterial strains used to produce Jennewein 2'-FL.
>
> RESPONSE TO INTERROGATORY NO. 2
>
> Jennewein objects to this interrogatory as overbroad, unduly burdensome and seeking information not reasonably calculated to lead to the discovery of admissible evidence or not proportional to the needs of this case to the extent that it encompasses products Jennewein does not import commercially into the U.S. or are not the subject of this Investigation, or strains used to produce such products.
>
> Subject to and without waiving general and specific objections, and subject to Jennewein's objections to Interrogatory No. 1, Jennewein responds to this interrogatory as follows: Jennewein identifies the production strain it uses to produce Jennewein 2'-FL for commercial importation into the United States as *E. coli* strain BL21 (DE3) #1540.
>
> FIRST SUPPLEMENTAL RESPONSE TO INTERROGATORY NO. 2 (11/5/18):
>
> Subject to Jennewein's prior objections to Interrogatory No. 22 [sic], Jennewein incorporates by reference its responses to Interrogatories Nos. 29, 59, and 60-61, and further identifies the [redacted] TTFL12, [redacted]

(CX-0237C at 1-2.) Again, November 5, 2018 was the day fact discovery closed.

Thus, on the question of whether Jennewein provided "extensive" or "sufficient" discovery on the TTFL12 strain, I find it did not. Only two documents provide any specific information on TTFL12: the undated "draft" article which describes the development strain and identifies it by name (*see, e.g.*, RX-0320C at -20191, Fig. 1); and the 2014 patent application specification, which

[redacted]

does not refer to TTFL12 by name and simultaneously discusses strains that *could* be TTFL12 (*see* SIB at 74 n.23 (discussing RX-0382 at ¶¶ [0084], [0085])) as well as strains that are definitely not TTFL12 [redacted] (*see id.* (discussing RX-0382 at ¶¶ [0087], [0088])). An accused infringer's own patents (RX-0382 in the case of Jennewein) are generally not considered reliable evidence of an accused product's features in the first place. *See Forest Labs., Inc. v. Abbot Labs.*, 239 F.3d 1305, 1313 (Fed. Cir. 2001). Further, while Jennewein identified TTFL12 as falling under the scope of the investigation in its Ground Rule 7.2 disclosure, and identified the "draft" article, RX-0320C, as evidence of TTFL12's relevant features, it did not identify the patent application such that Glycosyn would have been on notice of it. Thus, in an effort to meet its burden on sufficient discovery, Jennewein has effectively pointed to just one document that Glycosyn could have used—the undated article (RX-0320C).

Moreover, the probative value of that article is low. While Jennewein argues it "includes a complete description of the genetic makeup of the TTFL12 strain; no more is required to conclude that the use of this strain cannot infringe the Asserted Claims" (RIB at 14 n.3), it does not show that any 2'-FL which Glycosyn might accuse of infringement was actually produced in this way. I find it perplexing why there were no other documents produced (or at least identified in Jennewein's briefing as having been produced) and/or identified to Glycosyn during discovery to confirm this basic fact, especially given: (1) the prevalence of batch or fermentation run records in this industry (*see* RIB at 145 ("Jennewein can readily determine the strain used to make any particular lot of 2'-FL. As Dr. Parkot testified, Jennewein can identify the strain used to produce each lot number of 2'-FL within four hours of a request.") (citing Hr'g Tr. at 348:10-21)); (2) the fact that Jennewein seems to have produced its first and only TTFL12 2'-FL during the discovery period of this investigation (RX-0385C at Q170 ("Q: When did Jennewein *start* producing 2'-FL

[redacted]

using the TTFL12 strain?" Dr. Jennewein himself testified, "[w]e performed a fermentation run in the summer of 2018." (emphasis added))); and (3) Jennewein's claim that TFFL12 is so fixed in design that [redacted] (RRB at 4 (citing Hr'g Tr. at 204:15-205:6)). RX-0320C may provide information on the conception of TTFL12, but it does not sufficiently identify and describe a product that could serve as an accused product.

The discovery responses which Jennewein and the Staff point to add little. Again, while TTFL12 was identified on September 14, 2018 as a product alleged to be within the scope of the investigation (CX-0226), the earliest interrogatory responses identified as mentioning TTFL12 are those Jennewein provided on the last day of discovery (CX-0237C at 1-2). Perhaps more important are Jennewein's responses to Glycosyn's request for admission on importation. Here, the request asked Jennewein to admit that #1540 was the only strain they use to produce 2'-FL imported into the U.S. (CX-0216C at 5.) Jennewein had initially answered with reference to just the #1540 strain, but updated that answer to include the [redacted] and then never updated it again. This was done despite Jennewein's *first ever importation* of TTFL12-based 2'-FL on October 11, 2018. (RIB at 11 (citing, *inter alia*, RX-0278C; RX-280C; Hr'g Tr. at 347:6-22).) Then, on the very last day of fact discovery, Jennewein added TTFL12 to its response to an interrogatory asking for simply "all corresponding bacterial strains used to produce Jennewein 2'-FL." (CX-0237C at 1-2.) In total, these responses put Glycosyn on notice of just three things: a strain referred to as TTFL12 exists and was described in an unpublished, undated article [redacted] (CX-0226; CX-0320C); at some point the strain was used to create an unspecified amount of 2'-FL (CX-2037C at 1-2); but that 2'-FL had not been imported into the United States (CX-0216C at 5).

[redacted]

It is the burden of the respondent to provide the "extensive" or "sufficient" discovery on the redesigned product, *Two-Way Radio*, Comm'n Op. at 23, and Jennewein has not met this burden, from either a document production or discovery response perspective. An earnest effort to force TTFL12 into the investigation would have seen Jennewein prove to Glycosyn the nature of TTFL12, and how it had been used to produce imported 2'-FL, *before* the very last day of fact discovery. This was not done, however.

Admittedly, Glycosyn failed to take discovery of its own on this issue (*see* RIB at 9-10, 14, 66; RRB at 2-4) and to respond to Jennewein's own requests for admission on TTFL12 (*see* RIB at 68-69 (citing RX-0317C)). As Jennewein summarizes, "Glycosyn has been hard at work trying to keep this product out of this investigation on procedural grounds." (*Id.* at 9.) Nevertheless, it is Jennewein's burden to introduce TTFL12-based 2'-FL into the case, *Two-Way Radio*, Comm'n Op. at 23, and Jennewein's inaccurate response to Glycosyn's request for admission on importation was more than enough to dissuade Glycosyn from investigating anything other than the #1540 strain during discovery.

Accordingly, I do not find adjudication of whether the TTFL12 strain infringes to be appropriate at this time because the discovery on TTFL12 was not adequate.

2. Direct Infringement by the Jennewein #1540 and [redacted] Strains

Glycosyn has shown by a preponderance of the evidence that the Accused Strains (#1540 and [redacted] meet the limitations of asserted claims 1-3, 5, 8, 10, 12, 18, and 24-28 either literally or under the doctrine of equivalents, and thus, Jennewein directly infringes those claims. Jennewein has not been shown to infringe dependent claim 23.

[redacted]

a. Undisputed Claim Limitations

The parties do not dispute most of the asserted claim limitations of the '018 patent as compared to Jennewein's Accused Strains. (*See, e.g.*, CIB at 33-34; RIB at 18; SIB at 33-36; RRB at 8-41.) Commission Rule 210.31(d) states in relevant part, "[a]ny matter admitted under this section may be conclusively established unless the administrative law judge on motion permits withdrawal or amendment of the admission." 19 C.F.R. § 210.31(d). I agree with Glycosyn that this rule allows me to conclusively find for the purposes of this investigation that the Accused Strains meet each of the claim limitations admitted to in Jennewein's responses to requests for admission (CX-0215C; CX-0216C; CX-0217C), and I do so find. (CIB at 34 (citing CX-0215C at 1-2, 4-7, 8, 39-40; CX-0216C at 1-2, 4-7, 8, 39-40, 25-33, 68, 69; CX-0217C at 72-74).) As to independent claim 1, these limitations include:

> 1. A method for producing a fucosylated oligosaccharide in a bacterium, comprising
>
> providing an isolated *E. coli* bacterium comprising,
>
> (i) a deletion or functional inactivation of an endogenous β-galactosidase gene;
>
> . . . .
>
> (iii) an inactivating mutation in a colanic acid synthesis gene; and
>
> (iv) an exogenous lactose-accepting fucosyltransferase gene;
>
> culturing said bacterium in the presence of lactose; and
>
> retrieving a fucosylated oligosaccharide from said bacterium or from a culture supernatant of said bacterium.

('018 patent at cl. 1.)

With respect to the asserted dependent claims, Jennewein's method of producing 2'-FL practices the additional elements recited in dependent claims 2, 3, 5, 10, 12, 18, and 24-28. (*See* CIB at 63-64 (citations omitted).) The Staff agrees these claim elements are met. (*See* SIB at 57-

[redacted]

60.) Jennewein does not dispute the claims are practiced either, apart from their dependence on independent claim 1. (*See* RIB at 66; RRB at 8-41.)

In light of the evidence identified by Glycosyn and discussed by the Staff, and the lack of a dispute over these claims, I find they are met by Jennewein's Accused Strains. These claims include:

> 2. The method of claim 1, wherein said colanic acid synthesis gene comprises an *E. coli* wcaJ, wzxC, wcaD, wza, wzb, or wzc gene.
>
> 3. The method of claim 2, wherein said colanic acid synthesis gene comprises a wcaJ gene.
>
> . . . .
>
> 5. The method of claim 1, wherein said exogenous lactose-accepting fucosyltransferase gene encodes α(1,2) fucosyltransferase and/or α(1,3) fucosyltransferase.
>
> . . . .
>
> 10. The method of claim 1, wherein said bacterium further comprises a functional lactose permease gene.
>
> . . . .
>
> 12. The method of claim 10, wherein said lactose permease gene comprises an *E. coli* lacY gene.
>
> . . . .
>
> 18. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 5 units.
>
> . . . .
>
> 24. The method of claim 1, wherein said exogenous functional β-galactosidase gene comprises a recombinant β-galactosidase gene engineered to produce a detectable level of β-galactosidase activity that is reduced compared to the level of β-galactosidase activity in a wild-type *E. coli* bacterium.
>
> 25. The method of claim 24, wherein the level of β-galactosidase activity comprises between 0.05 and 5 units.

[redacted]

26. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 4 units.

27. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 3 units.

28. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 2 units.

('018 patent at cls. 2, 3, 5, 10, 12, 18, 24-28.)

b. Disputed Claim 1 Limitation "an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium"

In addition to those undisputed limitations listed above, claim 1 of the '018 patent requires:

(ii) *an exogenous functional B-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type E. coli bacterium*, wherein the level of β-galactosidase activity comprises between 0.05 and 200 units;

('018 patent at cl. 1 (emphasis added).)

For the emphasized portion of this limitation, Glycosyn alleges it is met in the Accused Strains both literally and under the doctrine of equivalents through the strains' use of *lacZα* and *lacZΩ* genes. (CIB at 35, 42.) More specifically, Glycosyn contends that *lacZα* encodes the "LacZα portion" and *lacZΩ* encodes the "LacZΩ portion" "of the full LacZ β-galactosidase enzyme" and thus, together, they "literally comprise a sequence of DNA that encodes β-galactosidase" under the claim construction ordered by Order No. 22. (*See id.* at 35-36.)

I disagree it is literally met. To repeat, the claim recites "a[] . . . functional β-galactosidase gene," which Order 22 construed as "a functional sequence of DNA that encodes β-galactosidase." (Order No. 22 at 29.) This limitation requires "*a* sequence" of DNA that encodes for the enzyme known as β-galactosidase. Jennewein has put forward persuasive evidence that *lacZα* and *lacZΩ* are, in fact, distinct sequences of DNA in which neither by itself comprises the full collection of

[redacted]

nucleotides needed for a β-galactosidase enzyme. (*See, e.g.*, RIB at 26-27 (citing Hr'g Tr. at 435:18-436:6; RX-0386C at Q56, 64-66; RX-0409C at Q329-330; RX-0408C at Q63-64).)

The Staff agrees with Jennewein (*see* SIB at 39) and Glycosyn acknowledges that *lacZα* and *lacZΩ* are distinct: "[i]n other words, β-galactosidase can be encoded by either two sequences of DNA, *i.e.*, *lacZα* and *lacZΩ* genes together, or by a single sequence of DNA, *i.e.*, the *lacZ* gene." (CIB at 37.) Nonetheless, Glycosyn disputes that "a sequence," as used in the ordered construction of "gene," means "that the 'functional sequence of DNA' be a single contiguous sequence within the bacterial genome." (CIB at 38.) Glycosyn offers no evidence in support, however, and I find a plain and ordinary meaning of "sequence" does imply contiguity. Indeed, if "sequence" did not mean a contiguous string of nucleotides (*i.e.*, a contiguous string of DNA), then Glycosyn and its expert would not bother to refer to *lacZα* and *lacZΩ* as separate genes, as they do in the excerpt above and throughout the record. (*See, e.g.*, CIB at 3, 11, 35, 36, 36 n.3, 38, 39, 43, 44, 64, 117; CX-0004C at Q62, 458, 462, 468, 477, 481, 578, 595, 596.)

Accordingly, Jennewein's Accused Strains do not literally infringe "an exogenous functional β-galactosidase gene" because they lack a single sequence of DNA which functions to create a β-galactosidase gene. As Glycosyn's own expert states, Jennewein "uses two shorter, functional sequences of DNA (*lacZα* and *lacZΩ*) which, together, encode β-galactosidase." (CX-0004C at Q475.) The use of such shorter functional sequences, which encode for enzyme fragments, is called α-complementation. (RX-0011 at -14798 ("[t]his complementation involves noncovalent reassociation of complementary fragments of the β-galactosidase subunit polypeptide chain, which then reassemble into an enzymatically active tetrameric structure.").)

Glycosyn also argues, however, that Jennewein's *lacZα* and *lacZΩ* meet "an exogenous functional β-galactosidase gene" under the doctrine of equivalents function-way-result test. (CIB

[redacted]

at 42.) Its expert testified that Jennewein's use of "two shorter, functional sequences" as compared to "one long, functional sequence" "is a quintessential example of 'equivalence,' because in both cases a functional β-galactosidase enzyme, with a low level of activity, is obtained." (CX-0004C at Q475.) To understand why Glycosyn's expert is correct, it is helpful to break the analysis into two parts: (1) "a[] . . . functional β-galactosidase gene"; and (2) "exogenous."

Regarding "a[] . . . functional β-galactosidase gene," the term was construed in Order 22 as "a functional sequence of DNA that encodes β-galactosidase." (Order 22 at 29.) As for function and result, there is no difference between the combination of *lacZα* and *lacZΩ* genes on the one hand, and any particular individual "functional β-galactosidase gene" on the other. The function and result of the "functional β-galactosidase gene" are baked right into its name—to provide expressible DNA which, when expressed through understood pathways, results in the creation of a β-galactosidase enzyme:

> Also described herein are bacterial host cells with the ability to accumulate a intracellular lactose pool while simultaneously possessing low, functional levels of cytoplasmic β-galactosidase activity, for example as provided by the introduction of a functional recombinant *E. coli* lacZ gene, or by a β-galactosidase gene from any of a number of other organisms (*e.g.*, the lac4 gene of Kluyveromyces lactis (*e.g.*, GenBank Accession Number M84410 (GI:173304), incorporated herein by reference).

(*See, e.g.*, '018 patent at 7:22-30.) Nowhere in this claim element is there any limit on: the amount or type of DNA; the location of the DNA in the genome; the amount or type of peptides expressed from that DNA; or the nature or way those peptides assemble into β-galactosidase.

Similarly, the function and result of the *lacZα* and *lacZΩ* genes is also the provision of DNA which, when expressed, results in the creation of a β-galactosidase enzyme. This function and result are communicated clearly in Jennewein's submission to the U.S. Food and Drug Administration (the "GRAS notice") for the #1540 strain. (*See* CX-0240C at -6804 (describing insertion of *lacZα* and *lacZΩ* "for the degradation of excess lactose"), -6805 ("Verification of *lacZ*

integrations and β-galactosidase activity"), -6806 ("The clones having the *lacZ* omega fragment integrated were analyzed for 2'-FL productivity and LacZ activity"), -6807 ("Clones showing β-galactosidase activity at 42°C but not at 30°C were selected for further modifications."); *see also* RX-0387C at Q77-78.)

And the way the result is achieved is substantially the same as claimed. Inasmuch as the "way" analysis focuses on gene expression, that is, the role of the "functional β-galactosidase gene," the claim term imposes no limits on the way the result is achieved apart from the basic process applicable to all DNA—the gene is transcribed and translated, resulting in peptides which, through folding and/or combination with one another, become the β-galactosidase enzyme. (*See* CX-0004C at Q53-54, 60 (discussing gene expression basics); RX-0384C at Q103-114 (discussing same); RX-0386C at Q93-97.) The evidence shows that this universal process also applies to *lacZα* and *lacZΩ* in the Accused Strains such that when these genes are expressed (*i.e.*, transcribed and translated), the peptides necessary to eventually become the β-galactosidase enzyme are created. (*See, e.g.*, CX-0004C at Q62, 468, 475-481; CDX-0032; RX-0384C at Q149-151; RDX-0005; RX-0386C at Q90, 94, 98, 102; RX-0387C at Q77-78; RX-0409C at Q21-24, 252; Hr'g Tr. at 435:5-14, 523:15-524:14, 615:16-25.) Inasmuch as the "way" analysis focuses on genome structure, because the first step in the method of claim 1 is "providing an isolated *E. coli* bacterium" possessing "a . . . functional β-galactosidase gene," the evidence shows that α-complementation was well-known in the art. (Hr'g Tr. at 265:5-16, 664:6-7.) Persons of ordinary skill would have known that using *lacZα* and *lacZΩ* as the relevant structure, instead of a single gene, would have been effective, albeit "overcomplicated." (Hr'g Tr. at 265:17-266:1, 664:6-7.)

I am not persuaded by Dr. Stephanopoulos' (Jennewein's expert) testimony on this point. His witness statement cites three basic differences between the claimed invention and the use of

[redacted]

lacZα and *lacZΩ*: (1) the two gene fragments were inserted at different times and in different genome locations; (2) assembling a β-galactosidase enzyme using *lacZα* and *lacZΩ* involves a process with more steps than assembling it after a single gene is expressed; and (3) the two gene fragments are temperature dependent, that is, there is no expression unless temperature conditions are satisfied. (RX-0409C at Q332-335.) The first two differences are seemingly foreseeable aspects of employing α-complementation, so these differences are not substantial. (*See* CX-0004C at Q477.) As for the third difference, Dr. Stephanopoulos points out that "Jennewein's [*lacZΩ*] is under temperature-sensitive repression CI857," which allows for temperature control of expression of the *lacZΩ* fragment. (*See* RX-0409C at Q335.) But as Dr. Prather (Glycosyn's expert) explains, CI857 is a protein added to the Accused Strains, and one which is not always effective. (Hr'g Tr. at 540:3-18, 543:21-23.) That is, when the CI857 is not present, or when it "leaks," expression of the *lacZα* and *lacZΩ* will not be temperature-dependent. (*Id.* at 540:15-18.) And because CI857 is apparently not a part of either the *lacZα* or *lacZΩ* gene fragments themselves, temperature-dependence has nothing to do with "providing . . . a . . . functional β-galactosidase gene," and it is therefore not a substantial difference between the way claim 1 of the '018 patent achieves its result and the way the Accused Strains do. (RX-0407C at Q26-28 ("A temperature-sensitive repressor is another genetic regulatory element that represses expression of a gene.").)

Jennewein makes two further arguments against equivalence. First, Jennewein argues its production process is such that [redacted] (RRB at 19.) Jennewein reasons that "[s]ince all parties admit *lacZΩ* is required to produce β-galactosidase, Jennewein's process cannot be equivalent to the claims." (*Id.*) I do not agree. Claim 1 covers a

[redacted]

method for producing a fucosylated oligosaccharide in a bacterium, comprising three overall steps: (1) providing a bacterium having certain characteristics; (2) culturing the bacterium in the presence of lactose; and (3) retrieving, in this case, 2'-FL. ('018 patent at cl. 1.) The claim limitation at issue here falls under the first step, requiring that the bacterium have a particular characteristic, namely, a functional β-galactosidase gene. (*Id.*) Jennewein's argument is about how the bacterium is cultured to produce 2'-FL, which falls under the second step. (*Id.*) How Jennewein cultures a bacterium has no bearing on whether the bacterium possesses a functional β-galactosidase gene. The combination of *lacZα* or *lacZΩ* is unquestionably functional—the fragments serve no other purpose except to produce β-galactosidase. (CX-0004C at Q481 ("That is their only function.").) That they can be repressed under certain conditions does not affect whether they are functional, and, similarly, [redacted] does not affect whether an equivalent to the claimed gene is present within the Accused Strains. (Hr'g Tr. at 631:3-6 ("Q. Is it fair to say that in your view, the [*lacZα* and *lacZΩ*] fragments are functional genes, they're just not beta-galactosidase genes? A. Correct.").) Jennewein's temperature-induced trigger is therefore irrelevant.

Second, Jennewein argues against equivalence because *lacZα* and *lacZΩ* were known to the '018 patent inventors, but they "chose not to disclose it in their patent or claim this foreseeable element as a form of β-galactosidase gene" [redacted] (RRB at 19 (citing Hr'g Tr. 94:12-15, 265:17-266:1; JX-0022C at 122:11-14).) Jennewein reasons "[t]hus, α-complementation cannot be equivalent to a normal β-galactosidase gene." (*Id.* (citing *Forest Labs.*, 239 F.3d at 1313).) Again, I do not agree, primarily because I do not see a connection between this supposed choice of the inventors and the function-way-result test. Moreover, to the extent inventor Dr. Massimo Merighi testified α-

[redacted]

complementation "seems like an overcomplication," he also testified moments later that "[b]ut alpha complementation [gives you] a functional beta-galactosidase polypeptide. So under that interpretation, yeah, we talk about it because the whole engineering we did was try to make a functional beta-galactosidase polypeptide inside a strain." (Hr'g Tr. at 266:5-11.)

Accordingly, the *lacZα* and *lacZΩ* genes in Jennewein's Accused Strains are equivalent to "a[] . . . functional β-galactosidase gene." *See Ajinomoto Co., Inc. v. Int'l Trade Comm'n*, Nos. 2018-1590, -1629, -- F.3d --, 2019 WL 3558560 at *9-10 (Fed. Cir. Aug. 6, 2019) (holding substantial evidence supported finding equivalence between two proteins exporting same aromatic compounds, consisting of 85-95% identical structure, and resulting in increased production of same L-tryptophan).

I also find the *lacZα* and *lacZΩ* genes are equivalent to "an *exogenous* functional β-galactosidase gene." Jennewein advances two arguments on this issue. First, it argues that "[n]either *lacZα* nor *lacZΩ* encodes for or can produce a functional β-galactosidase enzyme or β-galactosidase activity when exogenous, or outside of, the production strain." (RIB at 32 (citing RX-0409C at Q255).) But in the *Markman* process, the parties agreed to a construction of "exogenous" as "originating outside an organism, tissue, or cell." (Order 22 at 12.) Whether or not a gene, like *lacZα* and *lacZΩ* individually, can produce β-galactosidase activity outside of the production strain is irrelevant to where a gene "originated."

Jennewein secondly argues that because the *lacZα* in the Accused Strains was not added by Jennewein, but was present in the original BL21 (DE3) strain which Jennewein engineered to achieve the Accused Strains, the "exogenous" limitation is not literally present in those strains. (RIB at 32-33.) However, *lacZΩ* was not originally in strain 1540, but was added during the strain's development, and it is therefore exogenous. (CX-0213 at Fig. 2, -5158 ("Strain 1540 was

[redacted]

derived from its parental strain 1242 by integrating a heat inducible lacZΩ gene fragment . . . .").) Because *lacZα* and *lacZΩ* together are equivalent to "a[] . . . functional β-galactosidase gene," the exogenous nature of *lacZΩ* is enough to meet the limitation. It is the combination of *lacZα* and *lacZΩ* which is equivalent to the claimed "β-galactosidase gene," and this combination does not exist until *lacZΩ* is inserted into the bacterium's genome from outside the organism. Therefore, the combination is "exogenous" and satisfies the claim limitation at least under the doctrine of equivalents, whether or not the *lacZα* alone is literally endogenous or exogenous.

Accordingly, I find the *lacZα* and *lacZΩ* genes in Jennewein's Accused Strains are equivalent to "an exogenous functional β-galactosidase gene."

c. Disputed Claim 1 Limitation "wherein the level of β-galactosidase activity comprises between 0.05 and 200 units"

In addition to those undisputed limitations listed above, claim 1 of the '018 patent requires:

> (ii) an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium, *wherein the level of β-galactosidase activity comprises between 0.05 and 200 units*;

('018 patent at cl. 1 (emphasis added).)

For this limitation, "wherein the level of β-galactosidase activity comprises between 0.05 and 200 units," Order 22 clarified that the term is not indefinite and means "β-galactosidase activity is measurable at between exactly 0.05 and exactly [200/5/4/3/2] Miller Units, as defined in Miller, J.H., Experiments in Molecular Genetics (Cold Spring Harbor Lab. 1972) at 352-355." (Order 22 at 22-23.) Thus, regardless of whether the Miller protocol is scientifically sound or reliable (*see* RIB at 41 (citing RX-0008)), it is *the* test to be used to determine if a bacterium falls within the scope of the claims. Glycosyn provides a rough summary of the Miller protocol as follows:

[redacted]

> (1) taking a sample from a culture of growing cells, (2) "permeabilizing" the cells, (3) incubating the permeablized cells with a chemical compound known as ONPG (a colorless compound which is specifically recognized and cleaved by β-galactosidase to yield a yellow product), and (4) measuring with a spectrophotometer the amount of yellow color that develops over a known period of time.
>
> The values recorded by the spectrophotometer are then entered into a mathematical equation to yield the level of β-galactosidase activity in "Miller units."

(CIB at 48-49 (citing CX-0251; Hr'g Tr. at 315:19-318:12).)

Upon a review of the parties' testing methods, it is clear Jennewein's (both that which it conducted itself and hired third-party Battelle to perform) diverges further from the Miller protocol than Glycosyn's. Jennewein's methods are therefore less reliable evidence on whether Jennewein "provides" an "*E. coli* bacterium" which "comprises" Miller Unit activity within the claimed range. ('018 patent at cl. 1.)

Considering Glycosyn bears the burden on this issue, I begin with its testing and Jennewein's criticisms thereof. Many of these criticisms are not rooted in a failure to follow the Miller protocol, however, but rather a failure to: (1) perform additional steps Jennewein deems necessary or appropriate to properly identify exactly that amount of Miller Unit activity is attributable to what would be the "functional β-galactosidase gene" (*i.e.*, the combination of *lacZα* and *lacZΩ*) in the strain (*see* RIB at 38-39; RRB at 20-21, 24-27, 29); or (2) perform testing that reflects Jennewein's actual manufacturing process (*see* RIB at 38, 50, 54-55; RRB at 21-23, 28).

Starting with the issue of Jennewein's manufacturing process, Jennewein alleges Glycosyn improperly: tested with shaker flasks; did not culture the strains in the presence of lactose; [redacted] (RIB at 54-55 (citations omitted); *see* RRB at 28.) These criticisms are misplaced. The test is not whether Jennewein's

[redacted]

accused strains exhibit the Miller Unit activity level during Jennewein's production process, but whether Jennewein "provides" an "*E. coli* bacterium" which "comprises" Miller Unit activity within the claimed range when put through the procedures outlined in Miller. ('018 patent at cl. 1; Order 22 at 22-23.) In other words, Jennewein's manufacturing process could involve chilling the *E. coli* to 10°C or boiling to 100°C, for 10 minutes or 10 hours, and any other number of variations, but that would not bear on whether the *E. coli* which Jennewein "provides" to its process exhibits Miller Unit activity within the claimed range when put through Miller's protocol.

Jennewein also complains that the Miller protocol is simply unreliable on its face and "insufficient to prove infringement." (*See* RIB at 41 ("A paper by Giacomini shows that, even following Miller's methods, Miller Units varied wildly. . . . This variability means that the Miller assay is not reliable proof of infringement, particularly at very low levels near the limit of the assay's detection."), 53-54 (citing, *inter alia*, RX-0409C at Q196; RX-0008; RX-0037); *see also* RIB at 19 (citing *Apotex, Inc. v. Cephalon, Inc.*, No. 2:06-cv-2768, 2012 WL 1080148 at *11-12 (E.D. Pa. Mar. 28, 2012)).) This complaint is beside the point. The U.S. Patent and Trademark Office issued claims to Glycosyn which expressly define the invention's scope in terms of Miller Units customized by the Miller protocol. Thus, reliable or not, it is the test to be used—a point Jennewein concedes in other portions of its brief. (*See* RIB at 49 ("Third, Glycosyn failed to follow Miller in performing its testing, and its test results are thus unreliable.").) I also agree with the Staff that any complaint over unreliability in defining an invention by reference to Miller Units is effectively an indefiniteness argument that was not included in Jennewein's pre-hearing brief and is therefore waived. (SRB at 8-9 n.3.)

Jennewein makes two other unpersuasive arguments regarding the Miller protocol. First, Jennewein argues Glycosyn's results vary "significantly" (RIB at 53) or "much more . . . than other

[redacted]

testing" (*id.* at 55-56) such that they have a lack of reproducibility leading to unreliability. The argument is largely conclusory, however, offering no discussion of Glycosyn's results or why their variance is "significant[]." (RIB at 53 (citing Hr'g Tr. at 505:1-15 (discussing general importance of reproducibility)).) Based on my own review of the data, I do not find Glycosyn's results vary meaningfully more than Jennewein's. (*Compare* CX-0258C *with* CX-0292C *with* CX-0294C.) Second, Jennewein argues Glycosyn failed to subtract Miller Unit levels associated with *ΔlacZ* or *lacZ*⁻ control strains. (*See, e.g.*, RIB at 50-52.) This step is indisputably not found in Miller (*see generally* CX-0251), and, for reasons discussed further below, I do not find it has been shown to be necessary or even appropriate.

Finally, of all the criticisms Jennewein lodges against Glycosyn's testing, only two are based in a deviation from the Miller protocol: (1) Glycosyn failed to test with toluene in addition to SDS/chloroform (RIB at 56 (citing RX-0409C at Q214-216; RX-0408C at Q125; RX-0008; Hr'g Tr. at 509:4-16); and (2) Glycosyn failed to test at longer incubation times than 60 and 120 minutes (*id.* at 56-57 (citing RX-0409C at Q218; RX-0408C at Q113, 114, 139; Hr'g Tr. at 307:8-308:25, 309:7-16).) On the first, Miller teaches use of toluene and SDS/chloroform as alternative techniques. (CX-0251 at -1810, -1812.) Therefore, using one technique but not the other does not render testing unreliable. On the second, it was not wrong for Glycosyn to fail to test at "extended incubation times," because Miller does not specify a reaction time. Miller instead states "[s]top the reaction by adding 0.5 ml of a [stop solution] after sufficient yellow color has developed." (CX-0251 at -1810.) Glycosyn's expert persuasively testified that sampling should occur while the reactions are linear (a point reinforced by Miller (CX-0251 at -1809)) and she confirmed that, for her experimental assays, 60-minute incubations gave a sufficient amount of visible yellow color, and times after that no longer represented linear reactions. (CX-0004C at Q502.)

[redacted]

Turning now to Glycosyn's criticisms of Jennewein's testing, I find these have more merit, but to varied effect. For example, a primary dispute in this investigation is whether Jennewein's additional step of subtracting a *ΔlacZ* or *lacZ*⁻ control strain's Miller Units from each accused sample's measured Miller Units is necessary—a step performed in Jennewein's own testing and that of third-party Battelle. Jennewein argues this step "is not only appropriate, but necessary" (RIB at 39) to correct for any agent within the strain that causes "enzymatic cleavage of ONPG by other enzymes besides β-galactosidase" (RX-0409C at Q99).[3]

Jennewein's point is seemingly scientifically valid, but the fact of the matter is that the Miller protocol does not include this step. (*See generally* CX-0251.) Further, the record does not identify any such "other enzyme[] besides β-galactosidase," let alone one present in Jennewein's [redacted] and #1540 strains. (*See* RIB at 41, 43, 45, 52-54, 60, 104; RRB at 21-23, 28, 30.) Given the supposed importance of this control step, Jennewein's expert's immense metabolic engineering experience (RX-0384C at Q9-40), and the well-studied properties of *E. coli*, I do not understand how this agent was not identified. Indeed, when pressed, both parties' experts testified they were unaware of such substances. (Hr'g Tr. at 454:9-23, 680:3-10.)

And in many cases, Jennewein's subtraction resulted in *negative* Miller Unit levels for an accused sample. The Staff presents one such instance taken from Jennewein's in-house testing:

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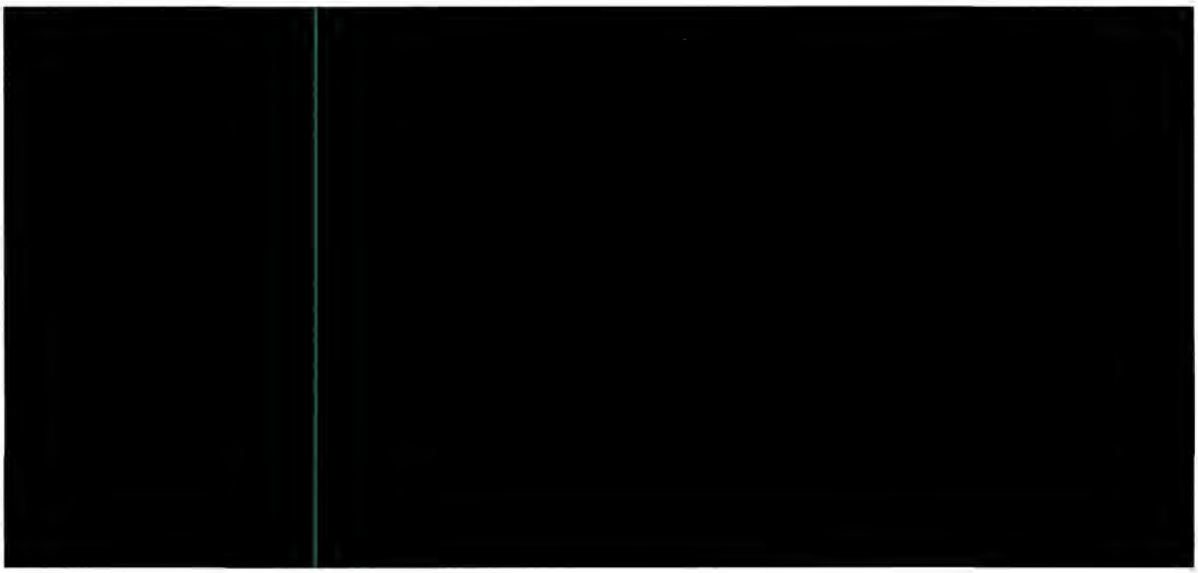
[3] Other sources of "background noise" Jennewein's expert identifies (RX-0409C at Q96-99; RDX-0013) are understood to be controlled for by techniques already disclosed in Miller itself (*see* CX-0251 at -1810-11 (describing 550 nm optical reading or centrifugation to correct for cell debris affecting 420 nm light reading); -1811 (describing Z buffer with no cells to correct for spontaneous splitting of ONPG)) or otherwise implemented in Jennewein's testing (RIB at 43 (describing washing for fermentation media), 52 (describing time=0 reading for spontaneous ONPG hydrolysis)).

[redacted]



(SIB at 51 (showing excerpt of RX-0029C); *see* RX-0029C (columns "O" and "P" at various worksheets).) There are negative results in Battelle's data as well:

(CX-0294C; *see generally* CX-0294C (columns "P" and "R"); CX-0292C (columns "P" and "R").)

These negative values in particular should have put Jennewein on notice that its negative control technique was unreliable on its face, or implemented unreliably, or some other assumption was incorrect. (*See* CIB at 55-56 [redacted] The

[redacted]

Staff notes that the Battelle scientist involved in the testing testified that such negative values "would correspond, correlate to a zero value," but, in the Staff's view, it is really "an impossible result." (SIB at 51 n.16 (citing Hr'g Tr. at 327:4-19).) I agree with the Staff.

I also find the scientist's explanation unacceptable given other evidence in the record that Jennewein may have chosen its [redacted] control strain over alternatives because of the effect it would have on infringement testing. The following email was produced during discovery (*see* Order No. 30) in which testing protocols were discussed between Jennewein personnel and a third party in the context of whether a "0.05" value would be met:

[redacted]

. . . .

Regarding the Miller assay:

[redacted]

(CX-0422C at -0306730-1; *see* CX-0004C at Q534-538; SIB at 53.) It is likely that the "0.05" value is the bottom of the claimed range "0.05 to 200 units," that is, Jennewein sought a control strain that would minimize the measured Miller Units. ('018 patent at cl. 1.)

Moreover, of the two testifying experts who offered contrasting opinions on whether negative control strain subtraction is necessary (*see, e.g.*, CX-0004C at Q534, 539; RX-0409C at 92-101, 196-201), Jennewein's expert was shown to have a significant lack of experience and familiarity with Miller testing prior to this litigation (*see* CIB at 57-59 (citing, *inter alia*, Hr'g Tr.

[redacted]

at 582:8-604:18)), while Glycosyn's expert has "performed the Miller assay many times [as] a graduate student [and] was able to reference my notes on those assays, which assisted me in my review of the documents in this investigation" (CX-0004C at Q86). I therefore assign Jennewein's expert's testimony less weight on this issue.

For at least these reasons, subtraction of a negative control strain was inappropriate for the purposes of determining infringement of "wherein the level of β-galactosidase activity comprises between 0.05 and 200 units." Nevertheless, Jennewein's data clearly shows the Miller Unit levels prior to the subtraction, so the reliability of Jennewein's testing can be assessed without reference to the negative control strain.

Two of Glycosyn's other critiques call that reliability into question. The first involves Jennewein's exclusive reliance on Miller Unit sampling at no less than 120 minute reaction times. (*See* RX-0388C at Q99 (Battelle testing); RX-0386 at Q220 (Jennewein in-house testing); RX-0408C at Q113 (Jennewein in-house testing); *see, e.g.*, RX-0292C (Battelle testing); CX-0294C (Battelle testing); RX-0029C (Jennewein in-house testing); CX-0275C; *see also* CIB at 56-57.) Jennewein justifies its choice "because it was authorized by Miller and Jennewein believed it needed to incubate its strains for a minimum of 120 minutes to obtain interpretable results in the Miller assay." (RRB at 31 (citing RX-0408C at Q113).) More specifically, Jennewein states "incubation time should be extended if the yellow color develops slowly, which would be expected for low-level β-galactosidase activity, such as near 0.05 Miller Units." (RIB at 56 (citing RX-0409C at Q218; Hr'g Tr. at 307:8-308:25, 309:7-16).) Yet, testimony from the Battelle scientist who performed the experiments indicates Jennewein instructed her to measure at 120 min without regard to how color was developing in the samples. (Hr'g Tr. at 318:17-320:6 ("Jennewein

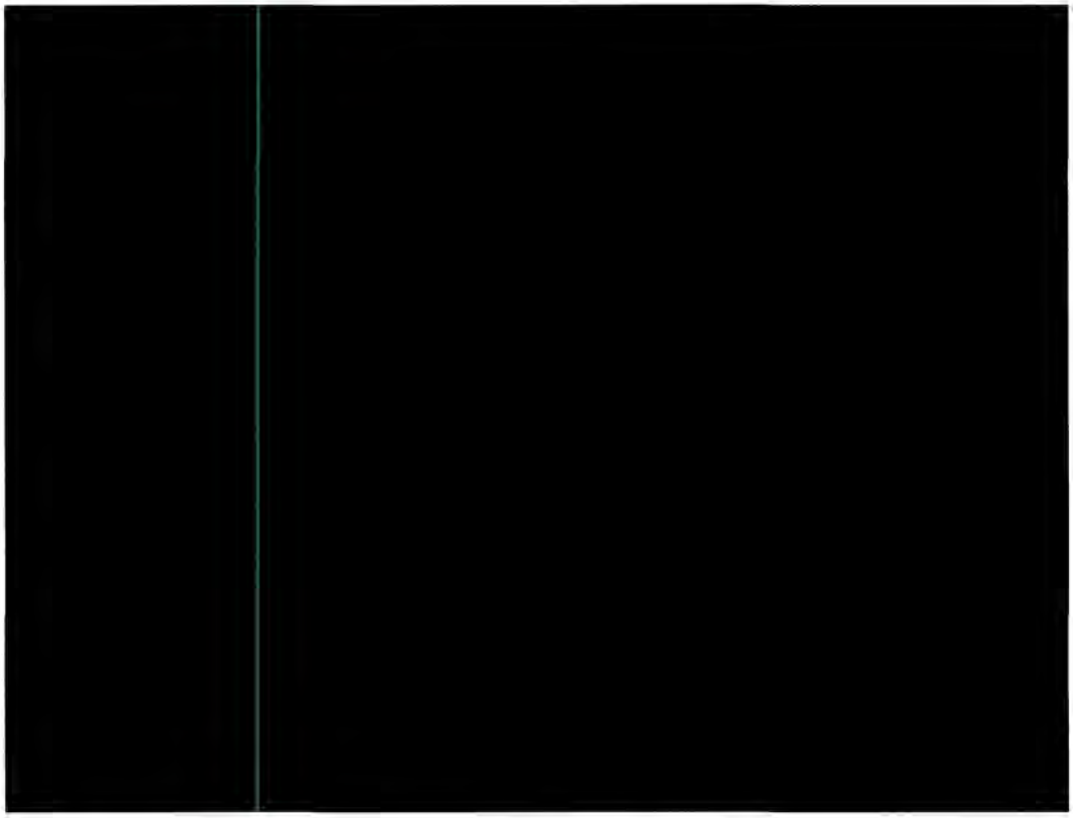
[redacted]

provided a protocol to me that I followed, and it was consistent with the Miller assay. So yes, that is what I did.").)

This is problematic because in Order 22, the presiding ALJ determined that "wherein the level of β-galactosidase activity comprises between 0.05 and 200 units" was not shown to be indefinite because the patent failed to identify for how long the activity level must be maintained or when it must be measured. (Order 22 at 21-22.) Order 22 concluded, "the claim is not ambiguous as to when the claimed activity range must be met—it need only be met at some point in time." (*Id.* at 22 (citation omitted).) Given this flexibility in the temporal scope of the claim, and Miller's instruction that the reaction should be stopped "after sufficient yellow color has developed" (CX-0251 at -1810), Jennewein's justification for its minimum 120 minute sample rings hollow.

Moreover, the evidence shows it likely would have made a difference to take a sample at an earlier time. In a chart Jennewein prominently presents as summarizing the highest Miller unit values third-party Battelle recorded (CX-0291C), a trend of decreasing Miller unit activity levels with respect to time is visible:

[redacted]



(CX-0291C at -308410; *see* RIB at 44.) Given this trend, Miller's instruction to stop the reaction when sufficient color is present, and the breadth of the claim term, it would seem readings at less than 120 minutes are required in order to ascertain if the activity falls within the range. (*See, e.g.*, CX-0004C at Q502, 513.) Indeed, the same Battelle scientist acknowledged a time less than 120 minutes would have been advisable:

> Q. And at your deposition, you testified that you probably should have done an OD420 nanometer reading for a time period less than 120 minutes; correct?
>
> A. I did, but due to time constraints while I was at their facility, I did not perform those – those steps. But what I did perform was consistent with what's described in the Miller assay, along with what's in the Jennewein protocol.
>
> Q. But you did testify that you probably should have measured a time point of less than 120 minutes; correct?
>
> A. Yes, I did.

[redacted]

(Hr'g Tr. at 320:17-321:3.) Glycosyn's test results support this conclusion. When it sampled at both 60 and 120 minutes, Miller Unit levels decreased over time. (*See* CX-0004C at Q503-504; CX-0258C; CX-0203C at CX-0203C.0004.) Glycosyn has also shown that in an earlier testing session, when Jennewein did sample at times less than 120 minutes, Miller Units within the claimed range were found. (CIB at 57 (citing CX-0241C; CX-0271C); *see* RX-0408C at Q101-106.) Unlike the negative control strain subtraction discussed above, the effect on Miller Unit activity resulting from measuring only at times after 120 minutes cannot be undone. The reliability of this testing is therefore diminished.

Glycosyn's second critique of Jennewein's testing is that Jennewein improperly took an initial OD420 nm (yellow light) reading before the ONPG reaction begun, and subtracted that reading from the OD420 nm reading taken at the 120 minute or greater sampling time. This is described in the briefs as the "time=0" or "t=0" reading. This step is clearly not found in Miller (*see generally* CX-0251), yet Jennewein describes its use as "to correct[] for the absorbance before β-galactosidase activity could start, which was at the t=0 time point." (RIB at 43 (citing CX-0388C at Q115, 120), 52, 52 n.11 (citing Hr'g Tr. at 592:18-22, 593:6-11; RX-0386C at Q202)). More specifically, Jennewein contends it is necessary to account for non-enzymatic hydrolysis of ONPG (*i.e.*, spontaneous ONPG hydrolysis). (RIB at 52-53 (citing Hr'g Tr. at 557:3-7), 45 (citing RX-0409C at Q98-99; Hr'g Tr. at 455:7-16, 559:9-13); RRB at 23 (citing, *inter alia*, RX-0385C at Q181-184).)

Setting aside whether this technique accurately controls for non-enzymatic (*i.e.*, spontaneous) hydrolysis of ONPG, it introduced significant effects into the results. Namely, this subtraction caused *negative* values of Miller Units in some circumstances even before the negative control strain values were considered (*see* CX-0292C at Column "O"; CX-0294C at Column "O";

RX-029C at Column "O"), and in other circumstances, greatly diminished the OD420 nm value that serves in the numerator position of the Miller equation:

$$\text{Units} = 1000 \times \frac{OD_{420} - 1.75 \times OD_{550}}{t \times v \times OD_{600}}$$

OD_{420} and OD_{550} are read from the reaction mixture,
OD_{600} reflects the cell density just before assay,
t = time of the reaction in minutes,
v = volume of culture used in the assay, in ml.

(CX-0251 at -1811; *see* CX-0292C at Columns "H" and "J"; CX-0294C at Columns "H" and "J"; RX-0029C at Columns "I" and "J".) The effect of this "control" is clear—Miller Unit values will decrease—and while Jennewein's records make it possible to undo this subtraction, I decline to wade through the dozens of samples to do so. The fact remains this step is not in Miller and greatly affected the results.

To the extent Jennewein argues its time=0 subtraction is effectively the same as Miller's ONPG hydrolysis control (CX-0251 at -1811), I find it is not. Miller teaches that correction for ONPG hydrolysis is only needed if the reaction runs for extended periods, like overnight, and should be measured via a blank with no cells. (*See* CRB at 17-18; CX-0251 at -1811.) Clearly, Jennewein's 120 minute samples and time=0 readings on samples with cells do not meet these criteria.

Taken altogether, there is insufficient reason to discount or view as wholly unreliable Glycosyn's testing of the Accused Strains, but there is such reason to discount Jennewein's. Apart from reliability concerns, Glycosyn's testing simply hewed more closely to the Miller protocol, *i.e.*, the terms in which the invention is defined. The Staff takes the position that Glycosyn's testing is therefore more relevant for infringement analysis purposes (SIB at 56), and I agree. That

[redacted]

testing showed a large majority of samples exhibiting Miller Unit activities within the claimed range. (*See* CX-0004C at Q504-505; CX-0258C; *see also* CX-0004C at Q516, 527; CX-0241C.) It is therefore more likely than not that Jennewein's Accused Strains meet the limitation "wherein the level of β-galactosidase activity comprises between 0.05 and 200 units" as in claim 1. It is also more likely than not that Jennewein's Accused Strains infringe claim 1 of the '018 patent.

d. Disputed Claim 8 "the method of claim 1, wherein said exogenous functional β-galactosidase gene comprises an *E. coli* lacZ gene"

Dependent claim 8 of the '018 patent requires:

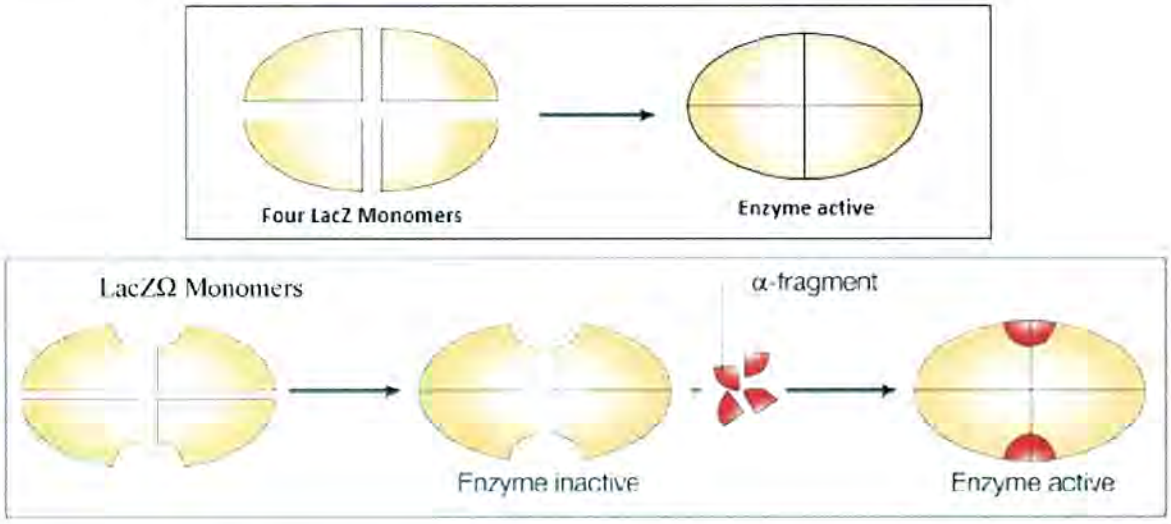
> The method of claim 1, wherein said exogenous functional β-galactosidase gene comprises an *E. coli lacZ* gene.

('018 patent at cl. 8.)

For this claim, which depends from independent claim 1 and adds further narrowing detail to the "exogenous functional β-galactosidase gene" recited therein, Glycosyn alleges it is met by Jennewein's Accused Strains both literally and through the doctrine of equivalents. (CIB at 64-65.) Jennewein's *lacZα* and *lacZΩ* genes are neither individually nor collectively a "functional β-galactosidase gene" in the literal sense, so they are also not literally "an *E. coli lacZ* gene," despite Jennewein's GRAS notice describing *lacZα* and *lacZΩ* as "originating from *E. coli* K12 DH5α." (CIB at 64 (citing CX-0213) (emphasis removed).) Therefore, claim 8 is not literally infringed.

Regarding doctrine of equivalents, the function and result of the '018 patent's "*E. coli lacZ* gene" is no different than the function and result of the "functional β-galactosidase gene" of claim 1—namely, to provide expressible DNA which, when expressed through understood pathways, results in the creation of a β-galactosidase enzyme. (*See, e.g.*, '018 patent at 7:22-30.) To be sure, the "way" the shared result is achieved is more specific in the "*E. coli lacZ* gene" than the more generic "functional β-galactosidase gene" of claim 1. The parties are in agreement as to the

technical details of this process, however; and those details are best explained with the following joint demonstrative:



(CDX-0032; RDX-0005 (excerpted); *see* CX-0004C at Q62; RX-0384C at Q149-151; *see also* SIB at 7-8.) In this figure, and as explained by both experts, the upper box is a depiction of how four LacZ peptides (*i.e.*, monomers), produced from the naturally occurring "*E. coli lacZ* gene" spontaneously fold and combine into the tetramer (*i.e.*, four monomers) or homeotetramer (*i.e.*, four identical monomers) which is the β-galactosidase enzyme. (CX-0004C at Q54, 62; RX-0384C at Q98, 109, 150.) Similarly agreed to, the lower box is a depiction of how four LacZΩ peptides, produced from the *lacZΩ* gene, and four LacZα peptides, produced from the *lacZα* gene, spontaneously combine into the β-galactosidase homeotetramer. (CX-0004C at Q62; RX-0384C at Q150-151.) As shown, the LacZΩ and LacZα peptides complement each other so as to result in a structure similar to a LacZ peptide, with spontaneous assembly into β-galactosidase.

Jennewein's expert nonetheless asserts that due to nucleotide differences between the combination of *lacZα* and *lacZΩ* and *lacZ*, "combining LacZα and LacZΩ leads to a heterodimeric enzyme that differs from wild-type LacZ." (RX-0384C at Q157; *see* Hr'g Tr. at 565:1-3.) In fact,

however, four of those heterodimers spontaneously combine to form the complete LacZ. Indeed, an article cited by Jennewein's expert (albeit on the written description issue) describes the structure produced by α-complementation as "tetrameric," rather than dimeric. (RX-0011 at -14798 ("[t]his complementation involves noncovalent reassociation of complementary fragments of the β-galactosidase subunit polypeptide chain, which then reassemble into an enzymatically active tetrameric structure.").) That is, with *lacZ* the β-galactosidase result starts with four subunits, and with *lacZα* and *lacZΩ* the β-galactosidase result starts with eight subunits; this is not a substantial difference. And the various peptides are otherwise created in substantially the same way—amino acids produced by the two step process of DNA transcription and translation.

Jennewein additionally emphasizes how *lacZα* and *lacZΩ* are not simply chopped portions of *lacZ*, and include their own start codons, stop codons, promoters, and other regulatory elements (RIB at 33-37; RRB at 18, 38-39), as well as how the LacZα and LacZΩ peptide combination are not "contiguous" or bonded in the same way as LacZ monomers are (RRB at 17-18). These structural differences are undisputed, but all they show is that the limitation is not literally met, as opposed to a substantial difference in function (supply necessary DNA), way (create spontaneously folding and combining proteins), or result (a β-galactosidase enzyme). (*See* Hr'g Tr. at 221:20-222:7 ("Q. . . . Why do you use two fragments? A. . . . the fact is that the lacZ gene cannot be completely regulated by itself in the E. coli – in E. coli, unfortunately. That is [why] we're talking about the full length gene here. And if you cut the gene into several fragments, then this improves its ability to be regulated. . . . that also enhances – lowers the stability of the protein, which is also advantageous.").)

[redacted]

Accordingly, I find the *lacZα* and *lacZΩ* genes in Jennewein's Accused Strains are equivalent to the "*E. coli lacZ* gene" of claim 8. Thus, the Accused Strains infringe claim 8 of the '018 patent.

e. Disputed Claim 23 "the method of claim 1, wherein said exogenous functional β-galactosidase gene is inserted into an endogenous gene"

Dependent claim 23 of the '018 patent requires:

> The method of claim 1, wherein said exogenous functional β-galactosidase gene is inserted into an endogenous gene.

('018 patent at cl. 23.)

For this claim, Glycosyn alleges it is met in the Accused Strains under the doctrine of equivalents. (CIB at 65.) Specifically, Glycosyn argues that the development of the strains saw Jennewein intentionally insert the *lacZα* gene into an endogenous gene known as yihQ. (*Id.* at 66 (citing CX-0240C; CX-0297C).) Glycosyn acknowledges, however, Jennewein's claim that this version of *lacZα* "simply fell out" and ceased to exist in the strain. (*Id.* (citing CX-0237C at 7-9; JX-0012C at 29-30, 79:23-80:5).) Glycosyn argues this makes no difference because it was subsequently discovered that *lacZα* nevertheless continued to exist in the strain from a much earlier insertion "into the *int* gene of the DE3 prophage" by other groups of scientists. (*Id.* (describing a BL21 host strain converted to BL21 (DE3).) Glycosyn concludes, "[w]hat is clear, is that the difference between Dr. Parschat inserting the *lacZα* gene into the endogenous gene *yihQ* gene, and someone else inserting the *lacZα* into the DE3 prophage's *int* gene are so insubstantial that Jennewein never even noticed it for years, and only after this investigation began." (*Id.* at 66-67 (citing *Toro Co. v. White Consol. Indus.*, 266 F.3d 1367, 1370 (Fed. Cir. 2001)).) Glycosyn does not address *lacZΩ*.

[redacted]

The Staff's argument on this point is persuasive: "both the *lacZΩ* fragment and the DE3 prophage itself," into which the *lacZΩ* fragment was inserted, "were introduced into the original host strain." (SIB at 60 (citing CX-0004C at Q598 (Prather).) That is, "either both are exogenous to Jennewein's production strains or both are endogenous." (*Id.*) But because claim 23 requires an exogenous gene inserted into an endogenous gene, the Accused Strains cannot literally infringe it. And because this claim limitation cannot be met through the doctrine of equivalents without vitiating it entirely, *Warner-Jenkinson*, 520 U.S. at 39 n.8, dependent claim 23 is not infringed.

E. Domestic Industry – Technical Prong

According to Glycosyn's post-hearing briefing, and not contested by Jennewein or the Staff, the following domestic industry products are alleged to practice the following claims of the '018 patent:

Product	**Claims**
Glycosyn's *E. coli* production strains of which *E. coli* strain E997 is representative	1-3, 5, 8-14, 18, 22-28

(CIB at 15-16.) With respect to those strains allegedly represented by E997, Glycosyn argues:

> Glycosyn has developed strain E997 as well as several other *E. coli* bacterium strains that practice claims 1-3, 5, 8-14, 18, and 22-28 of the '018 Patent, and thus are domestic industry strains. *See* CX-0059C (curated 258 strains.xlsx). Since Fall of 2015, Glycosyn has documented the amounts of 2'-FL produced by these domestic industry strains to be [redacted], with about [redacted] being produced by E997. *See* CX-0131C (!All Runs Summary.xlsx); CX-0064C (!All Runs Summary.xlsx).

(*Id.* at 92; *see id.* at 15 (citing CX-0004C at Q99, 123); *see also* CX-0004C at Q164.) I do not observe any dispute from Jennewein or the Staff over Glycosyn's contention of representativeness

[redacted]

of E997. I therefore accept Glycosyn's claim of representation for the purposes of evaluating domestic industry.

Further, for the reasons explained below, I find Glycosyn has shown by a preponderance of the evidence that its production of 2'-FL using its E997 strain practices claims 1-3, 5, 8, 10-14, 18, 22, and 24-28 of the '018 patent. Glycosyn has not shown it practices claims 9 or 23.

1. Undisputed Claim Limitations

As with infringement by the Accused Strains, discussed above, and as reflected in the parties' post-hearing briefing, the practice of a large majority of the '018 patent claim limitations by Glycosyn's E997 strain is not in dispute. (*See, e.g.*, CIB at 92; RIB at 69-72; SIB at 76-86; RRB at 41-43; SRB at 20-22.) With respect to independent claim 1, and in reference to claim limitation identifiers used within the witness statement of Glycosyn's expert (CX-1004C), Glycosyn asserts "that [it] literally produces 2'-FL, a fucosylated oligosaccharide, in a bacterium using a method that practices claim elements 1(pre), 1(a), 1(c), 1(d), 1(e), and 1(f)," an assertion supported by its expert's witness statement. (CIB at 92 (citing CX-0004C at Q110-126, 127-134, 169-175, 176-187, 188-192, 193-209).) Glycosyn also demonstrates that, for the remaining limitation, E997 includes "an exogenous functional β-galactosidase gene comprising a detectable level of B-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium." (*Id.* (citing RPB at 76; CX-0004C at Q127-134).) The Staff agrees these limitations are met. (*See* SIB at 77-79.) Jennewein does not dispute the limitations are met, either. (*See* RIB at 69-72; RRB at 41-43.)

In light of the evidence identified by Glycosyn and discussed by the Staff, and the lack of dispute, I find they are practiced by Glycosyn's E997 strain. These limitations include:

> 1. A method for producing a fucosylated oligosaccharide in a bacterium, comprising

providing an isolated *E. coli* bacterium comprising,

(i) a deletion or functional inactivation of an endogenous β-galactosidase gene;

(ii) an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium,

. . . .

(iii) an inactivating mutation in a colanic acid synthesis gene; and

(iv) an exogenous lactose-accepting fucosyltransferase gene;

culturing said bacterium in the presence of lactose; and

retrieving a fucosylated oligosaccharide from said bacterium or from a culture supernatant of said bacterium.

('018 patent at cl. 1.)

With respect to the asserted dependent claims, Glycosyn argues it "practices the additional claim elements present in dependent claims 2, 3, 5, 8, 9, 10, 11, 12, 13, 14, 18, 22, 23, 24, 25, 26, 27, and 28 of the '018 Patent." (CIB at 96 (citing CX-0004C at Q210-294; CX-0065).) Jennewein indeed does not dispute this. (*See* RIB at 69-72; RRB at 41-43.) The Staff, however, does challenge Glycosyn's practice of claims 9 and 23, and I address these below. (SIB at 82-86.)

I also address the β-galactosidase activity level of claim 1 below. Otherwise, in light of Glycosyn's expert evidence, and the lack of a dispute from Jennewein or the Staff, I find the following claims are practiced by Glycosyn's E997 strain:

2. The method of claim 1, wherein said colanic acid synthesis gene comprises an *E. coli* wcaJ, wzxC, wcaD, wza, wzb, or wzc gene.

3. The method of claim 2, wherein said colanic acid synthesis gene comprises a wcaJ gene.

. . . .

5. The method of claim 1, wherein said exogenous lactose-accepting fucosyltransferase gene encodes α(1,2) fucosyltransferase and/or α(1,3) fucosyltransferase.

. . . .

8. The method of claim 1, wherein said exogenous functional β-galactosidase gene comprises an *E. coli* lacZ gene.

. . . .

10. The method of claim 1, wherein said bacterium further comprises a functional lactose permease gene.

11. The method of claim 10, wherein said lactose permease gene is an endogenous lactose permease gene.

12. The method of claim 10, wherein said lactose permease gene comprises an *E. coli* lacY gene.

13. The method of claim 1, wherein said bacterium further comprises an exogenous *E. coli* rcsA or *E. coli* rcsB gene.

14. The method of claim 1, wherein said bacterium further comprises an inactivating mutation in a lacA gene.

. . . .

18. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 5 units.

. . . .

22. The method of claim 1, wherein said bacterium comprises the genotype of

(a) ampC::(PtrpBλcI+), PlacI q (ΔlacI-lacZ)lacY+, ΔwcaJ, thyA::Tn10, Δlon::(kan, lacZ+); or

(b) ampC::(PtrpBλcI+), PlacI q (ΔlacI-lacZ)lacY+, ΔwcaJ, thyA::Tn10, Δlon::(kan, lacZ+), ΔlacA.

. . . .

24. The method of claim 1, wherein said exogenous functional β-galactosidase gene comprises a recombinant β-galactosidase gene engineered to produce a detectable level of β-galactosidase activity that is reduced compared to the level of β-galactosidase activity in a wild-type *E. coli* bacterium.

[redacted]

25. The method of claim 24, wherein the level of β-galactosidase activity comprises between 0.05 and 5 units.

26. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 4 units.

27. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 3 units.

28. The method of claim 1, wherein the level of β-galactosidase activity comprises between 0.05 and 2 units.

('018 patent at cls. 2, 3, 5, 8, 10-14, 18, 22, 24-28.)

2. Disputed Claim 1 Limitation "wherein the level of β-galactosidase activity comprises between 0.05 and 200 units"

The only claims and limitations in dispute for the domestic industry technical prong are the β-galactosidase activity level of claim 1, which Jennewein contests, and dependent claims 9 and 23, which the Staff contests. Claim 1 of the '018 patent requires:

> (ii) an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium, *wherein the level of β-galactosidase activity comprises between 0.05 and 200 units*;

('018 patent at cl. 1 (emphasis added).)

For this limitation, Glycosyn's evidence shows that "E997, and other Glycosyn strains that contain a re-introduced lacZ gene at the same location and direction, reproducibly exhibit β-galactosidase activity between 1 and 3 Miller units," which is well below the approximately 1000 Miller units exhibited by wild-type *E. coli* bacteria. (CIB at 94 (citing CX-0024C; CDX-0070C; CX-0021C; CX-0049C; CX-0050C; CX-0251.) Jennewein, however, complains that "Glycosyn relies solely on its own in-house testing to support the technical prong of the domestic industry requirement" as specified by an internal index card of instructions. (RIB at 70 (citing Hr'g Tr. at 76:5-12, 271:19-272:8, 514:18-22; RX-0409C at Q349).) Jennewein repeats its non-infringement position (discussed and rejected above) that the testing method suffers from no negative controls

[redacted]

(*id.* at 70-71) and adds, as Glycosyn anticipated, criticisms of Glycosyn's incubation temperature as well as the [redacted] (*See id.* at 71-72.)[4]

As noted above, failure to subtract negative control strain Miller Units does not constitute deficient testing. Jennewein's remaining criticisms regarding temperature and redundant sample preparation steps also lack merit. On temperature, Glycosyn's results show that testing was done [redacted] but also at 28°C and 30°C—the former of which Jennewein claims is the correct temperature. (RIB at 71; RRB at 41-42; CX-0004C at Q165-167; CX-0048C.) As shown below, Miller Unit levels within the claimed range were met at all temperatures:

[redacted]

(CX-0048C at -122123.) Regarding Glycosyn's [redacted] which Jennewein correctly observed is redundant according to Miller (CX-0251 at -1811), I am persuaded that use of just one of these preparation steps would have increased Miller Unit values but not so much as to travel outside of the claimed 0.05 to 200 range. (CX-0251C at -1810-1811 (describing formulae in which 550 nm readings are used to lower Miller Unit

[4] While Jennewein and Glycosyn refer to the 28°C as an incubation temperature, it is likely more accurately described as a reaction temperature. (CX-0251 at -1810 (cells are grown at 37°C but driven to 28°C right before ONPG is added).)

[redacted]

calculated amounts); Hr'g Tr. at 536:1-9.) Indeed, Jennewein's argument is limited to an assertion that the Miller Units would simply be "altered"—a premise that it otherwise provides little support for. (RIB at 72 (citing RX-0409C at Q350 (withdrawn testimony)); RRB at 42 (citing Hr'g Tr. at 305:7-15; RX-0409C at Q212 (discussing Jennewein strains and inapplicable)).)

Accordingly, I find Glycosyn's E997 strain practices this limitation of independent claim 1, and in light of the other limitations not in dispute, all of independent claim 1.

3. Disputed Claim 9 "the method of claim 8, wherein the lacZ gene is inserted into an endogenous lon gene"

Dependent claim 9 of the '018 patent requires:

> The method of claim 8, wherein the lacZ gene is inserted into an endogenous lon gene.

('018 patent at cl. 9.)

Glycosyn's own expert interpreted Glycosyn's GRAS Notice No. 735 as evidence that the 'lon' gene was modified with a 'complete deletion and replacement with a gene cassette . . . .' (CX-0004C at Q229; *see* CX-0065 at Table 1.) Clearly, "complete deletion" of a gene precludes insertion into that gene, so claim 9 is not practiced. Glycosyn does not dispute this in their reply brief. (*See* CRB at 47.)

4. Disputed Claim 23 "the method of claim 1, wherein said exogenous functional β-galactosidase gene is inserted into an endogenous gene"

Dependent claim 23 of the '018 patent requires:

> The method of claim 1, wherein said exogenous functional β-galactosidase gene is inserted into an endogenous gene.

('018 patent at cl. 23.)

For the same reasons outlined above with respect to claim 9, I agree that claim 23 is not practiced. Glycosyn does not dispute this in their reply brief. (*See* CRB at 47.)

[redacted]

F. Validity and Enforceability

Jennewein's initial post-hearing brief identifies the following invalidity and unenforceability theories against the asserted claims of the '018 patent:

Claims	Theory
1-3, 5, 8, 10, 12, 18, and 23-28	Rendered obvious under 35 U.S.C. § 103 by Samain (RX-0002) in view of Kawano (RX-0014) and the knowledge of one of skill in the art as shown by Drouillard (RX-0015), Geisser (RX-0016), and Dekany (RX-0017).
1-3, 5, 8, 10, 12, 18, and 23-28	Indefinite under 35 U.S.C. § 112, ¶ 2 (included solely for right of appeal in light of Order 22)
1-3, 5, 8, 10, 12, 18, 23, and 24	Lack of enablement under 35 U.S.C. § 112, ¶ 1
1-3, 5, 8, 10, 12, 18, 23, and 24	Lack of written description 35 U.S.C. § 112, ¶ 1
1-3, 5, 8, 10, 12, 18, and 23-28	Unenforceable due to inequitable conduct

1. Asserted Prior Art

Jennewein alleges the "Samain" reference, U.S. Patent No. 7,521,212 (RX-0002) is prior art to the '018 patent because it issued from an application filed on May 24, 2002 and further claims priority from international applications to July 7, 1999. (RIB at 75.) Glycosyn does not contest the prior art status of Samain (*see* CIB at 96-109; CRB at 47-54), and I find it qualifies as prior art under pre-AIA 35 U.S.C. § 102(a), (b), and (e).

Jennewein alleges the "Kawano" reference, a publication found in "Volume 33 of Nucleic Acids Research" (RX-0014) is prior art to the '018 patent because it was published in 2005. (RIB at 75.) Glycosyn does not contest the prior art status of Kawano (*see* CIB at 96-109; CRB at 47-54), and I find it qualifies as prior art under pre-AIA 35 U.S.C. § 102(a) and (b). 35 U.S.C. §

[redacted]

102(e) only applies to patent applications and issued patents, which Kawano is not; Jennewein's contention to the contrary is not well-taken. (*See* RIB at 75.)

Jennewein alleges the "Drouillard" reference, a publication found in "Volume 118 of the Angewandte Chemie (German for 'Applied Chemistry') journal" (RX-0015) is prior art to the '018 patent because it was published in 2006. (RIB at 77.) Glycosyn does not contest the prior art status of Drouillard (*see* CIB at 96-109; CRB at 47-54), and I find it qualifies as prior art under pre-AIA 35 U.S.C. § 102(a) and (b).

Jennewein alleges the "Geisser" reference, a publication found in "the Journal of Chromatography A" (RX-0016) is prior art to the '018 patent because it was published in 2005. (RIB at 77.) Glycosyn does not contest the prior art status of Geisser (*see* CIB at 96-109; CRB at 47-54), and I find it qualifies as prior art under pre-AIA 35 U.S.C. § 102(a) and (b).

Jennewein alleges the "Dekany" reference, published application number WO 2010/115935 (RX-0017) is prior art to the '018 patent because it "was filed on April 7, 2010, and claims priority to a Danish application filed on April 7, 2009." (RIB at 78.) Glycosyn does not contest the prior art status of Dekany (*see* CIB at 96-109; CRB at 47-54), and I find it qualifies as prior art under pre-AIA 35 U.S.C. § 102(a).

2. 35 U.S.C. § 103 (Obviousness)

Jennewein contends that "claims 1-3, 5, 8, 10, 12, 18, and 23-28 of the '018 patent are each obvious, and thus are invalid, based on Samain [RX-0002] in combination with Kawano [RX-0014] and optionally one of Drouillard [RX-0015], Geisser [RX-0016], or Dekany [RX-0017]." (*Id.*) More specifically, and with respect to claim 1 from which all other asserted claims depend, Jennewein's theory is that Samain teaches all elements of this claim except for "(ii) an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium, wherein the level of β-galactosidase

[redacted]

activity comprises between 0.05 and 200 units." (*See* RIB at 79 (citing RX-0384C at Q201, 202; Hr'g Tr. at 707:2-712:19).) For this missing element, Jennewein claims it is taught by Kawano, and that a person of ordinary skill in the art would have been motivated to incorporate this teaching of Kawano into Samain's fucosylated oligosaccharide-producing strains. (*See id.* at 79-80 (citing RX-0384C at Q206-209; RX-0014 at -2244-45).)

Jennewein's expert testified in support of that motivation in several places, as part of his '230 and '018 patent discussions:

> In my opinion, it would have been obvious to use a low level of β-galactosidase activity in Samain's *E. coli* strain, less than wild-type activity, to solve the known problem of purifying oligosaccharides from lactose, as taught by Druillard, Geisser or Dekany, but keeping the level low enough to avoid preventing 2'-FL production as taught by Samain.

(RX-0384C at Q203 (citing RX-0015 at *1810; RX-0016 at *18; RX-0017 at *1-5));

> Lactose as a feedstock would necessarily be present in significant amounts in the fermentation medium as I explained above, and would be difficult and impractical to separate from 2'-FL, particularly at large scale, due to these known difficulties in separating 2'-FL from lactose. Keeping the level of lactose inside the cell low also would have been desired to avoid lactose toxicity and degrading the substrate for 2'-FL production, for which some level of β-galactosidase activity would have been an obvious solution.

(*id.* at Q204);

> To avoid impacting 2'-FL production, but still allow excess lactose to be eliminated, a low level of B-galactosidase activity would have been desired, including as low as 0.05 to 200 units.

(*id.* at Q206);

> A POSA would have been motivated to combine Kawano's low level of β-galactosidase activity with Samain to address the known problem of purification of fucosylated oligosaccharides like 2'-FL from lactose, while not destroying too much lactose substrate to prevent production of any 2'-FL. β-galactosidase was known to destroy lactose.

(*id.* at Q209):

[redacted]

> One of ordinary skill would have been motivated to modify Samain with a reasonable expectation of success by introducing a low-level of β-galactosidase activity according to Kawano to aid in the purification of the fucosylated oligosaccharides produced by eliminating other oligosaccharides present, like lactose.

(*id.* at Q219 (citing RX-0015 at *1810; RX-0016 at *18; RX-0017 at *1-5); *see also id.* at Q259, 262 (citing RX-0015 at *1810; RX-0016 at *18; RX-0017 at 1-5)). The expert further testified that a person of ordinary skill would have known how to accomplish this given "the teachings of Kawano, which teaches a POSA how to engineer *E. coli* to have a low level of β-galactosidase activity, including activity of 130-200 Miller units." (*Id.* at Q206 (citing RX-0014 at Table 2, Fig. 1); *see id.* at Q216, 258.)

I find that a person of ordinary skill in the art would not have been motivated to combine the teachings of Samain and Kawano, without the benefit of hindsight from the '018 patent, for two primary reasons.

First, a fair reading of Samain shows that it teaches away from the proposed combination. Samain not only fails to teach "(ii) an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium, wherein the level of β-galactosidase activity comprises between 0.05 and 200 units," but it repeatedly insists that no β-galactosidase activity be present to avoid consuming the lactose "precursor" outside the production pathway of 2'-FL:

> [S]aid method comprising the steps (i) of obtaining a cell that comprises at least one recombinant gene encoding an enzyme capable of modifying said exogenous precursor or one of the intermediates in the biosynthetic pathway of said oligosaccharide from said exogenous precursor necessary for the synthesis of said oligosaccharide from said precursor, and also the components for expressing said gene in said cell, *said cell lacking any enzymatic activity liable to degrade said oligosaccharide, said precursor and said intermediates*[.]

(RX-0002 at 2:38-47 (emphasis added));

[redacted]

> According to one preferred embodiment of the invention, the bacterium is *Escherichia coli*. According to another embodiment of the invention, the cell is a yeast that is preferably *Saccharomyces cerevsae, Saccharomyces pombe* or *Candida albicans. The cell according to the invention lacks any enzymatic activity liable to degrade said oligosaccharide, said precursor or said metabolic intermediates.*

(*id.* at 3:35-41 (emphasis added));

> The β-galactosides are normally hydrolyzed in the cytoplasm of the bacterium by the β-galactosidase encoded by the LacZ gene. In order to overcome this problem, a lacZ− bacterial mutant lacking β-galactosidase activity is used when the precursor used is lactose and/or a β-galactoside. *One of the objects of the invention is thus also to provide the method according to the invention that is characterized in that said cell lacks enzymatic activity liable to degrade said precursor or said metabolic intermediates.*

(*id.* at 7:6-14 (emphasis added));

> In the method according to the invention, *said cell may be lacking in enzymatic activity liable to degrade said precursor(s).* According to one preferred embodiment, the method is characterized in that said cell has a genotype chosen from $LacZ^-$ and/or $NanA^-$.

(*id.* at 7:25-30 (emphasis added));

> FIG. 1: . . . *Lactose (β-D-Gal-[1-4]-β-D-Glc) is transported into the cell by lactose permease (Lac permease). The lactose cannot be hydrolyzed in the cell since the strain is a $LacZ^-$ mutant.*

(*id.* at 10:66-11:9 (emphasis added); *see also id.* at 11:40-51 (emphasis added));

> FIG. 9: . . . *Lactose and sialic acid (NeuAc) are internalized in the cell by lactose permease (lacy) and sialic acid permease (nanT). These two compounds are not degraded in the cell since the strain is a $lacZ^-$ and $nanA^-$ mutant.* The expression of CMP-NeuA synthase and of α-2,3-sialyl-transferase allows the activation of the sialic acid internalized into CMP-NeuAc and its transfer onto the intracellular lactose.

(*id.* at 11:63-12:3 (emphasis added)).

Samain achieves this lack of β-galactosidase activity by maintaining a $LacZ^-$ status in multiple disclosed embodiments (through deletion or inactivation):

Thus, according to one preferred embodiment . . . it is characterized in that said cell is a bacterium of $LacZ^-$, $LacY^+$ genotype, said enzyme is β-1,3-N-acetyl-glucosaminyl-transferase, said substrate is glycerol, said inducer is isopropyl β-D-thiogalactoside (IPTG) and said precursor is lactose.

. . . .

According to a second preferred embodiment, the method according to the invention is used for the production of lacto-N-neo-tetraose and polylactosamine; it is characterized in that said cell is a bacterium of $LacZ^-$, $LacY^+$ genotype[.]

. . . .

According to a third preferred embodiment, the method according to the invention is used for the production of allyl 3-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-β-D-galactopyranoside, (β-D-GlcNac-[1→3]-β-D-Gal-1→O-allyl); it is characterized in that said cell is a bacterium of $LacZ^-$, $LacY^+$ genotype[.]

. . . .

According to a fourth preferred embodiment, the method according to the invention is used for the production of analogs of lacto-N-neo-tetraose and of polylactosamines in which the glucose residue is replaced with an allyl group; it is characterized in that said cell is a bacterium of $LacZ^-$, $LacY^+$ genotype[.]

. . . .

According to a fifth preferred embodiment, the method according to the invention is used for the production of allyl-β-D-lactosamine (β-D-Gal-[1→4]β-D-GlcNac-1→O-allyl); it is characterized in that said cell is a bacterium of $LacZ^-$, $LacY^+$genotype[.]

(*id.* at 7:43-8:19);

Another subject of the invention relates to a method described above for the production of 3′-sialyllactose (α-NeuAc-[2→3]-→-D-Gal-[1→4]-β-D-Glc) or 6′-sialyllactose (α-NeuAc-[2→6]-β-D-Gal-[1→4]-β-D-Glc), characterized in that:

said cell is a bacterium of $LacZ^-$, $LacY^+$, $NanA^-$ or $NanT^+$genotype[.]

(*id.* at 9:1-12);

According to a seventh preferred embodiment, the method according to the invention is used for the production of 3′-fucosyllactose (β-D-Gal-[1→4]-

[redacted]

> (α-L-Fuc-[1→3]-D-Glc) or 2′-fucosyllactose (β-D-Gal-[1→2]-(α-L-Fuc-[1→3]-D-Glc), characterized . . . in that the cell has a wcaj$^-$ lacZ$^-$genotype and overexpresses the rcsA gene and in that said precursor is lactose.

(*id.* at 9:39-46; *see also id.* at 16:1-15 ("The strain JM 109 is lacZ$^-$, that is to say that it is incapable of hydrolyzing lactose.")).

Notably, Jennewein's expert does not squarely address this important aspect of Samain's disclosure in his direct witness testimony. He responds in conclusory fashion, "Q. What about Glycosyn's argument that the prior art teaches away from their invention? A. I do not find that Jennewein's patent or Samain 'teach away' from the claimed inventions or evidence skepticism relating to the alleged inventions." (RX-0384C at Q315; *see* RIB at 96-97 (citing same).) Based on the above excerpts, Samain clearly expresses skepticism as to the value of re-introducing LacZ activity into its strains. Similarly, Jennewein is wrong in asserting that the above excerpts amount only to "lacking a limitation" and not "teaching away." (*See* RRB at 45.) Samain's consistent emphasis on a LacZ$^-$ status for its strains is too great to be written off in this way.

Jennewein cites *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1355 (Fed. Cir. 2012) and *Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731, 739 (Fed. Cir. 2013) to show otherwise (RIB at 45), but I am not persuaded. For one, *Santarus* actually supports teaching away by Samain. In that case, the court held that a reference did not teach away from a drug formulation claim limitation because it advocated for a first version of that formulation while also advocating for a second. 694 F.3d at 1355 ("Although Pilbrant 'ruled out' conventional dosage forms such as tablets, capsules, or granules with non-enteric coated PPIs, it states that a 'rapidly dissolving suspension of micronized omeprazole is the second best choice as the reference formulation.'"). But it held the reference *did* teach away from the first version, specifically through a discussion of stomach degradation problems it would encounter. *Id.* In this case, there is no instance of Samain

advocating for LacZ activity, and, like the first version of the formulation in *Santarus*, Samain discourages LacZ use because of precursor consumption problems.

In *Galderma Labs.*, the court held that the prior art articles only taught an optimal ingredient percentage for a pharmaceutical (0.1%), as opposed to discouraging the patent's claimed percentage (0.3%), before disagreeing with the lower court over whether the references taught away. 737 F.3d at 738-9 ("Moreover, there is nothing in either of these references to indicate that increasing the concentration to 0.3% would be unproductive . . . ."). In this case, Samain actively discourages LacZ activity in its strains, setting it apart from *Galderma Labs.*

And Jennewein's expert agreed under cross-examination that "the teachings of Samain are so compelling that you can't fathom a reason that someone would use an *E. coli* strain with a low level of beta-galactosidase activity to produce 2'-FL, as opposed to using a strain with zero beta-galactosidase activity":

> Q. And the reason Samain doesn't teach this element is because Samain teaches no beta-galactosidase activity, not a low level of beta-galactosidase activity; correct?
>
> A. Yes.
>
> Q. And you think that zero beta-galactosidase activity is the ideal situation; correct?
>
> A. Yes.
>
> Q. And, in fact, the teachings of Samain are so compelling that you can't fathom a reason that someone would use an *E. coli* strain with a low level of beta-galactosidase activity to produce 2'-FL, as opposed to using a strain with zero beta-galactosidase activity; correct?
>
> A. Correct.
>
> . . . .
>
> Q. Okay. And you can't fathom that they would do that with any low level of beta-galactosidase activity, whether it's .04, .05, .06, or .07 units; correct?
>
> A. Correct.

[redacted]

(Hr'g Tr. at 625:17-626:20.)

Jennewein also seeks to bolster its motivation to combine theory based on the disclosed use of a certain "JM 109" or "JM109" bacterial strain. (*See* RIB at 73-74, 83, 85, 90.) Jennewein argues:

> But, as Dr. Stephanopoulos explains and Dr. Prather acknowledges, Samain discloses a JM109 strain of *E. coli*, which already possesses a low level of β-galactosidase activity. RX-0384C (Stephanopoulos WS) at Q/A 218; Tr. (Prather) at 712:17-713:19; *see* RX-0002 (Samain) at 12:5-22 (Example 1). Dr. Stephanopoulos also testifies that this would not change were the strain to be used for 2'-FL production. RX-0384C (Stephanopoulos WS) at Q/A 218. Indeed, the ordinarily skilled artisan would have been motivated to have used a strain with a low level of β- galactosidase activity (such as the JM109 strain described in Example 1 of Samain) in order to avoid destroying the lactose feedstock necessary to produce lactose-containing oligosaccharides like 2'-FL. *Id.*; *see* RX-0002 (Samain) at 7:6-15.

(*Id.* at 73-74 (wherein cited expert testimony further cites RX-0008 (Giacomini) at *88).) In fact, the JM 109 strain disclosed in Samain has zero β-galactosidase activity (*see* RX-0002C at 16:1-15), although the seemingly identical strain disclosed in Giacomini has substantial β-galactosidase activity (*see* RX-0008C at -14693). Dr. Prather testified that it was "impossible to believe that those were actually the same strains," and in any event Giacomini merely analyzes the effects of various parameters on measuring β-galactosidase activity using the Miller assay, and says nothing about 2'-FL production. (Hr'g Tr. at 748:14-15; RX-0008C.) So the disclosure of JM 109 in both Samain and Giacomini would not motivate a skilled artisan to combine their teachings.

Nor does Kawano provide a motivation to combine. Although Kawano "teaches inserting a β-galactosidase gene into a gene construct in *E. coli*, producing a low-level β-galactosidase activity, including 130-220 Miller Units" (RIB at 76 (citing RX-0014 at -22445, Table 2; Hr'g Tr. at 462:25-463:2)), Kawano also teaches insertion of the same gene so as to produce much higher levels of β-galactosidase activity—along the lines of 5,000-12,000 Miller Units (RX-0014 at -

[redacted]

22443, Table 1). In fact, Kawano discloses an extremely wide range of Miller Unit activities resulting from the insertion of a β-galactosidase gene into *E. coli*:

Table 1. Activities and genomic locations of eight fragments selected for high activity

Strain no.	β-Galactosidase MU	Source of fragment in *E.coli* Position, size and orientation[c]	Nearest Gene	Position and orientation[c]	RO[1]	ORF->[b]
M1789[d]	12 200	121 678 <- 145 bp 128 116	*aroP*[e]	120 178 <- 121 551	S	---->
M1791	10 100	960 788 171 bp -> 960 958	*rpoA*[f]	961 218 -> 962 891	S	---->
M1792	9100	4 194 326 <- 170 bp 4 194 495	*rsd*[g]	4 193 910 <- 4 194 386	S	---->
M1793	6700	189 380 <- 204 bp 189 583	*map*	188 712 <- 189 506	S	---->
M1794	6100	1 019 354 <- 165 bp 1 019 518	*ompA*[h]	1 018 236 <- 1 019 276	S	---->
M1795	6200	1 695 029 <- 164 bp 1 695 192	*mdR*	1 694 486 <- 1 695 076	S	---->
M1796	6200	2 797 076 165 bp -> 2 797 240	*ygaW*	2 797 185 -> 2 797 634	S	---->
M1797	5700	621 461 <- 163 bp 621 623	*fepD*	620 408 <- 621 412	S	---->

Table 2. Activities and genomic locations of 20 most active fragments selected at random

Strain no.	β-Galactosidase Rank	MU	Source of fragment in *E.coli* Position, size and orientation[d]	Nearest Gene[a]	Position and orientation[d]	RO[c]	-ORF->
M1493	1	3200	2 990 280 <- 166 bp 2 990 445	*sgcH*	2 990 116 -> 2 991 492	O	<----
M1490	2	2900	1 527 795 <- 163 bp 1 527 962	*rhsE*	1 525 914 -> 1 527 962	O	<----
M1485	3	2100	2 764 194 <- 168 bp 2 764 361	*yjjN*	2 763 939 -> 2 765 012	O	<----
M1479	4	1300	2 939 936 212 bp -> 2 939 725	*gcvA*	2 939 672 -> 2 940 589	S	---->
M1476[i]	5	1100	2 510 624 <- 170 bp 2 510 793	*panH*	2 509 511 <- 2 510 726	S	---->
M1473	6	970	3 743 676 <- 230 bp 3 743 905	*suaO*	3 743 724 -> 3 744 710	O	<----
M1471	7	900	3 795 597 151 bp -> 3 795 747	*rfaL*	3 794 575 -> 3 795 834	S	---->
M1469	8	620	1 048 436 <- 155 bp 1 048 590	*xnuC*	1 047 911 <- 1 048 489	S	---->
M1468	9	570	4 279 164 <- 153 bp 4 279 316	*yjcE*	4 277 559 -> 4 279 208	O	<----
M1465	10	470	2 040 776 152 bp -> 2 040 927	*sodB*	2 040 390 -> 2 040 920	S	---->
M1463	11	450	1 710 148 <- 176 bp 1 710 323	unnamed[j]	1 709 136 <- 1 709 846	S	---->
				nlp	1 709 547 -> 1 710 182	[O]	<----
M1448	12	290	29 444 <- 121 bp 29 564	unnamed[j]	28 875 <- 29 231	S	---->
				dapB	28 374 -> 29 195	[O]	<----
				carA	29 756 -> 30 799	[O]	<----
M1447	13	270	1 769 832 <- 220 bp 1 770 051	*ydiM*	1 769 095 -> 1 770 309	O	<----
M1439	14	200	155 915 173 bp -> 156 087	*ecpD*	155 461 <- 156 201	O	<----
M1438	15	200	1 331 533 <- 147 bp 1 331 679	*topA*	1 329 072 -> 1 331 669	O	<----
M1437	16	180	217 647 <- 152 bp 217 798	*proX*	217 057 <- 218 775	S	---->
M1433	17	160	2 188 009 <- 145 bp 2 188 153	*yehB*	2 186 450 <- 2 188 930	S	---->
M1429	18	150	2 200 816 <- 167 bp 2 200 982	*yehI*	2 198 299 -> 2 201 931	O	<----
M1428	19	150	939 285 132 bp -> 939 416	*ycfS*	938 651 -> 939 943	S	---->
M1422	20	130	1 015 608 156 bp -> 1 015 763	*ycbZ*	1 015 762 <- 1 017 348	O	<----
				fabA	1 015 175 <- 1 015 801	[O]	<----

(RX-0014 at -22443, Table 1, -22445, Table 2 (annotated).) As shown in the above combined table, the lowest Miller Unit level reported is 130. While Kawano makes reference to additional strains with promoters causing Miller Unit activities below 130, it does not disclose the details of those strains (*see id.* at -22444, Figure 1) nor does it disclose why any particular activity level would be preferable over any other (*see generally id.*)—Kawano is solely directed to "a direct experimental approach for identifying chromosomal sequences with promoter activity" (*id.* at -22441) and not any particular use for resultant β-galactosidase.

[redacted]

This 130 Miller Unit level is important to a motivation to combine because it is the testimony of Jennewein's expert, given in the context of enablement, that "beta-galactosidase activity well above 5.8 would be expected to destroy lactose too quickly for the cell to use it to produce 2'-FL":

> Q. So you agree that those claims are enabled?
>
> A. Up to about 5 Miller units, I think so, yes.
>
> Q. It's your opinion that beta-galactosidase activity well above 5.8 units *would be expected* to destroy lactose too quickly for the cell to use it to produce 2'-FL; is that right?
>
> A. Correct.

(Hr'g Tr. at 644:11-17 (emphasis added); RX-0384C at Q186 (stating same); *see* RX-0384C at Q177-178 ("One better fit would be linear, for example one which shows about zero 2'-FL production at approximately 40 [Miller units]. This would be realistic as it reflects that higher β-galactosidase activity would essentially prevent a cell from making a decent amount of 2'-FL.").) I emphasize "would be" in the above excerpt because enablement, like obviousness, is evaluated from the perspective of one having ordinary skill in the art:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § 112 (pre-AIA); *Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 999 (Fed. Cir. 2008) ("The 'enablement requirement is satisfied when one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation.'") (citation omitted).

Thus, Jennewein's expert pleads both sides of the same coin: a person of ordinary skill in the art would be motivated to incorporate Kawano's 130 Miller Unit plasmids into Samain's

[redacted]

processes to help purify the oligosaccharides (RX-0384C at Q257-258), but would also expect that any Miller Unit activity above 5.8 would degrade lactose faster than it could be used for oligosaccharide production (*id.* at Q186). This contradictory picture significantly diminishes the persuasiveness of the purported motivation to combine.

Nor do the other references cited by Jennewein support a motivation to combine. Geisser (RX-0016), for example, is not directed to enzymatic production through modified organisms at all, but instead to "[t]he successful separation of the disaccharide lactose from a complex mixture of human milk oligosaccharides (HMOS) with the continuous chromatography of simulated moving bed (SMB) technique." (RX-0016 at Abstract.) Glycosyn's expert persuasively testified that "to the extent a person of skill in the art could learn anything from Geisser about β-galactosidase activity, they would understand that a high level, not a low level, of β-galactosidase activity would be preferred" to enhance the separation of lactose from other oligosaccharides in the milk. (CX-0487C at Q157.) Drouillard (RX-0015) discloses synthesis of 2'-FL through metabolically engineered *E. coli*, but it claims in both of its setups that no leftover lactose remained, that is, it does not address 2'-FL purification at all, nor does it even reference β-galactosidase. (RX-0015 at -15184 ("After 22 h of incubation, the lactose was completely consumed" and "To produce [2'-FL] without [LNnF-1] . . . . After 25 h incubation, lactose was completely consumed and converted into [2'FL].").) Lastly, Dekany discloses enzymatic methods for creating oligosaccharides, but only in background and with general discouragement:

> Either genetically engineered microorganisms or mammals are used in biotechnological methodologies for the synthesis of 2'-O-fucosyllactose. Such technologies use complex enzymatic systems facilitating both the biosynthesis of precursors and the required glycosylations. To date, such approaches face severe regulatory approval hurdles due to the use of genetically engineered organisms and potential contaminations of non-natural oligosaccharides.

(RX-0017 at -22356-7);

[redacted]

> Enzymatic methodologies suffer from the low availability of enzymes, extremely high sugar nucleotide donor prices and regulatory difficulties due to the use of enzymes produced in genetically modified organisms.

(*id.* at -22359). I therefore do not see this reference as useful or related to a motivation to combine β-galactosidase activity into the enzymatic techniques disclosed in Samain.

Apart from the lack of motivation to combine, some secondary considerations of non-obviousness further undermine Jennewein's case. Jennewein does not dispute the existence of a long felt, but unresolved need. (RRB at 50.) As for teaching away, Samain and three Jennewein patents all disclose the importance of inactivating the *lacZ* gene to preserve lactose for 2'-FL production. (CIB at 107 (citing CX-0487C at Q191-198).) The Jennewein patents demonstrate the existence of the conventional outlook: any other lactose-consuming processes should be deleted or inactivated during 2'-FL production. (*See* CX-0504 at 6:4-20; CX-0506 at [0014].) As the re-introduction of a functional β-galactosidase enzyme into *E. coli* during 2'-FL production is a central inventive aspect of the '018 patent, I find the requisite nexus is met here. *Merck & Cie*, 808 F.3d at 837; *In re Huai-Hung Kao*, 639 F.3d at 1068. And as for unexpected results, Jennewein's own expert was surprised that using a low level of β-galactosidase activity to produce oligosaccharides works, since it is contrary to what he believes even today is the preferable method for producing oligosaccharides, namely, use of an *E. coli* strain with no β-galactosidase activity. (Hr'g Tr. at 625:12-626:20.) Moreover, a non-testifying expert's issued patent states that the use of a low level of β-galactosidase activity had unexpected and surprising results in the production of oligosaccharides. (CX-0507 at 7:11-15.) For clarity, that reference, filed after the '018 patent, teaches:

> Surprisingly, it was determined that microorganisms that produce less β-galactosidase activity than a microorganism with a non-defective lacZ gene are the best producers of 2-FL (as compared to microorganisms that express normal levels of β-galactosidase or express no β-galactosidase).

[redacted]

(*Id.* at 7:11-15.) So non-obviousness is supported by a long felt, but unresolved need, teaching away, and unexpected results.

However, I am not persuaded that the failure of others supports a finding of non-obviousness. To be sure, Glycosyn's evidence shows it is not only hard to make 2'-FL in bioengineered organisms, but also hard to make it in sufficient quantities for commercial purposes, such as an ingredient in baby formula, so much so that "many have tried and failed." (RRB at 50; CIB at 105 (citing CX-0004C at Q52; Hr'g Tr. at 18:3-12; CX-0001C at Q34-35; RX-0320C at -20187).) In particular, the evidence shows that "there was no prior art solution for manufacturing fucosylated oligosaccharides that did not suffer from either low yields or purification difficulty" even though others, such as Jennewein, Abbott, and Nestlé, tried. (CIB at 106-107 (citing CX-0487C at Q191-198).) Nonetheless, Jennewein is the only current commercial provider of 2'-FL in the United States. (*See id.* at 93; RX-0384C at Q314.) And the failure of others is readily attributable to the inability to make 2'-FL in sufficient quantities and with necessary purity required for use in baby formula, while also making it cost-efficient. (*See* CIB at 105-106; CX-0487C at Q172, 178-181.) None of these goals are recited or necessarily accomplished through the simple practice of the '018 patent claims. (*See, e.g.*, '018 patent at cls. 1-28 (not reciting amount of fucosylated oligosaccharide produced, cost, or purity level).) Based on the stage of Glycosyn's collaboration with production partner FrieslandCampina, it seems too early to tell if the '018 patent answers the identified *commercial* needs. It was confirmed at the hearing that such production has not even begun. (Hr'g Tr. at 45:3-21, 48:1-17.)

I therefore do not find that the failure of others supports a finding of non-obviousness. The other three secondary considerations asserted by Glycosyn do support such a finding, however, and Jennewein has additionally failed to demonstrate a motivation to combine references. On

[redacted]

balance, therefore, neither claim 1 of the '018 patent, nor any of the dependent claims, are invalid for obviousness.

3. 35 U.S.C. § 112, ¶ 1 (Enablement)

In its opening brief, Jennewein contends "[c]laims 1-3, 5, 8, 10, 12, 18, 23, and 24 are invalid for failing to satisfy the enablement requirement of 35 U.S.C. § 112, ¶ 1." (RIB at 99.) Jennewein presents two specific arguments that "[t]he '018 patent's specification does not enable the full range of β-galactosidase activity" because it only shows fucosylated oligosaccharide production at an activity level of 1-2 Miller Units, while claim 1 recites a much broader range of 0.05 to 200 Units. (*See id.* at 100 (citing '018 patent at 18:23-32).)

First, Jennewein contends that "it would require undue experimentation to make a fucosylated oligosaccharide at such higher levels of β-galactosidase activity." (RIB at 109; *see, e.g.*, RIB at 101-102 ("[A] person of ordinary skill in the art would need undue experimentation to produce 2'-FL at these high level[s] of β-galactosidase activity."), 102 ("A person of ordinary skill in the art would need to conduct periodic experiments over the entire range of 0.05 to 200 . . . to ensure that the β-galactosidase level at each measurement would both (a) not be so high as to halt production of the fucosylated oligosaccharides and (b) eliminate residual lactose after 2'-FL production to allow isolation of the 2'-FL product, as claimed by Glycosyn during prosecution of the '018 patent's parent."), 102 ("significant experimentation would be necessary to ensure that the full scope of values within the claimed range of 0.05 to 200 units would 'strike a balance between production of desired fucosylated oligosaccharides and the level of β-galactosidase produced"), 106 ("Three data points over a relatively narrow range would be deemed as insufficient to show that strains having activity up to 200 units could in fact make 2'-FL.").) This position is tied to the claim limitation "retrieving a fucosylated oligosaccharide from said bacterium or from a culture supernatant of said bacterium." ('018 patent at cl. 1.) It revolves

around the argument that at higher β-galactosidase activity levels, the β-galactosidase "would destroy intracellular lactose faster than it could be processed into significant amounts of 2'-FL" such that "it would require undue experimentation to make a fucosylated oligosaccharide at such higher levels of β-galactosidase activity." (RIB at 109.)

To the extent this argument avers lack of enablement for producing "significant," useful, or "commercial levels" of a fucosylated oligosaccharide (RIB at 100 (citing RX-0384C at Q186)), it is entirely misplaced. No asserted claim requires any particular amount of fucosylated oligosaccharide to be produced or "retriev[ed]." (*See, e.g.*, '018 patent at cl. 1.)

To the extent this argument avers lack of enablement for producing any fucosylated oligosaccharide whatsoever at high β-galactosidase activity levels, there is a lack of clear and convincing evidence on this point. Jennewein relies on the testimony of its expert to make the claim (*see* RIB at 108-109 (citing RX-0384C at Q186))[5], but this testimony is contradicted by Jennewein's own obviousness arguments:

> *Furthermore, should the claims encompass producing any amount of 2'-FL, 2'-FL would be produced even in the presence of β-galactosidase activity within the claimed range.* This occurs because the β-galactosidase enzyme and the 2'-FL-producing fucosyltransferase enzyme are competing simultaneously for lactose. *See* Tr. (Prather) 730:15-731:14, RX-0384 (Stephanopoulos WS) at Q/A 195. . . . As shown in RDX-0012, should fucosyltransferase [be] present, some 2'-FL will be produced, even though less 2'-FL would be produced if β-galactosidase is also present. *See id.* It is also worth noting that Jennewein's fucosyltransferase attaches fucose to the galactose moiety of lactose.

(RIB at 83-84 (emphasis added).) That is, Jennewein concedes in its discussion of obviousness that simultaneous competition between β-galactosidase and fucosyltransferase will still result in

[5] Jennewein also cites hearing testimony from Glycosyn's expert here, but that testimony does not support the concept that competition will prevent any 2'-FL production. (RIB at 108-109 (citing Hr'g Tr. at 730:16-21, 731:1-14).)

[redacted]

some 2'-FL production, even when that competition is stiff. A person of ordinary skill would know this. (Hr'g Tr. at 730:15-731:14, 743:5-18, 737:14-738:20.)

Even setting aside this concession, I agree with Glycosyn (CIB at 112) and the Staff (SIB at 98) that Jennewein's expert testimony on the destruction of 2'-FL at higher β-galactosidase activity levels is largely conclusory and thus entitled to little weight. *Cephalon, Inc. v. Watson Pharms., Inc.*, 707 F.3d 1330, 1338 (Fed. Cir. 2013). For example, the expert claims that the data points contained in Dr. McCoy's declaration submitted during prosecution are better fit by a linear line than the exponential fit Dr. McCoy employed, but he provides no explanation for why it would be better—especially with regard to the science of simultaneous competing enzymatic pathways he acknowledges elsewhere. (*Compare* RX-0384C at Q178, 195 (discussing RDX-0012) *with* Hr'g Tr. at 743:5-18.) The expert's claim that "β-galactosidase activity well above 5.8 units would be expected to destroy lactose too quickly for the cell to use it to produce 2'-FL" is similarly conclusory. (*See* RX-0384C at Q186.) Dr. Stephanopoulos did not perform any experiments or cite any disclosures in connection with his contention that high β-galactosidase activity will prevent any 2'-FL production. (Hr'g Tr. at 644:13-646:4.)

Thus, I find it far from clear and convincing that higher β-galactosidase activity levels (*i.e.*, higher than ~6 Miller Units) would result in no 2'-FL production whatsoever. Jennewein does not explicitly address the *Wands* factors on this point, and, therefore, neither do I. (*See* RIB at 106-110.)

Jennewein's second enablement contention is that "undue experimentation would be required to modify microorganisms having β-galactosidase activity for the entire range." (RIB at 102; *see* RIB at 100 ("The specification fails to enable the full scope of the claim limitation 'the level of β-galactosidase activity comprises between 0.05 and 200 units' of claim 1 of the '018

[redacted]

patent."), 101 ("[T]he evidence showed that undue experimentation is required to produce strains with any specific activity in the claimed range."), 103 ("The specification . . . leav[es] a person of ordinary skill completely in the dark about how to create modified bacteria that could, taken together, cover the entire claimed range."), 105 ("The highly complex nature of this invention in this unpredictable field also contributes to a high level of experimentation necessary to achieve the claimed range of β-galactosidase activity.").) This position is tied to the claim limitation "(ii) an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium, *wherein the level of β-galactosidase activity comprises between 0.05 and 200 units*." ('018 patent at cl. 1 (emphasis added).)

This contention is a closer call. The '018 patent specification only discloses a single species of bacteria which produces between 1 and 2 Miller units of β-galactosidase activity:

> The lon mutation in E390 increases intracellular levels of RcsA, and enhances the intracellular GDP-fucose pool. The inserted lacZ+ cassette not only knocks out lon, but also converts the lacZ− host back to both a lacZ+ genotype and phenotype. The modified strain produces a minimal (albeit still readily detectable) level of β-galactosidase activity (1-2 units), which has very little impact on lactose consumption during production runs, but which is useful in removing residual lactose at the end of runs, is an easily scorable phenotypic marker for moving the lon mutation into other lacZ− *E. coli* strains by P1 transduction, and can be used as a convenient test for cell lysis (*e.g.* caused by unwanted bacteriophage contamination) during production runs in the bioreactor.

('018 patent at 18:19-32; *see* RIB at 103; SIB at 94 (not disputing Examiner's observation); *see generally* CIB at 109-116.) Thus, the issue is whether this limited species disclosure sufficiently enables a person having ordinary skill in the art to practice the limitation "(ii) an exogenous functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium, *wherein the level of β-galactosidase activity comprises between 0.05 and 200 units*," over the full range without undue experimentation.

[redacted]

Resolving this issue requires consideration of the *Wands* factors: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. *Wands*, 585 F.2d at 737.

In reviewing these factors, I have avoided relying on the evidence cited in Dr. McCoy's declarations during prosecution. Declarations submitted during prosecution, while undisputedly part of the intrinsic record, are not part of the specification, but it is the specification that is the focus of the enablement inquiry. And as for the *Wands* factors themselves, factor one, "the quantity of experimentation necessary," outweighs all others in significance, and I consider it last.

The second and third *Wands* factors, "the amount of direction or guidance presented" and "the presence or absence of working examples," favor Jennewein. The '018 patent specification provides just one example of an engineered bacterium with Miller Units of any amount (1-2 units). ('018 patent at 18:9-32.) And although Glycosyn's expert testified that "[t]he '018 specification and the documents cited therein provide significant guidance on how to modify a bacterium to express different levels of β-galactosidase activity and/or produce different amounts of 2'-FL," her testimony is conclusory. (CIB at 115 (citing CX-0487C at Q59-64).) She merely cites passages in the '018 patent (CX-0487C at Q61 (citing '018 patent at 16:31-35, 18:12-13)) which mention that an increased cellular pool of lactose and the lon replacement mentioned above were achieved using "λ Red combineering" or "λ Red recombineering." The expert does not explain what this technique is or how it can be used to achieve varied β-galactosidase activity levels.

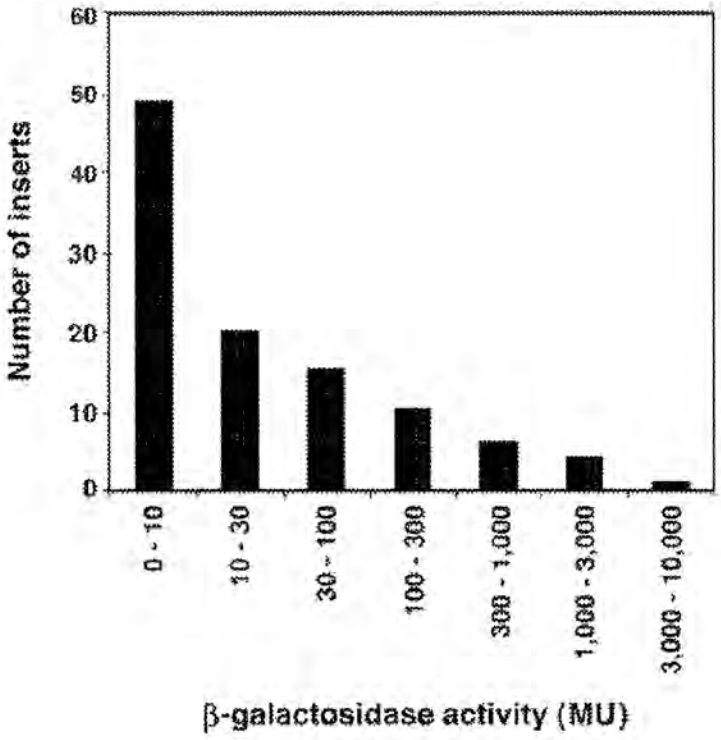
The fourth and eighth factors, "the nature of the invention" and "the breadth of the claims," do not favor either side. While the obviousness discussion above identifies "wherein the level of

β-galactosidase activity comprises between 0.05 and 200 units" as a key distinguishing feature over the prior art, engineering a bacterium with this level of activity is not by itself an aspect of the invention. (*See, e.g.*, RX-0014 at -22443-5, Table 1, Fig. 1, Table 2.) Rather, the benefit of the invention comes from the combined use of a bacteria producing the claimed activity range, alongside those other techniques implemented for increased oligosaccharide production within the bacteria. And the recited 0.05 to 200 Miller unit range is not particularly broad. Prior art references such as Kawano (RX-0014) show that, depending on the promoter used, β-galactosidase activity within an *E. coli* bacterium can run anywhere between 0 and 12,200 Miller units. (*See* RX-0014 at -22443, Table 1, -22445, Table 2.)

The fifth, sixth, and seventh factors, "the state of the prior art," "the relative skill of those in the art," and "the predictability or unpredictability of the art," also do not favor either side. There is persuasive evidence in the record that this art is generally unpredictable, in that those skilled in the art understand and expect experimentation to be performed before conclusions on genetic or enzymatic activity can be reached. (*See* Hr'g Tr. at 676:17-678:4 ("You would not know the results. You expect results, but you do not know the results until you do the experiment. . . . You have to do the experiment."); CX-0002C at Q36 ("This is how genetic engineering works, you try several different modifications unit you get the result you want."); *see generally* JX-0002 at -2961-2968 (rejecting claims due to unpredictability in the field); RX-0384C at Q185, 190; Hr'g Tr. at 296:13-23, 640:16-641:5, 505:1-15, 147:18-149:18; CX-0053C at -117388; CX-0488C at Q20-23, 39.) Yet, there is also evidence showing the person of ordinary skill in the art at the time of invention would have known how to conduct this experimentation and would be aware of various *E. coli lacZ* promoters to try. (*See, e.g.*, JX-0002 at -2934 (citing prior

art investigation of promoters); RX-0014; Hr'g Tr. at 619:4-624:12; CX-0468; CX-0469; CX-0487C at Q64.)

Turning finally to the first *Wands* factor, "the quantity of experimentation necessary," I find this favors Glycosyn. Again, Kawano is instructive. While Jennewein is correct that Kawano explicitly teaches bacteria strains for only a portion of the claimed 0.05-200 Miller Unit range (RIB at 105), it is also true that of Kawano's 105 randomly selected strains for potential promoter activity, a vast majority exhibited Miller Unit activity levels within the 0.5-200 range. This is explained alongside Kawano's Figure 1:



[redacted]

Figure 1. The distribution of promoter (β-galactosidase) activities of 105 random fragments of *E.coli* as assayed in the promoterless *lacZ* tester plasmid, pRS551. We defined a sequence as having potential promoter activity when the β-galactosidase activity of the strain was increased by 3-fold or more over that of the strain with the parental plasmid pRS551 (i.e. to >10 MU). We found that 56 (53%) of the inserts (tested in only one orientation) exhibited promoter activity by this criterion. However, some of the inserts may contain more than one promoter. Applying the Poisson distibution, $P(0) = e^{-\lambda}$, where $P(0)$ is the probability of finding no activity (i.e. the null class of plasmids expressing 0–10 MU = 47%), and solving for λ (the average number of potential promoters per insert), we calculate there are on average 0.76 promoters per fragment (in one of the two possible orientations). We therefore conclude that there are ~1.52 (twice 0.76) promoters per 163 bp or one full promoter in either direction per ~107 bp.

(RX-0014 at -22444.) This data strongly suggests that when a person of ordinary skill in the art, and familiar with *E. coli* gene manipulation techniques, searches for promoters to use with a functional β-galactosidase gene to accomplish "wherein the level of β-galactosidase activity comprises between 0.05 and 200 units," they will find one with little trouble, possibly just through a review of the literature. Kawano shows that the process is not like searching for a needle in a haystack. "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed[.]" *Wands*, 858 F.2d at 737.

On balance, although several factors are neutral and two factors favor Jennewein, the weightiest factor, the quantity of experiment necessary, favors Glycosyn, so much so that it outweighs the factors that favor Jennewein. Therefore, Jennewein has not shown by clear and convincing evidence that the asserted claims of the '018 patent are not enabled.

4. 35 U.S.C. § 112, ¶ 1 (Written Description)

In addition to lack of enablement, Jennewein argues "[c]laims 1-3, 5, 8, 10, 12, 18, 23, and 24 are also invalid for failing to satisfy the written description requirement of 35 U.S.C. § 112, ¶

[redacted]

1." (RIB at 110.) Specifically, Jennewein refers to the α-complementation technique used in its Accused Strains and argues "[i]f interpreted broadly enough (as Glycosyn does) to encompass α-complementation, the patent fails to show possession of the full scope of the term 'functional . . . β-galactosidase gene." (*Id.* at 111.) This argument is clearly conditioned on interpretation of the claims as covering α-complementation. (*See* RIB at 113 ("Glycosyn's argument that Jennewein literally infringes the '018 Patent requires the claims to literally encompass not just α-complementation, but also the unique form of α-complementation employed by Jennewein."); RRB at 58 ("As the written description requirement cannot be applied to equivalents, Jennewein is not conflating the written description requirement with the doctrine of equivalents."); *id.* ("If interpreted broadly enough . . . to include α-complementation, the specification fails to show possession of the full scope of the term 'functional . . . β-galactosidase gene . . . ."); SRB at 28-29 ("The Staff agrees with Jennewein that [α-complementation] does not *literally* infringe the asserted claims. . . . If the Administrative Law Judge adopts this interpretation of the claim language, then Jennewein's written description argument is moot.").) As explained above, Jennewein's α-complementation technique does not fall within the literal scope of "functional . . . β-galactosidase gene." Therefore, Jennewein has failed to prove that the claims in suit fail the written description requirement.

5. Inequitable Conduct

A patent may become unenforceable if "the applicant misrepresented or omitted material information with the specific intent to deceive the PTO." *Therasense*, 649 F.3d at 1287. According to Jennewein:

> Glycosyn intentionally withheld information that was plainly material to patentability and was known to it during prosecution of the '018 Patent and its parent (the '230 Patent). Co-inventor Dr. John McCoy intentionally withheld information that contradicted his affirmative representations to Examiner Rebecca Prouty, which she relied upon to grant the '018 patent

[redacted]

> Accordingly, inequitable conduct renders the Asserted Claims unenforceable.

(RIB at 118.) More specifically, Jennewein contends that Dr. McCoy knew of certain Glycosyn testing data that, as characterized by Jennewein, "reveals that bacterial strains having β-galactosidase activity within the claimed range of 0.05 to 200 Miller units actually failed to produce 2'-FL. . . . but chose not to disclose any of it to the Examiner." (RIB at 123.) Jennewein has not shown inequitable conduct by clear and convincing evidence, with respect to both materiality and intent.

Understanding why requires consideration of the prosecution history. On August 8, 2014, the Examiner rejected the claims of the application that would become the '230 patent "under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement." (JX-0002 at -2728.) The Examiner explained the rejection as follows:

> The specification includes no evidence that the presence of any modified *lacZ* gene wherein the bacterium has between 0.5 and 200 units of β-galactosidase activity when grown under inducing conditions is not detrimental to producing a fucosylated oligosaccharide as would be expected since β-galactosidase will degrade the lactose acceptor necessary for the fucosylation, yet the claims clearly encompass any functional β-galactosidase gene having up to 100 fold more β-galactosidase activity than the single disclosed species.

(*Id.* at -2730-1.) The Examiner issued a parallel rejection based on the same facts under enablement. (*See id.* at -2732-34.)

On February 9, 2015, Glycosyn amended the claims (JX-0002 at -2916-22) and provided a first declaration from Dr. John McCoy to overcome the written description and enablement rejections (*id.* at -2924-7). On May 8, 2015, the Examiner issued the same rejections. (JX-0002 at -2953-68.) With respect to the declaration, the Examiner stated:

> Applicants argue that the declaration of John McCoy shows that even relatively high levels of β-galactosidase produced by the *LacZ*$^{+}$ bacteria of FIG. 2 did not deplete the lactose pool such that the desired fucosylated

[redacted]

> oligosaccharide end product was not made by the engineered bacteria. However, this is not persuasive as the declaration does not show that the range of activity of the bacteria of Figure 2 of the declaration encompasses the claimed range of 0.05-200 units claimed. Without any indication of the level of B-gal activity present in the bacteria of Fig. 2 of the declaration, the declaration does not provide evidence that the claimed range of B-gal activities will not deplete the lactose pool such that the desired fucosylated oligosaccharide end product will not be made.

(JX-0002 at -2964-5.) The Examiner provided similar commentary in the context of the renewed enablement rejection. (*See id.* at -2966-8.)

On November 9, 2015, Glycosyn responded and amended the claims. (JX-0002 at -3025-31.) With respect to the § 112 rejections, and the previous declaration in particular, Glycosyn argued:

> Fig. 2 of the Declaration is a photograph of the art-recognized X-GAL colorimetric assay for β-galactosidase in which low levels of the enzyme appear as light blue colonies/streaks and high levels appear dark blue [,] thus providing an art-recognized and standard indication of β-galactosidase enzyme activity. Applicant's statement (copied above) also addresses the Examiner's concern that the claims may encompass bacteria that do not make the fucosylated oligosaccharide, stating that even relatively high levels of β-galactosidase produced by the LacZ+ bacteria (dark blue streaked colonies in Fig. 2) did not deplete the lactose pool such that the desired fucosylated oligosaccharide end product was not made by the engineered bacteria. In view of the foregoing clarifications and arguments, Applicant respectfully requests withdrawal of this rejection.

(JX-0002 at -3038-9.)

Following this, on January 22, 2016, the claims were again rejected on the same written description and enablement grounds. (*See* JX-0002 at -3044-53.) In the context of the alleged written description problem and the X-GAL assay image above, the Examiner stated:

> However, this is not persuasive as it is not clear how much β-galactosidase activity is necessary to obtain a light blue or dark blue color and a quick internet search by the examiner did not provide this information such that there is still no indication whether the colonies of Fig. 2 of the declaration span the claimed range or not.

[redacted]

(JX-0002 at -3051.) However, the Examiner invited Glycosyn to submit a declaration stating "that the bacteria of Figure 2 of [a] previous declaration all successfully produced fucosylated oligosaccharides and include strains with B galactosidase activities of about 20 units (or more)," and, if so submitted, "the examiner will withdraw the instant rejection." (JX-0002 at -3051.)

In April 2016, Dr. McCoy submitted the suggested declaration, containing data for three exemplary 2'-FL producing strains, E997, E890x416/pG217, and E890x422/pG217, and affirmatively stated that "good levels of 2'-FL are produced in all 3 strains." (RX-0396 at 3.) These strains had β-galactosidase activities of 1.5, 2.5, and 5.8 Miller Units, respectively. (*Id.*) The declaration also contained an extrapolation of the measured data to 200 Miller Units in graph form, accompanied by a statement that "even strains producing 200 Miller Units of galactosidase would be capable of producing significant levels of 2'-FL in the fermenter (>2g/L)." (RX-0396 at 4.) After filing the declaration, first in the prosecution of the '230 patent, and then in the prosecution of the '018 patent, all claims were allowed. (JX-0002 at -1750; JX-0004 at -304-310.)

Jennewein contends, in summary, that:

> Dr. McCoy withheld material information not once, but at least three times. First, he withheld the fact that the only strain with beta-galactosidase activity of about 200 Miller Units that Glycosyn had actually tested prior to McCoy's declaration in fact failed to make 2'-FL. CX-0053C at 7. Second, he withheld the fact that two strains that Dr. McCoy represented as producing 2'-FL actually failed to produce it reliably. *Id.* at 6. Third, demonstrating a pattern of lack of candor, he also withheld material information from the European Patent Office.

(RIB at 134-135.) I consider these points individually.

First, Jennewein argues that CX-0053C, a slide deck summarizing certain research and development activities and dated almost a year before Dr. McCoy's second declaration, shows no 2'-FL was created by a single strain [redacted] with approximately 200 Miller Units of β-galactosidase activity. (RIB at 125 (citing CX-0053C).) But

[redacted]

these test results were not germane to the invention, because the [redacted] strain was not comparable to the strains Dr. McCoy identified in this second declaration, for two reasons. First, the [redacted] made it a poor candidate for creating 2'-FL, regardless of its β-galactosidase activity. As Dr. Merighi, the creator of the slide deck, testified, [redacted] was a [redacted] so it was not fully expressing the pathway for making 2'-FL. So it didn't surprise me too much that we were not making it. I was hoping that we would make some." (Hr'g Tr. at 281:8-25; *see* CX-0053C at -117382 ("Next: Make a lon- version").) In contrast, each of the E997, E890x416/pG217, and E890x422/pG217 strains used as the basis for Dr. McCoy's declaration (and shown in CX-0053C) were [redacted] (*Id.* at 287:24-288:5.) Indeed, Dr. Merighi, a non-party, testified that comparing [redacted] and [redacted] is not meaningful. (*Id.* ("You showed me the slide, it was the [redacted] units. That was not ready for apple to apple comparison, because it was [redacted] correct. So these strains are all [redacted] so you can compare them.").) Second, it is not a mere "technicality" (RRB at 62) that the 2'-FL production rate in a large scale fermentor does not match smaller tube-scale runs. (*See, e.g.*, CX-0053C at -117379, -117381, -117388; CX-0488C at Q9, Q20-22, 39; Hr'g Tr. at 147:18-150:25, 295:20-296:23, 639:20-641:19, 725:14-727:9; RX-0409C at Q167.) Dr. McCoy, in particular, testified at length about the differences between the two test methods. (Hr'g Tr. at 147:18-150:25.) The fact that Dr. McCoy's declaration was in the context of the former (JX-0002 at -3211 ("significant levels of 2'FL in the fermentor")), whereas Dr. Merighi's experiment was the latter (CX-0053C at -117382 ("(tube scale)")), diminishes the relevance of the [redacted] result.

Second, Jennewein argues that of the three strains discussed in Dr. McCoy's declaration as producing "good levels of 2'-FL," CX-0053C shows two, E890x416/pg217 and E890x422/pG217,

[redacted]

actually failed to make 2'FL. (RIB at 132.) Jennewein bases this claim on the following line from CX-0053C:

(RIB at 132 (citing CX-0053C at -117381).) As Dr. McCoy testified, however, this comment could not have referred to testing of E890x416/pg217 and E890x422/pG217, because those tests (which are documented a few pages earlier in CX-0053C) did show 2'-FL production. (Hr'g Tr. at 115:1-2 (bullet point 5 is "clearly not referring to the ones that we were just looking at, because they produced 2'-FL").) And Dr. Merighi, the bullet point's author, testified that he was unsure what it referenced, but that he thought it was a distinct strain, [redacted] (*Id.* at 287:19-23.)

Third, Jennewein points to other β-galactosidase experimental data that Dr. McCoy did not submit to the USPTO, including one set that was submitted to the European Patent Office for similar prosecution purposes. (*See* RIB at 131-132 (citing RX-0067C; JX-0019C at 350:19-21 (non-designated)).) Jennewein asserts that Dr. McCoy "demonstrate[ed] a pattern of lack of candor" by withholding information from the European Patent Office. (RIB at 135.) But Jennewein makes no effort to demonstrate that he had a duty to disclose such allegedly withheld information to the EPO. (*See id.* at 134-135.) Moreover, the information pertains to a strain, E1277, that produced 2'-FL with β-galactosidase activity far outside the claimed range, and therefore of little relevance. (RIB at 131.) And Jennewein's discussion of the evidence cites principally to a 246-page laboratory notebook of Dr. McCoy, which appears to be admitted as CX-0025C, but without citing to page numbers. (*Id.* at 131-132.) Nor does it appear that Jennewein questioned Dr. McCoy about this exhibit during the hearing. On balance, Jennewein has failed to prove that Dr. McCoy withheld anything from the PTO regarding E1277, and I do not address this argument further.

[redacted]

Overall, Dr. McCoy's failure to disclose the [redacted] tube-run experiment and what Dr. Merighi believed was the [redacted] tube run, as recorded in CX-0053C, was not material to the patentability of the claims. The Federal Circuit has explained, "the materiality required to establish inequitable conduct is but-for materiality. . . . in assessing the materiality of [withheld information], the court must determine whether the PTO would have allowed the claim if it had been aware of the undisclosed [information]." *Therasense*, 649 F.3d at 1291-92. Admittedly, it was material to patentability whether the claims were enabled at 200 Miller units. But if Dr. McCoy's second declaration had included the challenged tube runs, and also explained why he subjectively did not consider them relevant, there is every reason to believe the Examiner would have allowed the claims.

And because of his subjective views of the two challenged tube runs, the requisite deceptive intent is also lacking. As acknowledged by both parties, a specific intent to deceive must be "the single most reasonable inference able to be drawn from the evidence." *Therasense*, 649 F.3d at 1290 (citation omitted). Dr. McCoy, who testified at the hearing with a confident but otherwise unremarkable demeanor, does not view the [redacted] test result and the [redacted] tube runs [redacted] bullet point in CX-0053C as contradicting the statements made in his second declaration; Jennewein, by contrast, offers only innuendo and case citations in support of deceptive intent. (*See generally* CX-0488C at Q19-39; RIB at 134-36.) The most reasonable inference to be drawn from the evidence is that Dr. McCoy sincerely believed that the challenged evidence was immaterial, and there is therefore no inequitable conduct.

V. DOMESTIC INDUSTRY - ECONOMIC PRONG

In a patent-based complaint, a violation of Section 337 can be found "only if an industry in the United States, relating to the articles protected by the patent ... concerned, exists or is in the process of being established." 19 U.S.C. § 1337(a)(2). Under Commission precedent, this

[redacted]

"domestic industry requirement" of Section 337 consists of an economic prong and a technical prong. *Stringed Instruments*, Inv. No. 337-TA-586, Comm'n Op. at 12-14. The complainant bears the burden of establishing that the domestic industry requirement is satisfied. *See Certain Set-Top Boxes and Components Thereof*, Inv. No. 337-TA-454, ID at 294 (June 21, 2002) (not reviewed by Commission in relevant part).

The economic prong of the domestic industry requirement is defined in subsection (a)(3) of Section 337 as follows:

> (3) For purposes of paragraph (2), an 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 or mask work 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). The economic prong of the domestic industry requirement is satisfied by meeting the criteria of any one of the three factors listed above. Importantly, the Commission has clarified that investments in plant and equipment, labor, and capital that may fairly be considered investments in research and development are eligible for consideration under subsections (A) and (B), in addition to subsection (C). *See Solid State Storage Drives*, Comm'n Op. at 14.

Here, Glycosyn alleges a domestic industry exists under all three factors. I agree.

A. Qualifying Investments

For subsection (A), and investments in plants specifically, the evidence shows Glycosyn conducted engineering, research and development activities related to the production of 2'-FL by *E. coli* bacteria at two domestic locations in Medford, Massachusetts and Woburn, Massachusetts between 2015 and the filing of the amended complaint in May 2018. (CX-0003C at Q11-14, 23,

[redacted]

39-41.) The evidence also shows Glycosyn spent approximately [redacted] per month in rent on each location, such that between January 1, 2015 and May 16, 2018, Glycosyn invested [redacted] in these facilities. (*Id.* at Q44-52; CX-0087C.) Glycosyn acknowledges that, between 2015 and May 2018, however, these locations were used for the development of 2'-FL as well as other compounds which do not fall under the scope of the asserted claims. (CIB at 128, 130-132; *see* CX-0003C at Q7, 23, 31-38; CX-0002C at Q93, 111.) In order to accommodate expenditures unrelated to the '018 patent, Glycosyn applies an allocation percentage to its facility investments, wherein said percentage is based on the amount of time its scientists at these locations spent on developing 2'-FL production per the '018 patent. (*See* CIB at 129-131 (citing, *inter alia*, CX-0003C at Q26, 27, 30-32, 44-53; CX-0002C at Q33, 93, 94; CX-0089C; CX-0087C).) The resulting claimed investment in facilities directed to the development of 2'-FL produced under the claims of the '018 patent is summarized in the below table:

[redacted]

The Staff agrees with this [redacted] figure as the amount in facilities expenses attributable to the '018 patent for purposes of domestic industry under subsection (A). (SIB at 117; SRB at 34.)

Jennewein's dispute with respect to this investment in facility is that "Glycosyn attributes all of that rent to its domestic industry expenditures, even though it conducts R&D related to other activities [redacted] at this facility." (RIB at 139; RRB at 67.) This point is not well taken; Glycosyn has reasonably apportioned its facilities expenses based on its labor expenses. In any event, Glycosyn's witness testimony on this issue (CX-0003C at Q30-53; CX-0002C at Q33, 92-

[redacted]

94) is credible and its documentary records (CX-0089C; CX-0087C) are reliable. Thus, I find the record supports a facility investment amount of [redacted] for purposes of domestic industry, subsection (A).

With respect to equipment under subsection (A), Glycosyn has presented evidence showing its various investments in equipment used at the Medford and Woburn locations discussed above. (*See* CIB at 132.) Glycosyn's witness testified that equipment purchases include "fermenter machines, a recirculate chiller/pressure reducer, Visiferm DO optical oxygen sensor, steam generator, sterilizers, a Biosat B plus Fermentation Control System, and a Touch Panel and Conversion Kit for the Biosat B equipment" as well as other equipment and tools attributable to the development of 2'-FL. (CX-0003C at Q55 (citing CX-0085C).) That witness also categorized each purchase in the year it was incurred (*id.* at Q56 (citing CX-0085C)), identified the costs expended with the maintenance of this and previously purchased equipment (*id.* at Q57 (citing CX-0085C)), and described depreciation costs incurred in 2017 for that equipment purchased prior to 2015 (*id.* at Q58 (citing CX-0086C)). Further, Glycosyn witnesses identified an additional equipment purchase for the two locations made on behalf of Glycosyn in 2016 by an organization called Glycosyn Health Initiatives, Inc., "an organization that provides funding, donations, and research sponsorship to various institutions in support of 2'-FL research experiments," which included "a Synergy H4 M_Pate Reader, an anaerobic chamber, camera, and freezer." (*Id.* at Q56.) Additional testimony elicited at the evidentiary hearing explained that Glycosyn Health Initiatives, Inc., a non-party, and Glycosyn, the complainant, have "interlocking leadership and board members." (Hr'g Tr. at 28:22-29:23.) In sum, the claimed investments in equipment at Glycosyn's research and development facilities are summarized in the below table:

[redacted]

The Staff essentially agrees with this [redacted] figure as the amount in equipment investment attributable to the '018 patent for purposes of domestic industry under subsection (A). (SIB at 118 (calculating [redacted]); SRB at 34 (calculating [redacted])

Jennewein's dispute with respect to this investment in equipment is that it includes amounts "wholly unrelated to Glycosyn's 2'-FL R&D efforts" because there is no apportionment between "activities related to 2'-FL and activities related to other molecules unrelated to the claims of the '018 patent." (RIB at 139; *see* RRB at 68.) Jennewein provides examples of a security alarm system, certain sterilizers, and a fermentation control system as equipment which a Glycosyn witness admitted at the hearing may not be solely related to 2'-FL development. (*See* RIB at 139 (citing Hr'g Tr. at 52:14-21, 52:22-27, 53:8-17).) Jennewein further argues, *inter alia*, the timing of Glycosyn's switch to development of the [redacted] in mid-2017, as compared to several equipment purchases after this time, shows "Glycosyn's equipment expenses are therefore suspect and should be disregarded as unreliable." (*See id.* at 139-140.)

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[6] Both Glycosyn and the Staff incorrectly report this amount as [redacted]. (CIB at 132; SIB at 118.) It is understood that this is a typo; [redacted] would be the correct rounding-up of [redacted]

[redacted]

Here, I find Jennewein's criticisms have merit. Of primary importance, Glycosyn directly acknowledges, and the evidence shows, that its concentration on 2'-FL greatly diminished following July 2017. (*See* CX-0089C at -74622 (showing scientist time changing from 100% to 25%); CX-0002C at Q93 ("Around the end of 2017, our project with [redacted] started [redacted] of Glycosyn's resources went there starting around mid-2017.").) It is natural to assume, therefore, that the use of its equipment for 2'-FL development similarly diminished; yet Glycosyn has not applied any allocation percentage in the way it had done for facility and labor.

The Staff agrees that Glycosyn has not done this but contends applying the 2'-FL allocation percentage derived from labor records makes little difference. (SRB at 35.) In its reply brief, Glycosyn similarly does not dispute that no allocation was applied or that one should have been. (*See* CRB at 66.)

Given the record, and Glycosyn's application of an allocation to both of its facility and labor expenses, I find the same allocation should be applied to equipment. Glycosyn's witness does not sufficiently make clear that every item listed in the equipment record, CX-0085C, has been used solely for 2'-FL development work (*see* CX-0093C at Q54-59), which is important given the clear recognition that only [redacted] of scientists' time in 2017 and [redacted] in 2018 was related to 2'-FL (*see* CIB at 130-131). I do not agree, however, that this failure to allocate means all of the equipment investments are unreliable and should be disregarded, as Jennewein urges. When applied, Glycosyn's domestic investment in equipment, for purposes of subsection (A), becomes:

[redacted]

[redacted]

With respect to labor under subsection (B)[8], the evidence shows Glycosyn employed several scientists and corporate officers between 2015 and May 2018 to develop and improve manufacturing methods of 2'-FL under the '018 patent, with respect to both bacterium engineering and fermentation procedures. (*See* CIB at 125-133; CX-0002C at Q92-122; CX-0089C.) A Glycosyn witness identified, for each of these employees, "allocated amounts of salaries and benefits per year [] based on the percentage of time each individual employee spent dedicated to 2'-FL" in each of the years 2015 through May 2018. (CX-0003C at Q31-37 (citing CX-0089C).) That witness, Howard Newburg, explained that the allocation of time for the scientists, as reflected in CX-0089C, was created by one of the scientists, Dr. John McCoy, whereas he generated the allocation for corporate officers. (CX-0003C at Q32; *see* CIB at 130 (citing, *inter alia*, CX-0002C at Q93-94).) The document, CX-0089C, reflecting the allocations of time spent towards 2'-FL shows percentages of either [redacted] depending on the employee, prior to July 2017; and percentages of [redacted] or [redacted] depending on the employee, for July 2017 through May 2018. (CX-0089C at -74621-2.) The resulting claimed investment in labor directed to the development of 2'-FL produced under the claims of the '018 patent is summarized in the below table:

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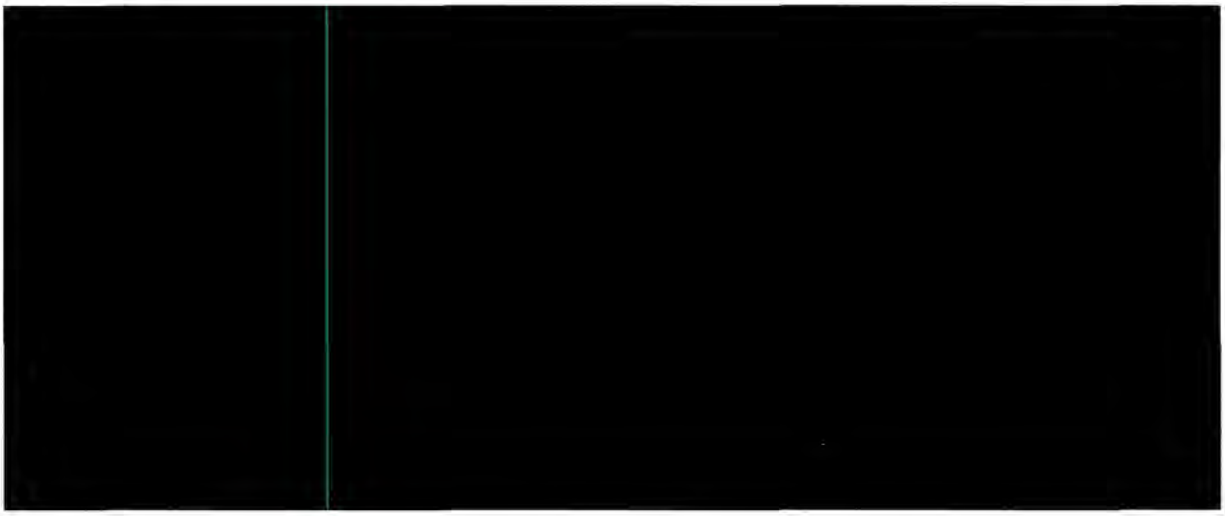
7 *See* FN 6.

8 As described below, Glycosyn names a fourth category of expenses as "Research and Development" and considers them as subsection (C) expenditures, rather than capital expenditures under subsection (B). (*See* CIB at 132-133, 138-140.)

[redacted]



The Staff agrees with this [redacted] figure as the amount in labor investment attributable to the '018 patent for purposes of domestic industry under subsection (B). (SIB at 120; SRB at 34.)

Jennewein's dispute with respect to this investment in labor is three fold. First, Jennewein criticizes Glycosyn for failing to break out labor associated with [redacted] to foreign corporation FrieslandCampina. (*See* RIB at 140-143.) Jennewein claims this assistance cannot be counted for multiple, disparate, reasons: (1) because it "reflect[s] work done outside of the U.S. [redacted] (2) "because it has not established that FrieslandCampina is practicing any claims of the '018 patent"; and (3) because FrieslandCampina did not sufficiently participate in discovery such that Glycosyn "[did not] request assistance from FrieslandCampina, Glycosyn cannot now rely on any activities related to FrieslandCampina in support of its domestic industry." (*See id.*) These arguments lack merit. That Glycosyn's research and development of 2'-FL production has some relation, or value, to FrieslandCampina does not take away from the fact that the investments occurred in the United States and have a connection to the '018 patent. Similarly, Jennewein cites no authority for discounting the labor costs of a domestic employee when that employee temporarily travels overseas and does work in a foreign location. Such hyper-particularity is not consistent with Commission precedent. *Stringed Instruments*, Inv. No. 337-

[redacted]

TA-586, Comm'n Op. at 26 ("[a] precise accounting is not necessary; as most people do not document their daily affairs in contemplation of possible litigation."). Even then, the record only supports finding that such physically-overseas [redacted] would have been a few days of labor. (*See generally* Hr'g Tr. at 60:18-61:1, 43:1-23, 50:7-51:23; CX-0003C at Q13-21; CX-0002C at Q92-94, 120, 122.) Nonetheless, the Staff's "understand[ing of] Mr. Newburg's testimony to mean that hours worked outside the United States were not included in Glycosyn's economic prong calculations" (SRB at 36 (citing Hr'g Tr. at 60:11-61:1)) is likely incorrect. CX-0089C is a record of gross wages and benefits paid to Glycosyn employees, not hours worked. (*See* CX-0089C at -74621-2.) Thus, unless employees who traveled and worked overseas were compensated apart from these gross wages, that expense is included in Glycosyn's economic prong calculations. And the fact that FrieslandCampina did not participate in discovery and may or may not be practicing the '018 patent outside the United States is irrelevant.

Jennewein's second criticism of the claimed labor investment is that it improperly includes general and administrative expenses. (RIB at 142 (citing *Certain Clidinium Bromide & Prods. Containing Same,* Inv. No. 337-TA-1109, Order No. 11 at 5-6 (July 25, 2018) (public version) ("*Clidinium Bromide*"); *Certain Kinesiotherapy Devices & Components Thereof,* Inv. No. 337-TA-823, Comm'n Op. at 29 n.8 (June 17, 2013) ("*Kinesiotherapy Devices*"), *rev'd on other grounds*, *Lelo*, 786 F.3d 879).) To make the argument, however, Jennewein conflates general and administrative expenses in support of domestic engineering with the more commonly prohibited sales and marketing expenses of an importer—and it is the latter which Jennewein's cited caselaw is concerned with. *See, e.g.*, *Clidinium Bromide*, Inv. No. 337-TA-1109, Order No. 11 at 5-6 ("Paying wholesalers to distribute pharmaceutical products is a cost of sale borne by pharmaceutical manufacturers selling to those entities, regardless of whether or not the

[redacted]

pharmaceutical is imported or made domestically. . . . [The] fees are nothing more than standard U.S. expenses of a mere importer, which should not be considered in a domestic industry analysis."). Even then, the Commission has shown latitude in including sales, marketing, or general administrative investments when they are provided in support of other qualifying activities:

> In the case at hand, PopSockets is not relying solely on marketing and sales expenditures to satisfy the economic prong. While PopSockets has included sales and marketing expenditures, it has also provided evidence of significant expenditures in its employment of labor in other qualifying activities, such as engineering, product development, product assembly, supply chain and operation management, and customer service, as well as capital expenditures for fixtures, furniture, software, and equipment used for design, engineering, and operation management, which are sufficient to establish the existence of a domestic industry under subsection (B).

Certain Collapsible Sockets for Mobile Electronic Devices and Components Thereof, Inv. No. 337-TA-1056, Comm'n Op. at 19-20 (July 9, 2018) (public version).

Jennewein's third criticism of the claimed labor investment is that Glycosyn's allocation percentage of time spend on 2'-FL is flawed and unreliable, pointing to testimony from Dr. Merighi, an ex-employee of Glycosyn, where he explained that "he did not devote all of his time to 2'-FL" [redacted] (RIB at 141 (citing Hr'g Tr. at 292:1-14).) Jennewein contrasts this with the record of CX-0089C, where [redacted] of Dr. Merighi's time is listed as spent on 2'-FL. (CX-0089C at -74621.) Neither the Staff nor Glycosyn addresses this discrepancy in their post-hearing briefs. (*See* CIB at 124-140; CRB at 64-68; SIB at 114-125; SRB at 33-39.) An expanded view of the testimony shows there many not necessarily be a conflict. Dr. Merighi states that at times he would have been [redacted] focused on 2'-FL or [redacted]

> Q. Just a couple more questions. At Glycosyn you worked on projects other than 2'-FL, correct?

[redacted]

A. Yes.

[redacted]

Q. So you didn't spend 100 percent of your time working on 2'-FL at Glycosyn, correct?

A. If you did – if the time is – what is – the five, six years? No. But I had like this big spring sometime where it would be [redacted] percent of my week was on 2'-FL [redacted]

Q. And then other times you would be devoted to other projects?

A. Yes, yes. I think at this time if you look at my notebook, it would be like a mix of – because we had to – we were supposed to keep the book in a chronological order, so you will see how much time I was doing one thing or the other. Just count the pages, because it's pretty much in chronological order.

(Hr'g Tr. at 292:1-19.) I therefore do not find this to be a reason to consider Glycosyn's records flawed or unreliable, and I determine that [redacted] of labor investment is attributable to the '018 patent for purposes of domestic industry under subsection (B).

With respect to research and development under subsection (C), Glycosyn's claimed investment includes the aforementioned plant, equipment, and labor expenses[9] in addition to a fourth category of miscellaneous research and development expenses allegedly attributable to 2'-FL development in the relevant time period of 2015 through May 2018. (CIB at 132-133, 138-140.) A Glycosyn witness identified these expenses as: (1) "costs for the FDA's GRAS assessment of Glycosyn's purified 2'-FL for the U.S. market"; (2) "manufacturing run of a test batch of 2'-FL [redacted] (3) "lab supplies purchased for use in Glycosyn's R&D of 2'-FL"; (4) "software subscriptions for its laboratory facilities, for Glycosyn scientists' use in their research and development efforts"; and (5) domestic travel

[9] For subsection (C) only, Glycosyn excludes its general and administrative labor costs.

[redacted]

expenses in "technical marketing efforts [redacted] (CX-0003C at Q61-65 (citing CX-0091C; CX-0092C; CX-0093C; CX-0094C; CX-0095C).) Of these, Glycosyn's witness applied the time allocation percentages derived from the labor to only the software subscriptions, to accommodate any usage not attributable to 2'-FL development. (*Id.* at Q63.) The resulting amounts of these miscellaneous investments are summarized in the below table:

[redacted]

Further, in light of subsection (C)'s requirement that a complainant must show a nexus between the research and development investment and the invention of the asserted patent, *see, e.g.*, *Solid State Storage Drives*, Inv. No. 337-TA-1097, Comm'n Op. at 14, Glycosyn applied a second allocation percentage "according to the proportion of Glycosyn's 2'-FL fermentation runs of using 2'-FL strains that practice the patented technology, as opposed to other 2'-FL strains." (CIB at 138.) A second Glycosyn witness testified that, based on a record of all fermentation runs since August 2015: [redacted] of 2'-FL runs in 2015 were done with '018 patent practicing bacteria strains; [redacted] of 2'-FL runs in 2016; [redacted] of 2'-FL runs in 2017; and [redacted] of 2'-FL runs in

[10] The documents reflecting purchases of lab supplies, CX-0093C through CX-0095C, are limited to the years 2015, 2016, and 2017.

[redacted]

2018. (CX-0002C at Q111 (citing CX-0131C); *see* CX-0002C at Q113.) Glycosyn further removed the labor costs associated with its general and administrative officers. (CIB at 138.) The resulting table of investments, for all categories Glycosyn alleges qualify for subsection (C), is as follows:

The Staff finds a [redacted] figure as the amount in research and development investment attributable to the '018 patent for purposes of domestic industry under subsection (C). (SIB at 122; *see* SRB at 34, 38.) In reaching this amount, which is higher than Glycosyn's, I understand the Staff either takes the position that general and administrative labor can be included or did not observe that Glycosyn removed this item.

Here, Jennewein's dispute is a general assertion that "Glycosyn has failed to provide sufficient evidence on the extent of any nexus between its investments and the '018 patent." (RIB at 142 (citing *Integrated Circuit Chips*, Inv. No. 337-TA-859, Comm'n Op. at 38 (Aug. 22, 2014) (public version)).) Jennewein does not, however, acknowledge Glycosyn's two-tier application of a 2'-FL-related allocation percentage (based on labor) and then a '018 patent-practicing allocation

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11 *See* FN 6.

[redacted]

percentage (based on fermenter runs) to its investments. I find this two-step allocation is probative of the value of investment related to the invention of the '018 patent; *i.e.*, the required "nexus." *Integrated Circuit Chips*, Comm'n Op. at 42 (holding domestic industry under subsection (c) can ordinarily be inferred from investment in a practicing [method] and "[r]equiring an extensive inquiry as to the adequacy of nexus when it is not challenged on the merits by respondents would unduly consume [] time and resources . . . ."). Again, Jennewein does not appear to dispute Glycosyn's claim of which strains, and thus which of its fermentation runs, practice the claims of the '018 patent.

I also find nexus based on the nature of Glycosyn's activities at its Massachusetts locations as compared to the subject matter of the asserted claim limitations. Glycosyn's activities, such as "all aspects of continued genetic engineering on our *E. coli* strains" and "improving the fermentation process for our production strains" (CX-0002C at Q92) relate directly to claim limitations, such as "providing an isolated *E. coli* bacterium comprising, (i) a deletion or functional inactivation of an endogenous β-galactosidase gene," "culturing said bacterium in the presence of lactose," and "retrieving a fucosylated oligosaccharide form said bacterium or from a culture supernatant of said bacterium" ('018 patent at cl. 1).

I therefore find the record supports Glycosyn's claimed investment amount in research and development with a nexus to the claims of the '018 patent, with certain exceptions. In the same way that software subscriptions were adjusted using the labor allocation percentages, and equipment investment more reasonably should have been (discussed above), I find Glycosyn's laboratory research and development supplies should be as well. Glycosyn's witness does not sufficiently make clear that every item listed in the purchase records, CX-0093C through CX-0095C, was solely for 2'-FL development work (*see* CX-0093C at Q62), which is important given

[redacted]

the clear recognition that only [redacted] of scientists' time in 2017 and [redacted] in 2018 was related to 2'-FL (*see* CIB at 130-131). When that allocation is applied, the record supports a research and development investment with a nexus to the claims of the '018 patent of [redacted] as in the below tables:

[redacted]

[redacted]

12 *See* FN 10.

13 *See* FN 6.

[redacted]

Finally, Jennewein makes an overall claim, seemingly against all of Glycosyn's investments, that "Glycosyn was no longer involved in that research at the time the Amended Complaint was filed, and had already moved to other projects" such that "Glycosyn cannot rely on R&D that was discontinued at the time of filing its Amended Complaint in support of domestic industry." (RIB at 143.) Jennewein contends "[p]ast expenditures may only be used to support a domestic industry claim if the complainant 'is continuing to make qualifying investments at the time the complaint is filed.'" (*Id.* (citing *Television Sets, Television Receivers, Television Tuners, and Components Thereof*, Inv. No. 337-TA-910, Comm'n Op. at 68 (Oct. 30, 2015) ("*Television Sets*"); *Motiva, LLC v. Int'l Trade Comm'n*, 716 F.3d 596, 601 n.6 (Fed. Cir. 2013)).)

I do not agree. Jennewein's sole support for this alleged cessation of activity is a line from a Glycosyn witness's deposition, which does not support the argument. (*See* RIB at 143 (citing JX-0020C at 151:20-152:3).) There, the witness testified, "Q. And for the second half of 2018, what do you expect will be the allocations of the employees for 2-FL [redacted]? A. I think there's still, at least a [redacted] (JX-0020C at 151:20-152:3.) I find additional evidence shows Glycosyn continues to make qualifying investments in 2'-FL. For example, the same witness testified that [redacted] "to continue the research in 2'-FL" (Hr'g Tr. at 44:20-45:13), and Glycosyn's records show it continued with 2'-FL fermentation runs throughout 2018 (*see* CX-0002C at Q113).

B. "Significant" or "Substantial"

The next step in the evaluation of domestic industry is to determine if the investment amounts identified above are "significant," as in subsections (A) and (B), or "substantial," as in subsection (C). The most recent precedential decision by the Court of Appeals for the Federal

[redacted]

Circuit addressing this determination is *Lelo*, which restated law applicable to a number of issues surrounding the economic prong of domestic industry. *See* 786 F.3d at 883-85. In particular, the Federal Circuit held that the statutory terms "'significant' and 'substantial' refer to an increase in quantity, or to a benchmark in numbers" and "[a]n 'investment in plant and equipment' therefore is characterized quantitatively, *i.e.*, by the amount of money invested in the plant and equipment." *Lelo*, 786 F.3d at 883. Continuing, the Federal Circuit held that: "[a]ll of the foregoing requires a quantitative analysis in order to determine whether there is a 'significant' increase or attribution by virtue of the claimant's asserted commercial activity in the United States." *Id.* In short, "Qualitative factors cannot compensate for quantitative data that indicate insignificant investment and employment." *Id.* at 885.

I find Glycosyn's investments in plant, equipment, and labor are "significant." Glycosyn conducts virtually all of its research and development in the United States, and has provided records showing its foreign expenses constitute a *de minimis* [redacted] in travel costs. (CX-0003C at Q64.) When compared against this [redacted] Glycosyn's domestic facility, equipment, and labor investment of [redacted] in facilities, [redacted] in equipment, [redacted] in labor) must provide a "'significant' increase or attribution" of value to its 2'-FL development under the rubric set by *Lelo*. 786 F.3d at 883. There is simply no other source but domestic activity to credit.

Moreover, the record shows Glycosyn's investment with respect to 2'-FL is significant even unto itself. A Glycosyn witness testified, using profit and loss schedules, that its company-wide operating expenses over the relevant time period total [redacted] (CX-0003C at Q67, 68; CX-0088C.) I have no trouble concluding Glycosyn's [redacted] in 2'-FL facility, equipment, and labor cost is a significant portion of this company-wide investment. For the same reasons, I

[redacted]

conclude Glycosyn's [redacted] in research and development costs with a nexus to the claims of the '018 patent are "substantial."

Jennewein's dispute over significance, and substantiality, is mainly that "the roughly [redacted] Glycosyn contends it invested in a domestic industry for the '018 patent since 2015 pales in comparison to the [redacted] at least, investment FrieslandCampina has made for its 2'-FL production facility [redacted]" (RIB at 141 (citing Hr'g Tr. at 46:13-16).) While this may be true, I disagree that this inter-company comparison is more indicative of significance (or lack thereof) than, for example, a comparison of Glycosyn's domestic versus foreign expenditures. It is also important to consider that the domestic industry article in question is not the 2'-FL which FrieslandCampina will produce, but the 2'-FL produced by Glycosyn in the United States under the methods of the '018 patent. (*See* CIB at 15, 92 (citing CX-0059C; CX-0131C; CX-0064C).) It cannot be reasonably disputed that Glycosyn's investments have significantly contributed, in a quantitative sense, to that production.

Jennewein also argues "[e]ven taken in their totality, the whole of Glycosyn's investments and employment are [redacted] Any investments and employment that would relate to exploitation of the '018 patent are [redacted] and Glycosyn has not offered any context for concluding that those investments would be 'significant' or 'substantial.'" (*Id.* at 144.) To the contrary, [redacted] is not a trivial amount and Glycosyn offered each of the quantitative contexts discussed above—comparison to its company-wide operating expenses and comparison to foreign expenditures. (CIB at 135-136, 139-140.)

Accordingly, I find Glycosyn satisfies the economic prong of domestic industry under each of subsections (A), (B), and (C).

[redacted]

VI. CONCLUSIONS OF LAW

1. The Commission has *in rem* jurisdiction over the Accused Product, 2'-FL.

2. The importation or sale requirement of Section 337 is satisfied.

3. Glycosyn has been shown to practice claims 1-3, 5, 8, 10-14, 18, 22, and 24-28 of U.S. Patent No. 9,970,018.

4. Glycosyn has not been shown to practice claims 9 or 23 of the '018 patent.

5. The domestic industry requirement is satisfied with respect to the '018 patent.

6. Jennewein directly infringes claims 1-3, 5, 8, 10, 12, 18, and 24-28 of the '018 patent.

7. Jennewein does not infringe claim 23 of the '018 patent.

8. No claims of the '018 patent have been shown to be invalid under 35 U.S.C. § 103.

9. No claims of the '018 patent have been shown to be invalid under 35 U.S.C. § 112.

10. The '018 patent has not been shown to be unenforceable.

11. There is a violation of Section 337 with respect to the '018 patent.

VII. RECOMMENDED DETERMINATION ON REMEDY AND BOND

The Commission's Rules provide that subsequent to an initial determination on the question of violation of section 337 of the Tariff Act of 1930, as amended, 19 U.S.C. § 1337, the administrative law judge shall issue a recommended determination concerning the appropriate remedy in the event that the Commission finds a violation of section 337, and the amount of bond to be posted by respondent during Presidential review of the Commission action under section 337(j). *See* 19 C.F.R. § 210.42(a)(1)(ii).

The Commission has broad discretion in selecting the form, scope, and extent of the remedy in a section 337 proceeding. *Viscofan, S.A. v. Int'l Trade Comm'n*, 787 F.2d 544, 548 (Fed. Cir. 1986). Under Section 337(d)(1), if the Commission determines as a result of an investigation that there is a violation of section 337, the Commission is authorized to enter either

[redacted]

a limited or a general exclusion order. 19 U.S.C. § 1337(d)(1). A limited exclusion order instructs the U.S. Customs and Border Protection ("CBP") to exclude from entry all articles that are covered by the patent at issue and that originate from a named respondent in the investigation. A general exclusion order instructs the CBP to exclude from entry all articles that are covered by the patent at issue, without regard to source. *Certain Purple Protective Gloves*, Inv. No. 337-TA-500, Comm'n Op. at 5 (Dec. 22, 2004). Under section 337(f)(1), the Commission may issue a cease and desist order in addition to, or instead of, an exclusion order. 19 U.S.C. § 1337(f)(1). The Commission generally issues a cease and desist order directed to a domestic respondent when there is a "commercially significant" amount of infringing, imported product in the United States that could be sold, thereby undercutting the remedy provided by an exclusion order. *See Certain Crystalline Cefadroxil Monohydrate*, Inv. No. 337-TA-293, USITC Pub. 2391, Comm'n Op. on Remedy, the Public Interest and Bonding at 37-42 (June 1991); *Certain Condensers, Parts Thereof and Prods. Containing Same, Including Air Conditioners for Automobiles*, Inv. No. 337-TA-334 (Remand), Comm'n Op. at 26-28, 1997 WL 817767, at *11-12 (U.S.I.T.C. Sept. 10, 1997).

Additionally, during the 60-day period of Presidential review under 19 U.S.C. § 1337(j), "articles directed to be excluded from entry under subsection (d) . . . shall . . . be entitled to entry under bond prescribed by the Secretary in an amount determined by the Commission to be sufficient to protect the complainant from any injury." *See* 19 U.S.C. § 1337(j)(3). "The Commission typically sets the bond based on the price differential between the imported infringing product and the domestic industry article or based on a reasonable royalty. However, where the available pricing or royalty information is inadequate, the bond may be set at one hundred (100) percent of the entered value of the infringing product." *Certain Industrial Automation Systems and Components Thereof Including Control Systems, Controllers, Visualization Hardware,*

[redacted]

Motion and Motor Control Systems, Networking Equipment, Safety Devices, and Power Supplies, Inv. No. 337-TA-1074, Comm'n Op. at 13 (Apr. 23, 2019) ("*Automation Systems*") (public version) (citation omitted).

Section 337 also mandates consideration of the effect of exclusion on (1) public health and welfare; (2) competitive conditions in the U.S. economy; (3) U.S. production of articles that are like or directly competitive with the articles subject to the investigation; and (4) U.S. consumers. 19 U.S.C. § 1337(d)(1). By publication in the *Federal Register*, the Commission has instructed me "to take evidence or other information and hear arguments from the parties and other interested persons with respect to the public interest in this investigation, as appropriate, and provide the Commission with findings of fact and a recommended determination on this issue, which shall be limited to the statutory public interest factors set forth in 19 U.S.C. 1337(d)(1), (f)(1), (g)(1)." 83 Fed. Reg. 28,865 (June 21, 2018).

A. LIMITED EXCLUSION ORDER

Should a violation be found, Glycosyn seeks a limited exclusion order "against the subject article, 2'-FL." (CIB at 147.) Glycosyn argues against any carve-out for 2'-FL made by any particular strain number in light of a general reluctance from the Commission to identify model numbers in exclusion orders (*id.* at 148 (citations omitted)) and the record evidence showing the only strain Jennewein actually uses to create imported 2'-FL is its #1540 strain (*id.* (citing, *inter alia*, RX-0387C at Q71, 75, 131-132; CX-0215C at 7)). The Staff agrees with Glycosyn here. (SRB at 40-41.)

Similarly, Glycosyn argues against a certification provision based on its view that there is no other strain "that does not infringe the '018 Patent, that is sufficiently fixed in design (and with regulatory approval) for sale to the United States market for foodstuffs." (*Id.* at 149 (citing *Certain*

[redacted]

Self-Cleaning Litter Boxes and Components Thereof, Inv. No. 337-TA-625, Comm'n Op. at 59-[60] (Apr. 28, 2009)).) Glycosyn also argues Jennewein is most likely incapable of so certifying. (*See* CRB at 71-72.) If a certification is used, Glycosyn insists that Jennewein should nonetheless be prohibited from importing 2'-FL for use in foodstuffs until "all necessary regulatory approval" has been granted (*id.*), and that Glycosyn should be afforded rights to audit Jennewein's production facilities (*id.* at 150). The Staff does not agree with the above proposals. (SRB at 41-42.)

Jennewein seeks a carve-out from a limited exclusion order for its TTFL12 strain for reasons of non-infringement, as well as a certification provision. (RIB at 144-145.) Jennewein argues that the process nature of the patent at issue, the '018 patent, is not grounds to refuse a certification provision. (*Id.* at 145 (citing *Certain Salinomycin Biomass & Preparations Containing Same Recommended Determination on Remedy & Bonding*, Inv. No. 337-TA-370 (Dec. 13, 1995); *Certain Acid-Washed Denim Garments and Accessories, Including Jeans, Jackets, Bags and Skirts*, Inv. No. 337-TA-324, Comm'n Op. at 22-23 (Aug. 14, 1992)).) Jennewein contends it is capable of providing such information. (*Id.* (citing Hr'g Tr. at 348:10-21).) Jennewein also challenges Glycosyn's premise that any regulatory approval is needed at all before 2'-FL from additional bacterial strains can be imported or sold (RRB at 71-74) and argues the requested audit rights are inappropriate on a number of grounds (*id.* at 75).

As determined above, a violation of Section 337 has taken place, and I therefore recommend to the Commission that a limited exclusion should issue according to statute. 19 U.S.C. § 1337(d)(1). As to those positions taken by Glycosyn on additional provisions for the exclusion order, I do not agree. Glycosyn's requested audit rights are without precedent and its request for prohibitions on importation until regulatory approvals have been met intrudes on the Food and Drug Administration's authority—in addition to placing an inordinate burden on the

[redacted]

Commission. I do not recommend the Commission include either provision in any limited exclusion order.

Certification presents a difficult question. The record evidence shows that 2'-FL produced by a first process is essentially indistinguishable from 2'-FL produced by another. (*See, e.g.*, Hr'g Tr. at 350:20-351:2; RX-0406C at Q60; CX-0002C at Q121; JX-0011 at 145:15-18 ("Q. Once Jennewein's 2'-FL is in powder form, is there any way to – to determine, using that powder, which strain was used to produce that 2'-FL? A. No.").) As the '018 patent is strictly a method patent, this creates two problems. First, there is no way for Customs and Border Patrol to discern on their own whether 2'-FL was made by an infringing process or not. Second, there is likely no way for Glycosyn to ascertain for itself whether Jennewein violates any exclusion order from importation records alone. (*See* CPB at 147-148 (describing knowledge gained through GRAS submission).) And Jennewein's ability to import 2'-FL (or any "fucosylated oligosaccharide") made under a non-infringing process must be maintained as well.

Accordingly, I see some sort of certification provision necessary, with certain heightened requirements. I therefore recommend the Commission include a certification provision, wherein said certification is required to state with particularity the grounds of non-infringement of the imported oligosaccharide and be accompanied by sufficient corroborating evidence of the type provided in discovery in this investigation.

B. BOND

Regarding bond during the presidential review period, the parties have stipulated to a 5% bond on Jennewein's 2'-FL during the 60-day-Presidential review period. (CIB at 150 (citing JX-0007); RIB at 145.) This is a reasonable amount to protect Glycosyn from harm during the review

[redacted]

period. Accordingly, I recommend the Commission set a bond in the amount of 5% of entered value.

C. PUBLIC INTEREST

Regarding the statutory public interest factors, Glycosyn contends there is no evidence of any significant adverse effects from an exclusion order. (CIB at 140-147.) Regarding health and welfare, Glycosyn argues "the evidence does not show that any of the infant formula products on the market today [redacted] (CIB at 140-141 (citing Hr'g Tr. at 26:23-28:21, 31:5-33:21; CX-0001C at Q37-50, 57-58; RX-0406C at Q86).) Thus, as of today, Glycosyn adds, Jennewein's 2'-FL "is not essential to the health and safety of babies in the United States, or necessary for any important public health or welfare need . . . ." (*Id.* at 141.) Regarding competitive conditions, Glycosyn notes that "infant formula supplemented with 2'-FL [] was introduced to the market only recently" (*id.* at 143 (citing, *inter alia*, JX-0010C at 30:1-23 ("It is very difficult to make any forecasts at this early stage about possible sales figures because it's a completely new product."))) and of the many infant formula products available, only a few contain small amounts of 2'-FL (*see id.* at 143-144). Glycosyn also identifies "numerous alternative, non-infringing 2'-FL producers that can step in and replace the excluded products, such as Glycosyn/FrieslandCampina, DuPont/Inbiose, Glycom, and eventually, BASF." (*Id.* at 146.) The Staff agrees with Glycosyn on these points. (SIB at 127-134.)

Jennewein emphasizes 2'-FL's "critical role[]" in infant development and the benefits of including it in infant formula, keeping in mind that Jennewein was the first and is the only company selling 2'-FL in the U.S. (RIB at 136-137 (citing RX-0358C at Q188).) Jennewein asserts that "Glycosyn makes no competitive products that could replace Jennewein's 2'-FL if it were

[redacted]

excluded from the U.S" (*id.* at 137 (citing, *inter alia*, Hr'g Tr. at 57:1-4, 57:22-58:3)), and "Glycosyn provided no evidence that alternate suppliers can replace Jennewein's 2'-FL in a commercially reasonable time or in sufficient quantities" (*id.* at 138).

Based on the record, I do not find the requested limited exclusion order would meaningfully impact public health and welfare, competitive conditions, domestic production of articles, or U.S. consumers. While it is clear that the purpose of providing 2'-FL in infant formula is to improve public health, the evidence shows that the otherwise well-established market has only recently begun including 2'-FL into its products, [redacted] The U.S. public is therefore not dependent on such products, as of yet. Moreover, assuming Jennewein is the only supplier of 2'-FL to the U.S. market, then all infant formula manufacturers or vendors in the U.S. will be affected equally—along with the consumers who purchase those formula products. To the extent these entities wish to continue using 2'-FL in their formula, the Staff, in particular, has persuasively shown that the demand can be met by competitors. (*See* SIB at 129-131 (citing, *inter alia*, RX-0327C at 25; CX-0009; CX-0011), 132; SRB at 43-44.)

Accordingly, it is my recommended determination that issuance of a remedial order in this investigation would not be contrary to the public interest.

[redacted]

VIII. INITIAL DETERMINATION AND ORDER

Based on the foregoing,[14] it is my Initial Determination that there is a violation of Section 337 of the Tariff Act of 1930, as amended, 19 U.S.C. § 1337, in the importation into the United States, the sale for importation, or the sale within the United States after importation of certain human milk oligosaccharides and methods of producing the same, in connection with the asserted claims of U.S. Patent No. 9,970,018.

Furthermore, it is my determination that a domestic industry in the United States exists that practices or exploits the asserted patent.

The undersigned hereby certifies to the Commission this Initial Determination, together with the Record of the hearing in this investigation consisting of the following: the transcript of the evidentiary hearing, with appropriate corrections as may hereafter be ordered; and the exhibits accepted into evidence in this investigation as listed in the appendices hereto.[15]

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.

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[14] The failure to discuss any matter raised by the parties or any portion of the Record herein does not indicate that said matter was not 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 brief which were otherwise unsupported by Record evidence or legal precedent have been accorded no weight.

[15] The pleadings of the parties filed with the Secretary need not be certified as they are already in the Commission's possession in accordance with Commission rules.

[redacted]

Confidentiality Notice:

This Initial Determination is being issued as confidential, and a public version will be issued pursuant to Commission Rule 210.5(f). Within seven (7) days of the date of this Initial Determination, the parties shall jointly submit: (1) a proposed public version of this opinion with any proposed redactions bracketed in red; and (2) a written justification for any proposed redactions specifically explaining why the piece of information sought to be redacted is confidential and why disclosure of the information would be likely to cause substantial harm or likely to have the effect of impairing the Commission's ability to obtain such information as is necessary to perform its statutory functions.[16]

SO ORDERED.

Cameron Elliot
Administrative Law Judge

[16] Under Commission Rules 210.5 and 201.6(a), confidential business information includes: information which concerns or relates to the trade secrets, processes, operations, style of works, or apparatus, or to the production, sales, shipments, purchases, transfers, identification of customers, inventories, or amount or source of any income, profits, losses, or expenditures of any person, firm, partnership, corporation, or other organization, or other information of commercial value, the disclosure of which is likely to have the effect of either impairing the Commission's ability to obtain such information as is necessary to perform its statutory functions, or causing substantial harm to the competitive position of the person, firm, partnership, corporation, or other organization from which the information was obtained, unless the Commission is required by law to disclose such information. *See* 19 C.F.R. § 201.6(a). Thus, to constitute confidential business information the disclosure of the information sought to be designated confidential must likely have the effect of either: (1) impairing the Commission's ability to obtain such information as is necessary to perform its statutory functions; or (2) causing substantial harm to the competitive position of the person, firm, partnership, corporation, or other organization from which the information was obtained.

CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME

INV. NO. 337-TA-1120

PUBLIC CERTIFICATE OF SERVICE

I, Lisa R. Barton, hereby certify that the attached **INITIAL DETERMINATION** has been served by hand upon the Commission Investigative Attorney, **Lisa Murray, Esq.** and the following parties as indicated, on

OCT 0 3 2019

Lisa R. Barton, Secretary
U.S. International Trade Commission
500 E Street SW, Room 112A
Washington, D.C. 20436

FOR COMPLAINANT GLYCOSYN LLC	
Michael C. Newman, Esq. **MINTZ LEVIN COHN FERRIS GLOVSKY AND POPEO PC** One Financial Center Boston, MA. 02111	( ) Via Hand Delivery (✓) Express Delivery ( ) Via First Class Mail ( ) Other: _____
FOR RESPONDENT JENNEWEIN BIOTECHNOLOGIE GmbH	
Gary M. Hnath, Esq. **MAYER BROWN, LLP** 1999 K Street, NW Washington, DC 20006	( ) Via Hand Delivery (✓) Express Delivery ( ) Via First Class Mail ( ) Other: _____

UNITED STATES INTERNATIONAL TRADE COMMISSION

Washington, D.C.

In the Matter of	
CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME	Inv. No. 337-TA-1120

ORDER NO. 22: CONSTRUING THE TERMS OF THE ASSERTED CLAIMS OF THE PATENTS AT ISSUE

(December 18, 2018)

TABLE OF CONTENTS

I. INTRODUCTION

This Investigation was instituted by the Commission on June 21, 2018 to determine whether certain human milk oligosaccharides and methods of producing the same infringe U.S. Patent Nos. 9,453,230 (the "'230 patent") and 9,970,018 (the "'018 patent"). *See* 83 Fed. Reg. 28865-6 (June 21, 2018). The Complainant is Glycosyn LLC ("Glycosyn"). The Respondent is Jennewein Biotechnologie GmbH ("Jennewein") (altogether, "the Parties").

Pursuant to Ground Rule 8, a *Markman* hearing was held October 16, 2018 regarding the interpretation of the certain terms of the patents at issue. Prior to the hearing, the Parties and the Commission Investigative Staff ("Staff") filed initial and amended joint claim construction charts setting forth a limited set of terms to be construed. The Parties and the Staff also filed initial and reply claim construction briefs, wherein each party offered its construction for the claim terms in dispute, along with support for its proposed interpretation.[1] At the beginning of the hearing, the Parties indicated one of the claim terms in dispute, "promotor-less," would not construction due to withdrawal of the relevant claims by Glycosyn. *See* Hr'g Tr. at 4:13-5:3.

II. IN GENERAL

The claim terms construed in this Order are done so for the purposes of this section 337 Investigation. Those terms not in dispute need not be construed. *See Vanderlande Indus. Nederland*

[1] For convenience, the briefs and amended chart submitted by the Parties are referred to hereafter as:

CIMB	Complainant's Initial *Markman* Brief
CRMB	Complainant's Reply *Markman* Brief
RIMB	Respondents' Initial *Markman* Brief
RRMB	Respondents' Reply *Markman* Brief
SIMB	Staff's Initial *Markman* Brief
SRMB	Staff's Reply *Markman* Brief
JC	Amended Joint Claim Construction Chart
Hr'g Tr.	*Markman* hearing transcript

BV v. Int'l Trade Comm'n, 366 F.3d 1311, 1323 (Fed. Cir. 2004) (noting that the administrative law judge need only construe disputed claim terms).

III. RELEVANT LAW

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

Claim construction focuses on the intrinsic evidence, which consists of the claims themselves, the specification, and the prosecution history. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (*en banc*); *see also Markman*, 52 F.3d at 979. As the Federal Circuit in *Phillips* explained, courts must analyze each of these components to determine the "ordinary and customary meaning of a claim term" as understood by a person of ordinary skill in art at the time of the invention. 415 F.3d at 1313. "Such intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." *Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc.*, 262 F.3d 1258, 1267 (Fed. Cir. 2001).

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude."' *Phillips*, 415 F.3d at 1312 (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). "Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of particular claims terms." *Id.* at 1314; *see also Interactive Gift*

Express, Inc. v. Compuserve Inc., 256 F.3d 1323, 1331 (Fed. Cir. 2001) ("In construing claims, the analytical focus must begin and remain centered on the language of the claims themselves, for it is that language that the patentee chose to use to 'particularly point [ ] out and distinctly claim [ ] the subject matter which the patentee regards as his invention."). The context in which a term is used in an asserted claim can be "highly instructive." *Phillips*, 415 F.3d at 1314. Additionally, other claims in the same patent, asserted or unasserted, may also provide guidance as to the meaning of a claim term. *Id.* "Courts do not rewrite claims; instead, we give effect to the terms chosen by the patentee." *K-2 Corp. v. Salomon S.A.*, 191 F.3d 1356, 1364 (Fed. Cir. 1999).

The specification "is always highly relevant to the claim construction analysis. Usually it is dispositive; it is the single best guide to the meaning of a disputed term." *Id.* at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). "[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Id.* at 1316. "In other cases, the specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor." *Id.* As a general rule, however, the particular examples or embodiments discussed in the specification are not to be read into the claims as limitations. *Id.* at 1323. In the end, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be ... the correct construction." *Id.* at 1316 (quoting *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998)).

In addition to the claims and the specification, the prosecution history should be examined, if in evidence. *Id.* at 1317; *see Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 913 (Fed. Cir. 2004). The prosecution history can "often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise

be." *Phillips*, 415 F.3d at 1317; *see Chimie v. PPG Indus. Inc.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005) ("The purpose of consulting the prosecution history in construing a claim is to exclude any interpretation that was disclaimed during prosecution.").

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

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

The construction of a claim term is generally guided by its ordinary meaning. However, courts may deviate from the ordinary meaning when: (1) "the intrinsic evidence shows that the patentee distinguished that term from prior art on the basis of a particular embodiment, expressly disclaimed subject matter, or described a particular embodiment as important to the invention;" or (2) "the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in either the specification or prosecution history." *Edwards Lifesciences LLC v. Cook*

Inc., 582 F.3d 1322, 1329 (Fed. Cir. 2009); *see also GE Lighting Sols., LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1309 (Fed. Cir. 2014) ("the specification and prosecution history only compel departure from the plain meaning in two instances: lexicography and disavowal."); *Omega Eng'g, Inc, v. Raytek Corp.*, 334 F.3d 1314, 1324 (Fed. Cir. 2003) ("[W]here the patentee has unequivocally disavowed a certain meaning to obtain his patent, the doctrine of prosecution disclaimer attaches and narrows the ordinary meaning of the claim congruent with the scope of the surrender."); *Rheox, Inc. v. Entact, Inc.*, 276 F.3d 1319, 1325 (Fed. Cir. 2002) ("The prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution."). Nevertheless, there is a "heavy presumption that a claim term carries its ordinary and customary meaning." *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002) (citations omitted). The standard for deviating from the plain and ordinary meaning is "exacting" and requires "a clear and unmistakable disclaimer." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1366-67 (Fed. Cir. 2012); *see Epistar Corp. v. Int'l Trade Comm'n*, 566 F.3d 1321, 1334 (Fed. Cir. 2009) (requiring "expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope" to deviate from the ordinary meaning) (citation omitted). As the Federal Circuit has explained, "[w]e do not read limitations from the specification into claims; we do not redefine words. Only the patentee can do that." *Thorner*, 669 F.3d at 1366.

A claim must also be definite. Pursuant to 35 U.S.C. § 112, second paragraph: "The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112, ¶ 2. In *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120 (2014), the Supreme Court held that § 112, ¶ 2 requires "that a patent's claims, viewed in light of the specification and prosecution history inform those skilled in the art about the scope of the invention with reasonable certainty." *Id.* at 2129. A claim is required to "provide objective boundaries for those of skill in the art," and a claim

term is indefinite if it "might mean several different things and no informed and confident choice is among the contending definitions." *Interval Licensing LLC v. AOL, Inc.*, 766 F.3d 1364, 1371 (Fed. Cir. 2014). A patent claim that is indefinite is invalid. 35 U.S.C. § 282(b)(3)(A).

Courts are not required to construe every claim limitation of an asserted patent. *See O2 Micro Intern. Ltd. v. Beyond Innovation Technology Co.*, 521 F.3d 1351, 1362 (Fed. Cir. 2008) (citations omitted). Rather, "claim construction is a matter of resolution of disputed meanings and technical scope, to clarify and when necessary to explain what the patentee covered by the claims, for use in the determination of infringement." *Id.* at 1362 (quoting *U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997)); *see also Embrex*, 216 F.3d at 1347 ("The construction of claims is simply a way of elaborating the normally terse claim language in order to understand and explain, but not to change, the scope of the claims.") (citation omitted). In addition, "[a] determination that a claim term 'needs no construction' or has the 'plain and ordinary meaning' may be inadequate when a term has more than one 'ordinary' meaning or when reliance on a term's 'ordinary' meaning does not resolve the parties' dispute." *O2 Micro*, 521 F.3d at 1361. Claim construction, however, is not an "obligatory exercise in redundancy." *U.S. Surgical Corp.*, 103 F.3d at 1568. "[M]erely rephrasing or paraphrasing the plain language of a claim by substituting synonyms does not represent genuine claim construction." *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 863 (Fed. Cir. 2004).

IV. LEVEL OF ORDINARY SKILL

In its opening brief, Glycosyn contends, for both asserted patents:

> [A] person of ordinary skill in the art for the purposes of this case would typically have a Ph.D in molecular biology, biochemistry, or chemical engineering, or an equivalent field, and 1-2 years of experience working with *E.coli* bacteria or related systems. Or such a person could have a lower level degree (e.g., a M.A.) in a similar field to those listed above, but a greater amount of relevant working

> experience (e.g., 5-6 years of experience working with *E.Coli* bacteria or related systems).

(CIMB at 17 (citing CIMB, Ex. 4 at ¶ 24).)

In its opening brief, Jennewein contends, for both asserted patents:

> [T]he person of ordinary skill in the field of the Asserted Patents is a person having a Ph.D. in molecular biology, biochemistry, biological or chemical engineering, or an equivalent field, and 1-2 years of experience working with E. coli bacteria or related systems. Or a person having a lower level degree (e.g., a M.A.) in a similar field to those listed above, but a greater amount of relevant working experience (e.g., 5-6 years of experience working with E. Coli bacteria or related systems).

(RIMB at 14.)

These proposed levels of skill are nearly identical, and the Staff indicates agreement with them. (SIMB at 9.) Accordingly, the undersigned finds that one of ordinary skill in the art would have (1) a Ph.D in molecular biology, biochemistry, or chemical engineering, or an equivalent field, and 1-2 years of experience working with *E. coli* bacteria or related systems, or (2) a lower level degree (*e.g.*, a M.A.) in a similar field to those listed above, but a greater amount of relevant working experience (*e.g.*, 5-6 years of experience working with *E. coli* bacteria or related systems).

V. THE ASSERTED PATENTS

A. The '230 Patent

The '230 patent, entitled "Biosynthesis of Human Milk Oligosaccharides in Engineered Bacteria," issued on September 27, 2016 to Massimo Merighi, John M. McCoy, and Matthew Ian Heidtman. The '230 patent is assigned on its face to Glycosyn LLC. The '230 patent generally relates to "compositions and methods for producing purified oligosaccharides, in particular certain fucosylated and/or sialylated oligosaccharides that are typically found in human milk." ('230 patent at Abstract.) In particular:

> The method for producing a fucosylated oligosaccharide in a bacterium comprises the following steps: providing a bacterium that

> comprises a functional β-galactosidase gene, an exogenous fucosyltransferase gene, a GDP-fucose synthesis pathway, and a functional lactose permease gene; culturing the bacterium in the presence of lactose; and retrieving a fucosylated oligosaccharide from the bacterium or from a culture supernatant of the bacterium.

(*Id.* at 1:48-55.)

The '230 patent has 40 claims. As of the date of this order, claims 21, 22, 27, 32, 34-38 are asserted in this Investigation. The asserted claims read as follows (with the first instance of the agreed-upon terms in *italics* and the first instance of the disputed terms highlighted in **bold**):

21. A method for producing a fucosylated oligosaccharide in a bacterium, comprising

providing an *E. coli* bacterium, said bacterium comprising a deletion or functional inactivation of the endogenous β-galactosidase gene; a **functional** *exogenous* wild type **β-galactosidase gene** inserted into an endogenous gene such that the resultant bacterium comprises a low level of β-galactosidase activity, wherein said **β-galactosidase activity comprises between 0.05 and 200 units**; an exogenous lactose-accepting fucosyltransferase gene comprising an α(1,2) fucosyltransferase gene, an α(1,3) fucosyltransferase gene, or an α(1,4) fucosyltransferase gene; an inactivating mutation in an endogenous *colanic acid synthesis gene*, wherein said colanic acid synthesis gene comprises an *E. coli* wcaJ, wzxC, wcaD, wza, wzb, or wzc gene; and a functional lactose permease gene, wherein said lactose permease gene comprises *E. coli* lacY; culturing said bacterium *in the presence of lactose*; and retrieving a fucosylated oligosaccharide from said bacterium or from a culture supernatant of said bacterium.

22. The method of claim 21, wherein said β-galactosidase gene inserted into an endogenous gene comprises an *E. coli lacZ gene*.

27. The method of claim 21, wherein said bacterium accumulates an increased intracellular lactose pool, wherein said increased intracellular lactose pool is at least 10% more than the levels in a wild type bacterium.

32. The method of claim 21, wherein said lactose permease gene is an *exogenous* lactose permease gene.

34. The method of claim 21, wherein said fucosylated oligosaccharide is 2'-fucosyllactose, 3-fucosyllactose, or lactodifucotetraose.

35. The method of claim 21, wherein said low level of **β-galactosidase activity comprises between 0.05 and 5 units**.

36. The method of claim 21, wherein said low level of **β-galactosidase activity comprises between 0.05 and 4 units**.

37. The method of claim 21, wherein said low level of **β-galactosidase activity comprises between 0.05 and 3 units**.

38. The method of claim 21, wherein said low level of β-**galactosidase activity comprises between 0.05 and 2 units**.

B. **The '018 Patent**

The '018 patent, entitled "Biosynthesis of Human Milk Oligosaccharides in Engineered Bacteria," issued on May 15, 2018 to Massimo Merighi, John M. McCoy, and Matthew Ian Heidtman. The '018 patent is assigned on its face to Glycosyn LLC, and recorded as a continuation of continuation of a divisional application from the application which became the '230 patent. The '018 patent generally relates to "compositions and methods for engineering bacteria to produce fucosylated oligosaccharides, and the use thereof in the prevention or treatment of infection." ('018 patent at Abstract.) In particular:

> The method for producing a fucosylated oligosaccharide in a bacterium comprises the following steps: providing a bacterium that comprises a functional β-galactosidase gene, an exogenous fucosyltransferase gene, a GDP-fucose synthesis pathway, and a functional lactose permease gene; culturing the bacterium in the presence of lactose; and retrieving a fucosylated oligosaccharide from the bacterium or from a culture supernatant of the bacterium.

(*Id.* at 1:53-60.)

The '018 patent has 28 claims. As of the date of this order, claims 1-5, 8, 10, 12, 18, 20, 21, 23-28 are asserted in this Investigation. The asserted claims read as follows (with the first instance of the agreed-upon terms in *italics* and the first instance of the disputed terms highlighted in **bold**):

1. A method for producing a fucosylated oligosaccharide in a bacterium, comprising *providing* an isolated *E. coli* bacterium comprising, (i) a deletion or functional inactivation of an endogenous β-galactosidase gene; (ii) an *exogenous* **functional β-galactosidase gene** comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type *E. coli* bacterium, wherein the level of **β-galactosidase activity comprises between 0.05 and 200 units**; (iii) an inactivating mutation in a *colanic acid synthesis gene*; and (iv) an exogenous lactose-accepting fucosyltransferase gene; culturing said bacterium *in the presence of lactose*; and retrieving a fucosylated oligosaccharide from said bacterium or from a culture supernatant of said bacterium.

2. The method of claim 1, wherein said *colanic acid synthesis gene* comprises an *E. coli* wcaJ, wzxC, wcaD, wza, wzb, or wzc gene.

3. The method of claim 2, wherein said *colanic acid synthesis gene* comprises a wcaJ gene.

4. The method of claim 1, wherein the bacterium comprises an increased intracellular guanosine diphosphate (GDP)-fucose level, wherein the increased intracellular GDP-fucose level is at least 10% more than the level of GDP-fucose in a wild-type bacterium.

5. The method of claim 1, wherein said exogenous lactose-accepting fucosyltransferase gene encodes α(1,2) fucosyltransferase and/or α(1,3) fucosyltransferase.

8. The method of claim 1, wherein said *exogenous* functional β-galactosidase gene comprises an *E. coli lacZ gene*.

10. The method of claim 1, wherein said bacterium further comprises a functional lactose permease gene.

12. The method of claim 10, wherein said lactose permease gene comprises an *E. coli* lacY gene.

18. The method of claim 1, wherein the level of **β-galactosidase activity comprises between 0.05 and 5 units**.

20. The method of claim 1, wherein said bacterium comprises an increased intracellular lactose level, wherein the increased intracellular lactose level is at least 10% more than the level in a wild-type bacterium.

21. The method of claim 1, wherein said *exogenous* **functional β-galactosidase gene** is an *E. coli lacZ gene* lacking an operably linked promoter, and said *colanic acid synthesis gene* comprises an *E. coli* wcaJ, wzxC, wcaD, wza, wzb, or wzc gene.

23. The method of claim 1, wherein said *exogenous* **functional β-galactosidase gene** is inserted into an endogenous gene.

24. The method of claim 1, wherein said *exogenous* **functional β-galactosidase gene** comprises a recombinant β-galactosidase gene engineered to produce a detectable level of β-galactosidase activity that is reduced compared to the level of β-galactosidase activity in a wild-type *E. coli* bacterium.

25. The method of claim 24, wherein the level of **β-galactosidase activity comprises between 0.05 and 5 units**.

26. The method of claim 1, wherein the level of **β-galactosidase activity comprises between 0.05 and 4 units.**

27. The method of claim 1, wherein the level of **β-galactosidase activity comprises between 0.05 and 3 units.**

28. The method of claim 1, wherein the level of **β-galactosidase activity comprises between 0.05 and 2 units.**

VI. CLAIM CONSTRUCTION

A. Construction of the Agreed-Upon Claim Terms

Prior to the *Markman* hearing, the Parties reached agreement regarding the construction of five terms:

Claim Term	Relevant Claims	Agreed Construction
"providing"	'230 patent claim 21 '018 patent claim 1	*A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, furnishing, supplying, making available, or preparing.
"in the presence of lactose"	'230 patent claim 21 '018 patent claim 1	*A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, lactose is available to the bacterium
"exogeneous"	'230 patent claims 21, 32 '018 patent claims 1, 5, 8, 21, 23, 24	*A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, originating outside an organism, tissue, or cell
"colonic acid synthesis gene"	'230 patent claim 21 '018 patent claims 1-3, 21	*(B) patentee as lexicographer:* By 'colanic acid synthesis gene' is meant a gene involved in a sequence of reactions,

		usually controlled and catalyzed by enzymes that result in the synthesis of colanic acid.
"*E. coli* lacZ gene"	'230 patent claim 22 '018 patent claims 8, 21	*A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, a structural gene that encodes the β-galactosidase protein and is part of the lac operon in the DNA of *E. coli*

(JC at 4.)

B. Construction of the Disputed Claim Terms

1. "β-galactosidase activity comprises between 0.05 and [200 units / 5 units / 4 units / 3 units / 2 units]"

The Parties disagree on the proper claim construction and have proposed the following constructions:

Relevant Claims	Glycosyn	Jennewein	Staff
'230 patent claims 21, 35-38 '018 patent claims 1, 18, 25-28	*(B) patentee as lexicographer:* β-galactosidase activity is measurable at between exactly 0.05 and exactly [200/5/4/3/2] Miller Units, as defined in Miller, J.H., *Experiments in Molecular Genetics* (Cold Spring Harbor Lab. 1972) at 352-355	*INDEFINITE:* This term is not amenable to definition with reasonable certainty to one of ordinary skill in the art, and is therefore indefinite under 35 U.S.C. 112. In the alternative, to the extent that the Commission finds the term is not indefinite and requires construction, Respondent proposes the following construction: *(A) plain and ordinary meaning;* *(B) patentee as lexicographer &*	*(B) patentee as lexicographer &* *(C) disavowal of scope* β-galactosidase activity is measurable at between exactly 0.05 and exactly [200/5/4/3/2] Miller Units, as defined in Miller, J.H., *Experiments in Molecular Genetics* (Cold Spring Harbor Lab. 1972) at 352-355

		(C) disavowal of scope "β-galactosidase activity between exactly 0.05 and exactly [200 units/5 units/ 4 units/3 units/2 units] at substantially all times during culturing of the bacterium and retrieval of the fucosylated oligosaccharide, when measured according to the assay procedures described in J.H. Miller, "Experiment 48," *Experiments in Molecular Genetics*, Cold Spring Harbor, NY (1972) 352-355."	

(JC at 2-3.)

In its opening brief, Glycosyn argues this term is not indefinite. (CIMB at 18.) Glycosyn explains that "β-galactosidase is an enzyme that catalyzes the cleavage of β-galactosidase (*i.e.*, sugars such as lactose) into two parts" and is well-known in the art. (*Id.* (citing Prather Decl. (CIMB, Ex. 4) at ¶ 34).) Glycosyn continues, "[t]he 'activity' of an enzyme is a measure of its ability to convert a certain amount of 'substrate' per unit time" (*id.* at 19 (citing Prather Decl. at ¶ 43)) and "[o]ne of the tests that measures the activity of β-galactosidase, the 'Miller assay,' which reports activity in 'Miller units,' was developed almost 50 years ago (*id.* (citing CIMB, Ex. 5)). Glycosyn alleges this is "a well-described, uncomplicated procedure." (*Id.* (citing Prather Decl. at ¶ 46).) Glycosyn then goes on to describe the details of the Miller test. (*See id.* at 20, 21-22.)

Thus, reasons Glycosyn, a person of ordinary skill in the art reading the specification and claims of the asserted patents would understand that "units" as used in the claims refers to "Miller

units." (*Id.* at 20-21 (citing, *inter alia*, '230 patent at 7:26-33; '018 patent at 7:30-37).) Glycosyn argues that modifications of the Miller test are permitted and do not take away from a person of ordinary skill's understanding that they have performed the so-named protocol. (*Id.* at 22 (citing Prather Decl. at ¶ 47).) Glycosyn contends, accordingly, that "[b]oth Complainant and Respondent have been able to perform the Miller assay on their respective cultures of bacteria that produce β-galactosidase to measure 'measurable' amounts of β-galactosidase activity." (*Id.* (citing CIMB, Ex. 7 at 12, 33-34, 36-37; CIMB, Ex. 8).)

With this understanding, Glycosyn argues that "β-galactosidase activity comprises between 0.005 and [200 units/5 units/4 units/3 units/2 units]" should be afforded its plain and ordinary meaning" as defined by the specifications of the '230 and '018 patents. (*Id.* at 23 (citing '230 patent at 7:26-33; '018 patent at 7:30-37).) Glycosyn criticizes Jennewein's construction for "insert[ing] a temporal limitation that is found nowhere in the claim, specification, or prosecution history." (*Id.* (citing *3M Innovative Props. Co. v. Tredegar Corp.*, 725 F.3d 1315, 1333 (Fed. Cir. 2013)).) Glycosyn argues "[t]he '230 and '018 patents do not specify when the claimed β-galactosidase activity range must be measured, or for how long the claimed range must be achieved. That is because these parameters do not matter for purposes of the claimed invention." (*Id.* at 24-25 (discussing '230 patent at 5:65-6:7, 7:33-41, 9:32-44, 18:23-32; Prather Decl. ¶ 50).) Rather, according to Glycosyn:

> [T]he claimed β-galactosidase activity ranges merely need be present at times useful for the production of 2'-FL. See Prather Decl. at ¶ 51. This could be at the very beginning when the bacterium is being constructed (for "phenotypic marking of desirable genetic loci during construction of host cell backgrounds"); it could be later during the fermentation of the bacteria ("for detection of cell lysis due to undesired bacteriophage contaminations in fermentation processes"); or it could be even later at the end of the fermentation process ("for the facile removal of undesired residual lactose at the end of fermentations"). *Id.*

(*Id.* at 25.)

In its reply brief, Glycosyn argues there is no merit to Jennewein's contention that "comprises," as used in the claim and in connection to the claimed numerical activity range, renders the limitation meaningless under the intrinsic evidence and settled law. (*See* CRMB at 2 (referring to RIMB at 15).) Glycosyn contends "as noted by Staff, the sue of the term 'comprises' in this context allows for the possibility that 'the action of the β-galactosidase enzyme may also have other, unrecited effects' beyond the claimed β-galactosidase activity between 0.05 and 200 units;" and therefore, the term is sufficiently definite. (*Id.* at 3 (citing Prather Decl. at ¶ 50).) Glycosyn considers Jennewein's claim of indefiniteness (for failure to define when the β-galactosidase activity must be present) as the flip side of Jennewein's use of a temporal requirement in its alternate construction. (*Id.* (referring to RIMB at 16, 21-22).) Glycosyn argues both sides represent improper interpretations under settled law and the teachings of the specification. (*Id.* at 3-4 (citing, *inter alia*, *3M Innovative Props.*, 725 F.3d at 1333; *Broadcom Corp. v. Emulex Corp.*, 732 F.3d 1325, 1333 (Fed. Cir. 2013); *Bell Commc'ns Research v. Vitalink Commc'ns Corp.*, 55 F.3d 615, 622-23 (Fed. Cir. 1995); '230 patent at 7:33-41; Prather Decl. at ¶ 51); *see generally id.* at 6-7.)

Further, with respect to any ambiguity in how to implement the Miller test, Glycosyn highlights that principle which states "when a claim does specify a method of measurement, its omission of details about how to implement the method will not invalidate the claim if a person of ordinary skill in the art could infer the details from industry standards or professional judgment." (*Id.* at 5 (citing, *inter alia*, *Abbott GmbH & Co., KG v. Cenocor Ortho Biotech, Inc.*, 870 F. Supp. 2d 206, 230 (D. Mass. 2012)).) Glycosyn argues, through its expert declaration, that a person of ordinary skill could do exactly that. (*Id.* (citing Prather Decl. at ¶ 46-47).)

In its opening brief, Jennewein argues that "[t]his term fails to inform with reasonable certainty to one of ordinary skill in the art the proper scope of the claims, and is therefore indefinite

under 35 U.S.C. § 112, ¶2." (RIMB at 15.) Jennewein reasons that because the range is preceded by "comprises," an open-ended or unbounded term, "it is hopelessly unclear whether the inventors intended that β-galactosidase activity would be limited to the claimed range, or not." (*Id.* at 15; *see* RRMB at 2-3 ("The term comprises defines the *range* of β-galactosidase activity allowed, not the action of β-galactosidase.").) Jennewein adds "the term 'activity' in the context of the claims is not amenable to definition with reasonable certainty to one of ordinary skill in the art. Neither the claims nor the specification define at what point this activity must be present." (RIMB at 16; *see* RRMB at 4.) Jennewein explains:

> Complainant apparently contends that a process falls within the scope of the claim if there is activity in the claimed range for any amount of time, even if only a small percentage, and that the range can be exceeded during the remaining time. That cannot be correct. Should activity greatly exceed 200 units during most of fermentation, 2'-FL may not be produced. High level β-galactosidase activity is contrary to the purpose of the invention, at least because it could destroy the intracellular lactose pool and prevent 2'-FL production. Exh. 1, '230 Patent at 7:26-41. Furthermore, low level β-galactosidase activity is a key distinction between the invention and the Samain patent. Exh. 9, Confidential Deposition Transcript of John McCoy ("McCoy"), Sept. 10, 2018 at 286:11-291:10. A skilled artisan therefore would not be able to determine the claim's scope with reasonable certainty.

(RIMB at 16.) Jennewein further argues that different methods for measuring the claimed "Miller units" "may lead to inconsistent results," causing further indefiniteness. (*See id.* at 17-18 (citing *Dow Chem. Co. v. Nova Chemicals Corp. (Canada)*, 803 F.3d 620, 630 (Fed. Cir. 2015)); *see* RRMB at 4-5.) Should the undersigned not determine the term is indefinite, Jennewein argues the claimed range must be strict in light of the prosecution history of the asserted patents (*see* RIMB at 18-20 (discussing RIMB, Exs. 6, 7)), must be measured using the assay procedures in Miller, and the range must be satisfied "at substantially all times during culturing of the bacterium and retrieval of the fucosylated oligosaccharide . . . ." (*Id.* at 21.) Jennewein argues this is so because:

> Should the β-galactosidase activity fall outside of this low range, one of two failures could occur. When the activity is too high, the lactose feedstock will be destroyed before 2'-FL is finished being constructed. *Id.* at 7:33-35. But when the activity is too low, the residual lactose in the fermentation broth will not be destroyed in the retrieval step, rendering it impractical to retrieve 2'-FL from the culture, particularly at a commercial scale. *See id.* at 33-41.

(*Id.* at 22; *see* RRMB at 7 ("If Complainant's broad interpretation is adopted, the claims would have no limit on at what point, or for how long, β-galactosidase activity must be present during production and purification of 2'-FL"), 8-9 (citing inventor testimony), 10 ("Complainant's construction therefore allows activity that is contrary to the expressed purposes of the invention explained above – producing 2'-FL and allowing its facile purification from lactose").)

Further, in its reply brief, Jennewein emphasizes that should the term not be indefinite, "units must be measured according to the assay procedures in Miller." (RRMB at 5.) Jennewein faults Glycosyn for "want[ing] to adopt part of the Miller assay – the method for calculating units – but not the express description of how the assay should be performed." (*Id.* at 6.) Jennewein argues "[d]uring the prosecution of the '230 patent, the patentee made clear that units of β-galactosidase activity must be measured according to the assay procedures in Miller" (*id.* at 6 (citing RIMB, Ex. 6)) and so Glycosyn is now judicially estopped from arguing otherwise now (*id.* at 7 (citing *Typhoon Touch Techs., Inc. v. Dell, Inc.*, 659 F.3d 1376, 1381 (Fed. Cir. 2011); *Omega Eng'g., Inc. v. Raytek Corp.*, 334 F.3d 1314, 1323-24 (Fed. Cir. 2003)).)

In its opening brief, and with respect to indefiniteness, the Staff observes "[t]he term 'comprising' is specifically defined in the patent specification" which "simply provides that the claimed method may include 'additional, unrecited elements or method steps.'" (SIMB at 15-16 (citing '230 patent at 11:43-48); SRMB at 2-3.) The Staff argues one of ordinary skill would understand the use of "comprises" functions to "not exclude the possibility that the action of the β-galactosidase enzyme may also have other, unrecited effects" and "would easily be able to discern

the bounds of the invention with reasonable certainty, based on the exact numerical ranges claimed." (*Id.* at 16 (citing *Nautilus*, 134 S. Ct. at 2124).) The Staff further disputes the propriety of imposing a "at substantially all times . . ." requirement into the construction under the legal principle that an accused product which sometimes, but not always, practices a claim still practices the claim. (*Id.* at 16-17 (citing *Broadcom Corp. v. Emulex Corp.*, 732 F.3d 1325, 1333 (Fed. Cir. 2013)).)

In its reply brief, the Staff addresses Jennewein's additional grounds for indefiniteness and continues to disagree. Regarding the impact of "activity," the Staff faults Jennewein for "not explain[ing] why one of ordinary skill in the art would be unable to understand what 'β-galactosidase activity' is without first knowing when that activity occurs" primarily because the definition of "activity" is agreed ("the process of cleaving the disaccharide lactose into glucose and galactose, as performed by the intracellular β-galactosidase enzyme") and "does not change depending on when the activity occurs." (*Id.* at 3 (citing SIMB, Ex. 7 at 343).) The Staff reasons:

> If a β-galactosidase enzyme cleaves lactose at any point during a process, then there has been "β-galactosidase activity." If that activity is measurable at between 0.05 and 200 Miller units at any point in the process, then at that point it is within the scope of the invention disclosed in claim 1 of the '230 Patent and claim 1 of the '018 Patent. *See* SBr. exh. 2 ('230 Patent) at 123:67; SBr. exh. 3 ('018 Patent) at 111:49-50. The Staff submits that one of ordinary skill in the art would be able to discern "with reasonable certainty" whether the level of β-galactosidase activity at any given point in a process is within the scope of the invention. *See Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2124 (2014).

(*Id.*) Regarding Jennewein's assertion that different Miller tests will produce different results, the Staff argues "[t]he more reasonable interpretation of the text is that Miller is describing two interchangeable variations of the Miller assay, either of which would yield the same results. Respondent has cited no evidence that this is incorrect." (*Id.* at 4.) For similar reasons to those discussed above, the Staff does not agree with any of the additional limitations Jennewein places into its alternative proposed construction. (*See id.* at 5-6.) The Staff also argues Jennewein's

construction tries to limit the scope of the invention to the most efficient embodiment of the claim, which is improper. (*Id.* at 6 (citing *Linear Tech. Corp. v. International Trade Comm'n*, 566 F.3d 1049, 1058 (Fed. Cir. 2009); *Liebel–Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004); *RF Delaware, Inc. v. Pacific Keystone Techs., Inc.*, 326 F.3d 1255, 1263 (Fed. Cir. 2003)).)

Upon review of the evidence, the undersigned finds Jennewein has not shown by clear and convincing evidence that the term is indefinite. In particular, Jennewein's argument that "persons of ordinary skill in the art could not know whether they infringe the claims with reasonable certainty if they had a β-galactosidase activity outside of the recited range" (RIMB at 15-16; *see* RIMB, Ex. 4 at ¶¶ 39-41) is not persuasive. If a person of ordinary skill can know when their β-galactosidase activity falls outside of the recited range, then they can also know if that activity was within the recited range—which would exactly inform them of whether they infringe or not. Moreover, Jennewein's contention that a person of ordinary skill would not understand with reasonable certainty what the range means or how to measure it (*see* RIMB at 17-18; RRMB at 4-5 (discussing different methodologies of testing and "natural and man-made variations")) is undercut by Jennewein's own expert. For example, while that expert opines "Miller describes two alternative method steps to conduct the assay" and "[o]ne measurement is likely to profuse [sic] higher values on that count and other factors in the assay may act in different directions," that expert also makes predictions on the practical drawbacks of β-galactosidase activity falling above or below the claimed range without reference to which technique is employed and under what conditions:

> 12. Should β-galactosidase activity not fall within the claimed range during the entire process of producing 2'-FL, several problems would arise.
>
> 13. Higher levels of β-galactosidase activity would destroy lactose faster than a cell could covert lactose to 2'-FL. β-galactosidase activity above 200 units during fermentation would likely eliminate or greatly inhibit a cell's ability to produce 2'-FL. Resp. Br., Exh. 6 4/7/16 Declaration of John McCoy.

> 14. On the other hand, β-galactosidase activity below 0.05 units would likely make purification of 2'-FL impractical, particularly at commercial scale. This is because 2'-FL and lactose are difficult to separate from each other. β-galactosidase destroys lactose that remains after 2'-FL production is complete, allowing for easier purification of 2'-FL from the culture medium. Too low of a level β-galactosidase activity during [sic] would therefore lose this important benefit of destroying residual lactose in the cell culture after 2'-FL syntheses was complete.

(RRMB, Ex. A at ¶¶ 12-14.) Further, the undersigned finds Glycosyn's expert more persuasive on this issue. Glycosyn's expert states clearly:

> Miller assays are conducted in hundreds of labs across the world to this day. Any person of ordinary skill in the art at the time of the invention would not only be familiar with the Miller assay, but also would be able to follow it as its methodology is very clearly described in Miller's 1972 textbook.
>
> A person of ordinary skill in the art at the time of the invention would understand that there is flexibility contained within the procedure of the Miller assay, and that scientists routinely modify procedures of assays to better fit within their research needs.

(CIMB, Ex. 4 at ¶ 46.) Jennewein's expert, on the other hand, paradoxically argues both of "[a] person of ordinary skill in the art understood in 2011 that certain factors can alter the data obtained using the Miller assay, which would result in incorrect readings of β-galactosidase" (RIMB, Ex. 4 at ¶ 45) and "[a]n ordinary scientist would not know how the activity would change with alterations in these parameters, and could not predict if his process would infringe the claimed β-galactosidase activity based on these variations" (*id.* at ¶ 50).

With respect to the timing or duration of the activity within the claimed range, the claims' failure to "specify whether the activity must remain at a low level throughout the claimed process steps of culturing and retrieving or only during part of those steps, and if so, what part of those steps" (RIMB at 16; *see* RRMB at 4), the undersigned does not find this results in an indefinite claim. Rather, it results in a broad claim which is met when β-galactosidase activity falls within the

claimed range at some point. This is perfectly compatible with the principle that "[a]n accused product that sometimes, but not always, embodies a claimed method nonetheless infringes." *Bell Commc'ns*, 55 F.3d at 622-23.

Turning to Jennewein's alternate construction, the undersigned declines to include "at substantially all times during culturing of the bacterium and retrieval of the fucosylated oligosaccharide" in the construction. Jennewein argues this added temporal requirement is needed to "resolv[e] the claim's ambiguity" (**RRMB** at 7), but as discussed above, the claim is not ambiguous as to when the claimed activity range must be met—it need only be met at some point in time. Jennewein also argues the temporal requirement is needed for the invention to have its beneficial effects (*see* RIMB at 22; RRMB at 8-10) but none of the patent specification excerpts cited by Jennewein for support suggest this dependency (*see* '230 patent at 5:13-18, 5:47-6:8, 7:18-41, 9:28-44, 18:19-31).

Further, while Glycosyn and the Staff do not address it, the undersigned finds no reason to read "when measured according to the assay procedures described in [the Miller textbook]" into the claim. To the extent the use of this assay is implied or required when one of ordinary skill is measuring activity in Miller Units (*see* RRMB at 5), then it is already present through the claim's explicit recitation of Miller Units. Jennewein's argument that "[d]uring the prosecution of the '230 patent, the patentee made clear that units of β-galactosidase activity *must* be measured according to the assay procedures in Miller" (RRMB at 6 (emphasis added)) is completely unsupported by the prosecution history excerpt cited (RIMB, Ex. 6 at 6/4/14 Reply and Amendment at 11-12) where the patentee simply noted the assay is widely known. This was in no way a clear and unmistakable disclaimer to avoid rejection under *Thorner*, 669 F.3d at 1366-67.

Accordingly, "β-galactosidase activity comprises between 0.05 and [200 units / 5 units / 4 units / 3 units / 2 units]" is hereby **not found to be indefinite** and construed as "**β-galactosidase**

activity is measurable at between exactly 0.05 and exactly [200/5/4/3/2] Miller Units, as defined in Miller, J.H., *Experiments in Molecular Genetics* (Cold Spring Harbor Lab. 1972) at 352-355."

2. "functional . . . β-galactosidase gene"

The Parties disagree on the proper claim construction and have proposed the following constructions:

Relevant Claims	Glycosyn	Jennewein	Staff
'230 Patent claim 21 '018 Patent claims 1, 21, 23, 24	*(A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, a gene involved in producing a working β-galactosidase enzyme.	*(A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, "a gene that encodes a full-length working β-galactosidase enzyme"	*(A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, a gene that encodes a working β-galactosidase enzyme

(JC at 3.)

For this limitation, the Parties' constructions differ very narrowly. In its opening brief, Glycosyn explains "[i]t appears the parties all agree that a working β-galactosidase enzyme is a β-galactosidase enzyme that has the ability to cleave the glycosidic bond between galactose and glucose." (CIMB at 27.) Glycosyn argues, however, that Jennewein's construction involving "full-length" is improper on technical grounds because "[w]ith regard to the enzyme produced from the *lacZ* gene, 'a full-length working β-galactosidase enzyme' does not exist.'" (*Id.* at 28 (citing Prather Decl. at ¶ 41).) Glycosyn contends the claim term is deliberately broad as to whether β-galactosidase enzyme needs to be produced by a single full-length gene or multiple genes and "[t]here is nothing in the patents that places any significance on having a single gene produce a 'full-length' β-galactosidase enzyme, and nothing in the patent that expressly limits the 'functional . . . β-galactosidase gene' to a single 'full-length' gene." (*Id.* at 28.) Further, Glycosyn contends "[a] person of ordinary skill in the art at the time of the invention would have readily understood that

this low-level β-galactosidase activity could have been equally achieved by inserting a full-length *lacZ* gene, or by inserting complementary *lacZα* or *lacZΩ* β-galactosidase genes. (*Id.* at 28-29 (citing Prather Decl. at ¶ 38-42).)

Essentially, according to Glycosyn, "[t]he claims are not even limited to *lacZ*, but instead include any β-galactosidase gene (of which *lacZ* is the [sic] only one type)." (*Id.* at 29.) Glycosyn argues this is shown through principles of claim differentiation, where *lacZ* is expressly claimed in other dependent claims as the recited "β-galactosidase gene." (*See id.* (citing *Phillips*, 415 F.3d at 1314-1315); *see also* CRMB at 9-10 ("if the dependent claim term '*E. coli lacZ* gene' means '*E. coli lacZ* gene that encodes a full-length enzyme,' as Respondent suggests, then the independent claim would necessarily be broader and would not contain the additional 'full length' limitation.")) With this understanding, Glycosyn adds that there is no meaningful difference between its construction and the Staff's and "the term 'encoding' is just another way of saying 'involved in producing.'" (CIMB at 30 (citing CIMB, Ex. 4 at ¶ 33).)

In its reply brief, Glycosyn argues that Jennewein's arguments on whether a fragment of a β-galactosidase gene can be considered a "functional" gene are belied by Jennewein's technical documents. (*See* CRMB at 8 (citing CRMB, Ex. 15 at 16967).) Glycosyn argues one such document is "far better evidence of what a person of ordinary skill in the art would have understood was meant by a 'functional gene' than any litigation-inspired constructions presented by Jennewein now." (*Id.*) Lastly, Glycosyn argues that the specification's identification of only "full-length" β-galactosidase genes (*lacZ* and *lac4*) cannot limit the claims as that would be improper act of limiting the claims to the specification (*see id.* at 10 (citing *Phillips*, 415 F. 3d at 1323)); and, contrary to Staff's argument, it is not true that the only way to obtain a working enzyme is to encode a "full-length" enzyme. (*See id.* at 10-11 (discussing SIMB at 18-19).) Glycosyn suggests the Staff confuses the claim term "functional" as describing the enzyme as opposed to the gene. (*Id.* at 11.)

In its opening brief, Jennewein identifies the issue as "whether a proper construction should [] clarify that the β-galactosidase gene must 'encode' a 'full-length' working enzyme." (RIMB at 23.) Jennewein argues the claims themselves and the patents' specifications plainly answer this question in the affirmative. (*Id.*; *see id.* at 24 (discussing '230 patent at cls. 2, 22; '018 patent at cls. 8, 24).) Jennewein also points to its expert's declaration to support "a β-galactosidase gene would be understood by those of ordinary skill in the art to encode for the full-length β-galactosidase protein from its start codon to the termination codon, and would not encode merely a fragment of it. . . . A skilled artisan intending to cover a gene fragment would not have used use [sic] the word 'gene' alone. Instead the skilled artisan would have used 'fragment' or its equivalent to describe the gene." (*Id.* at 24 (citing RIMB, Ex. 4 at ¶ 26-28).) Jennewein adds that "[t]he specification of the Asserted Patents teaches only two specific β-galactosidase genes, *lacZ* and *lac4*, both of which encode a full-length, working β-galactosidase in a different species of bacteria (*E. coli* and *K. lactis*, respectively)." (*Id.* at 25 (citing '230 patent at 2:65-67, 7:34-35).)

On technical grounds, Jennewein explains:

> However, a fragment of the β-galactosidase gene does not encode the β-galactosidase enzyme, but rather only a fragment of the β-galactosidase enzyme. Moreover, a "functional β-galactosidase gene" must encode a functional β-galactosidase enzyme, i.e. a "working β-galactosidase enzyme," as the parties agree. In contrast, a gene that does not encode a working β-galactosidase enzyme—for example a fragment of a β-galactosidase gene that encodes only a non-working fragment of the enzyme—would not be a "functional β-galactosidase gene." Ex. 4, Stephanopoulos at ¶¶ 26-28.

(*Id.* at 23.) Jennewein also explains, with respect to the fragments associated with the technique known as alpha complementation:

> When expressed separately, each fragment produces a portion of the LacZ protein, but neither portion has β-galactosidase activity alone. *Id.* When *lacZα* and *lacZω* are simultaneously expressed in the same cell, their portions of the LacZ protein assemble into one of the four subunits of the LacZ β-galactosidase enzyme. *Id.* Assembly with the

> remaining three subunits into a homotetramer results in a functional β-galactosidase enzyme that has β-galactosidase activity. *Id.*

(RRMB at 12-13.)

Further, in its reply brief, Jennewein argues "[t]here is no support in the intrinsic evidence for Complainant's tortured reading of the claim language" and agrees with the Staff that Glycosyn's construction creates new ambiguities. (RRMB at 10 (citing SIMB at 18).) Jennewein generally disputes that a gene "involved in producing," as in Glycosyn's construction, is interchangeable with a gene that "encodes." (*See id.* at 11-12 (citing, *inter alia*, RRMB, Ex. [A] at ¶¶ 6-7; RRMB, Ex. D at 257-258).) Jennewein also alleges it is improper for Glycosyn to rely on Jennewein's accused process to define the claim term. (*See id.* at 13-14 (citing *NeoMagic Corp. v. Trident Microsystems, Inc.*, 287 F.3d 1062, 1074 (Fed. Cir. 2002)).)

With that said, Jennewein finds the Staff's construction amenable in light of the Staff's argument that the term "functional . . . β-galactosidase gene" would not be met by a gene that produces that enzyme only when another undefined gene or gene segment is simultaneously produced. (*See id.* at 11.)

In its opening brief, the Staff understands Glycosyn's construction to cover "any gene that is involved in producing such an enzyme, even if the gene can only do so in conjunction with other genes." (SIMB at 17.) The Staff argues this presents problems for partial genes and whether they are "functional" or not, as "[i]nfringement would depend on the presence or absence of 'other segments' that are not identified anywhere in the claim language, in the specification, or in the prosecution history." (*Id.* at 18; SRMB at 10.) On the other hand, the Staff finds Jennewein's construction acceptable except for the "full-length" term. (*See* SIMB at 18-19.) The Staff summarizes, "what is important in the context of the asserted patents is whether the gene in question encodes an enzyme that successfully performs its function." (*Id.* at 19.)

In its reply brief, the Staff argues the claim language "a functional promoter-less β-galactosidase gene inserted into an endogenous gene such that the resultant bacterium comprises a low level of β-galactosidase activity," when read in context, "indicates that the β-galactosidase gene must be fully 'functional' at the time it is inserted into an endogenous gene." (SRMB at 8.) This, according to the Staff, contradicts Glycosyn's construction. (*Id.*)

Upon review of the evidence, the undersigned first emphasizes that claim terms are not to be construed in light of the accused device. "[T]his court has repeatedly stated that a court must construe claims without considering the implications of covering a particular product or process." *SmithKline Beecham Corp. v. Apotex Corp.*, 703 F.3d 1331, 1339 (Fed. Cir. 2005) (citing *NeoMagic.*, 287 F.3d at 1074 ("It is well settled that claims may not be construed by reference to the accused device.")); *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1118 (Fed. Cir. 1985) ("It is only *after* the claims have been *construed without reference to the accused device* that the claims, as so construed, are applied to the accused device to determine infringement.")

Much of the parties' briefing involves argument over whether a technique known as "α-complementation" would fall under the scope of this term. (*See* CIMB at 26-27, 28-29; CRMB at 7-9, 10 ("There is no dispute that Respondent's *E. coli* strain produces a working β-galactosidase enzyme."), 11; RIMB at 24; RRMB at 12-14 (citing *NeoMagic*, 287 F.3d at 1074); SRMB at 7-10.) This technique is not discussed in the asserted patents. (*See generally* '230 patent; '018 patent.) Rather, it became clear at the *Markman* hearing, on the public record, that α-complementation is related to Jennewein's accused products in this Investigation. (*See, e.g.*, Hr'g Tr. at 64:5-19, 65:10-17, 69:4-10 ("this then means that there is no infringement of any claims of the asserted patents . . . .").)

Thus, the undersigned finds that briefing and argument which concerns whether or not α-complementation falls within the scope of or is covered by "functional . . . β-galactosidase gene" is not persuasive.

Moving on, the Parties' primary dispute is whether a "functional . . . β-galactosidase gene" can be any gene that is involved in the production of the β-galactosidase enzyme, as in Glycosyn's construction, or whether it must be a gene that encodes that enzyme, as in the Jennewein and the Staff's. Jennewein's construction also uses the term "full-length" to describe a functional enzyme (*see, e.g.*, RIMB at 25 ("A β-galactosidase enzyme would not be functional unless it is full-length or substantially full-length, for only those contain enough of the β-galactosidase structure that is responsible for producing enzymatic activity.")), but the undersigned finds this descriptor is misplaced given the term to be construed is "functional . . . β-galactosidase *gene*" and not "functional β-galactosidase enzyme." Indeed, Jennewein acknowledges that "full-length" is not critical to its proposed construction. (*See* RIMB at 27 (noting "full-length" is implicit in the Staff's construction which omits "full-length.").)

The undersigned finds Jennewein and the Staff's construction more persuasive. The asserted patents do not specifically explain what is meant when the modifier "β-galactosidase" is placed before the word "gene," which is what the present dispute turns on. Thus, consideration of extrinsic evidence is appropriate; and the Parties' experts' explanations of "gene" resolves the issue.

Glycosyn's expert explains "[a] gene is a sequence of DNA that contains the molecular 'code' for producing functional biological molecules, such as proteins." (CIMB, Ex. 4 at ¶ 32.) Jennewein's expert similarly explains, "[w]hen ordinary scientists read the term 'gene,' they think of the nucleotide (DNA) sequence encoding the amino acid sequence of the an entire protein." (RIMB, Ex. 4 at ¶ 26.) These explanations are consistent and are hereby adopted. Further consistent are both of Glycoysn's and Jennewein's constructions in their interpretation of "β-galactosidase" in

"β-galactosidase gene" to mean the creation or production of the enzyme β-galactosidase. Additionally, no party contends that anything other than the plain and ordinary meaning should apply to this term. (*See, e.g.*, CIMB at 25 (table).)

Thus, in light of the experts' statements and the parties' constructions, the undersigned finds the plain and ordinary meaning of "functional . . . β-galactosidase gene" is simply "a functional sequence of DNA that encodes β-galactosidase."

While Glycosyn's expert also states "to say that a gene 'encodes' a working enzyme is to say that it is 'involved in producing' a working enzyme" (*id.*, Ex. 4 at ¶ 33), Jennewein's expert squarely takes the opposition position, "[o]rdinary scientists generally do not describe a gene as merely being 'involved' in producing a protein like β-galactosidase. They normally say a gene 'encodes' β-galactosidase" (RIMB, Ex. 4 at ¶ 25). The undersigned finds Jennewein's expert more persuasive in light of the very particular and detailed nature of this art, and notes that Glycosyn provides no other evidence beyond its expert's opinion to support its "involved in producing" interpretation.

Accordingly, "functional . . . β-galactosidase gene" is hereby construed as "**a functional sequence of DNA that encodes β-galactosidase.**"

3. "wild type"

The Parties disagree on the proper claim construction and have proposed the following constructions:

Relevant Claims	Glycosyn	Jennewein	Staff
'230 Patent claims 21, 27 '018 Patent claims 1, 4, 20, 24	*(A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, the phenotype most commonly found in nature	*(A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, "the form most commonly found in nature"	*(A) plain and ordinary meaning:* plain and ordinary meaning, *i.e.*, the phenotype most commonly found in nature

(JC at 3-4.)

For this limitation, the Parties' dispute is also narrow. Glycosyn argues "[t]hroughout the claims and the specification, the term 'wild type' is used to compare observable traits of the E. coli organism as compared to the modified E. coli organism described in the claims." (CIMB at 34-35 (citing '230 patent at cls. 2, 8, 21, 27; '018 patent at cls. 1, 4, 20, 24); *see id.* at 35 (citing '230 patent at 5:6-18, 6:42-46, 16:43-49; '018 patent at 5:6-18, 6:42-46, 16:43-49).) Glycosyn reasons:

> The picture is clear: every time the term "wild type" is used in the patent claims, it is used in relation to observable traits of the *E. coli* organism. Such observable traits are referred to by persons of ordinary kill [sic] in the art as "phenotype." They are not a "form," as Respondent contends.

(*Id.* at 35.) Glycosyn argues it and the Staff's proposed construction "comports with how a person of ordinary skill in the art would understand the term 'wild type' at the time of the invention. . . . This also aligns with dictionaries commonly used by people of ordinary skill in the art in question at the time of the invention." (*Id.* at 35-36 (citing Prather Decl. at ¶ 36; CIMB, Ex. 13 at 68993-68997).) In its reply brief, Glycosyn contends Jennewein admits "phenotype is defined in term of observable traits or observable characteristics" and "wild-type is used in the patents to describe a phenotype." (CRMB at 14 (citing RIMB at 31).) To the extent Jennewein argues the existence of "wild-type" genotypes, in addition to phenotypes, Glycosyn urges the use of "form" in Jennewein's construction "does not capture this" and "adds complexity and confusion, and leaves the definition of wild-type less apparent and subject to further interpretation." (*Id.*)

In its opening brief, Jennewein highlights that "'[w]ild-type' appears in two contexts in the Asserted Patents: 'wild-type gene' and 'wild-type bacterium'" and argues its own construction "embraces the clear, plain meaning in both contexts: the form most commonly found in nature." (RIMB at 29-30.) Jennewein points out the '230 patent's recitation of both phenotype and genotype (*id.* at 30 (citing '230 patent at 18:19-23)) and extrinsic textbook evidence that defines "phenotype"

as "distinct from its genotype" (*id.* (citing RIMB, Ex. 10 at G8, G-13)). Jennewein summarizes, "[g]enes have both a phenotype *and* a genotype, and there is no reason to include one and exclude the other from the plain meaning of 'wild-type'" and a person of ordinary skill would understand "wild-type" is not limited to phenotype of a gene. (*Id.* (citing RIMB, Ex. 11 at 977, 1232; RIMB, Ex. 10 at 342).)

Regarding a phenotype as an "observable" characteristic or trait, Jennewein contends "[a] gene would not have an 'observable' trait or characteristic—that would be the gene's product, not the gene itself." (*Id.* at 31 (citation omitted).) Further, Jennewein reasons "[a]lthough a wild-type bacterium could have the same phenotype as a genetically engineered bacterium, in that case the bacterium would no longer be considered a 'wild type.'" (*Id.* (citing RIMB, Ex. 4 at ¶ 56).) Thus, Jennewein explains, "[t]he term 'wild-type' qualifies the thing that appears after it—here, either or a gene or bacteria" and "neither a 'gene' nor a 'bacteria' is a phenotype, and the claim needs no such additional requirement." (*Id.* at 32.)

In its reply brief, Jennewein asserts "[t]he parties agree that a 'wild-type' is the form as it exists in nature. A key aspect of this natural state of 'wild-type' is that it is unchanged by man." (RRMB at 18 (citing RIMB, Ex. 4 at ¶¶ 55-56; CIMB, Ex. 13); *see id.* at 20-21 (citing SIMB, Ex. 10 at 2370).) Jennewein contends the construction from Glycosyn and the Staff "eliminates this 'natural' aspect of 'wild-type' and would include man-made mutants." (*Id.* at 18-19.) Jennewein continues to add that discussions in the patent specifications of "levels of activity in a wild-type gene or bacterium does not mean that the gene or bacterium is limited to its phenotype" (*id.* at 19 (citing RRMB, Ex. A at ¶ 18)) and "[n]either the claims nor the specification define a wild-type gene as being synonymous with wild-type activity" (*id.*).

In its opening brief, the Staff points to extrinsic dictionary evidence which defines "wild type" as a phenotype, and other extrinsic dictionary evidence which defines the same as a genotype

or phenotype. (SIMB at 22 (discussing SIMB, Exs. 10, 11).) The Staff explains it prefers using "phenotype," as in Glycosyn's construction, over "form," as in Jennewein's construction, because "it is a slightly more accurate reflection of the manner in which the term 'wild-type' is used in the asserted patents." (*Id.* at 22-23.) The Staff reasons:

> Both patents are focused on the *behavior* of the engineered organisms, specifically on their ability to produce human milk oligosaccharides such as 2'-FL, rather than on the specific molecular makeup of the organisms' genetic structure. In other words, they are focused on the modified *E. coli* bacterium's phenotype rather than its genotype. The Staff's proposed construction reflects this fact.

(*Id.* at 23 (emphasis in original).) In its reply brief, the Staff repeats "the focus of both asserted patents is on the *behavior* of the engineered organism, specifically on its ability to produce human milk oligosaccharides such as 2'-FL, as well as the effect of the *behavior* of the specific *lacZ* gene on the organism's ability to produce 2'-FL." (SRMB at 15 (emphasis in original).) The Staff continues, "[a]ny genotype of a functional promoter-less β-galactosidase gene will do, so long as it has the effect of causing a low level of β-galactosidase activity. In other words, it is the effect of the gene on the bacterium, and not its physical structure, that is important." (*Id.*) Thus, the Staff concludes phenotype is the proper interpretation of "wild-type." (*Id.* at 16.) The Staff also faults Jennewein's comparison of phenotypes between man-made and wild organisms as unsupported by Jennewein's cited expert declaration. (*See* SRMB at 16-17 (discussing RIMB, Ex. 4 at ¶¶ 56, 58).)

Upon review of the evidence, the undersigned finds Jennewein's construction is more accurate. The claims of a patent are the starting point for claim construction. *Interactive Gift Express*, 256 F.3d at 1331. The claims of the asserted patents use "wild type" or "wild-type" as descriptors in two distinct contexts—for both a gene (*see* '230 patent at cls. 2, 5, 21, 24) and for a bacterium as a whole (*see* '230 patent at cls. 8, 27; '018 patent at cls. 1, 4, 20, 24). More specifically, "wild type" is used in the context of a gene which is inserted into another gene ('230 patent at cls.

2, 5, 21, 24) and then also in the context of comparing observable traits between two bacteria ('230 patent at cls. 8, 27; '018 patent at cls. 1, 4, 20, 24.)

Jennewein's construction is consistent with both of these contexts—the "wild type" gene or bacterium is the "form" or "type" of the gene or bacterium "most commonly found in nature." It is this type of the gene which is inserted into another gene (*see* '230 patent at cls. 2, 5, 21, 24) and the type of bacteria which is compared to the bacterium of the invention (*see* '230 patent at cls. 8, 27; '018 patent at cls. 1, 4, 20, 24). Jennewein's construction is further consistent with those portions of the patent specification which refer to "wild-type" in the contexts of a "coding sequence" (*see* '230 patent at 12:64-67 ("DNA fragment carrying . . . a wild-type E. coli lacZ+ coding sequence")) and "wild-type copy of the lacZ (β-galactosidase) gene" (*id.* at 16:43-47) or "supplying a wild-type thyA gene" (*id.* at 16:63-65).

Glycosyn and the Staff's construction, interpreting "wild-type" as a "phenotype" is arguably consistent in the context of comparing organisms with observable traits, but not in the gene context where there is no observable trait, or "phenotype" under comparison as, for example, in the following claims:

> 2. The method of claim 1, wherein the functional promoter-less β-galactosidase gene inserted into an endogenous gene comprises an exogenous wild type *E. coli* lacZ gene.
>
> 5. The method of claim 1, wherein said bacterium comprises a functional promoter-less wild-type *E. coli* lacZ$^+$gene inserted into an endogenous lon gene.
>
> 24. The method of claim 21, wherein said bacterium comprises a functional, wild-type, promoter-less *E. coli* lacZ$^+$gene inserted into an endogenous lon gene.

('230 patent at cls. 2, 5, 24.)

Every claim term is presumed to have meaning. *Innova/Pure Water*, 381 F.3d at 1119 ("While not an absolute rule, all claim terms are presumed to have meaning in a claim."). To have

meaning in these claims, "wild type" must refer to something other than "phenotype." Glycosyn and the Staff's construction is thus too narrow. Indeed, as demonstrated by these claims, Glycosyn is incorrect when it argues "[t]he picture is clear: every time the term 'wild type' is used in the patent claims, it is used in relation to observable traits of the *E. coli* organism." (CIMB at 35.)

Further, the balance of the extrinsic evidence supports Jennewein's broad construction. While the dictionary definition cited by Glycosyn does link "wild type" to phenotype, it does so in the context of a "wild type" as a "member[] of a species." (CIMB, Ex. 13.) Genes are not members of a species and as noted above, the asserted patents use "wild type" in the contexts of both overall organisms and genes themselves. Glycosyn's definition, is therefore of lesser probative value. The Staff's cited dictionary definition linking "wild-type" to phenotype is of similar little value as it too is in the context of a member of a species—"the phenotype that is characteristic of most of the members of the species occurring naturally and contrasting with the phenotype of a mutant." (SIMB, Ex. 11.) The Staff's rationale for including "phenotype" in its construction likewise comes from the viewpoint of the overall organism. (*See, e.g.*, SIMB at 23 ("In other words, [the patents] are focused on the modified *E. coli* bacterium's phenotype rather than its genotype. The Staff's proposed construction reflects this fact."); SRMB at 15 ("the Staff maintains that the focus of both asserted patents is on the *behavior* of the engineered organism . . . .")).

On the other hand, the Staff's second cited dictionary definition defines "wild type" in the proper context—that of genetic material—and states "the standard gene, or the standard genotype or phenotype of an individual, that is found in a wild or natural population [or] a form that is arbitrarily designated as such." (SIMB, Ex. 10.) Jennewein's cited dictionary definitions also define "wild type" in the proper context. A first definition defines "wild-type gene" as "the form of a gene [allele] normally found in nature" (RIMB, Ex. 11 at 977, 1232) and second definition states "the

'normal, nonmutant form of a *macromolecule*, cell or organism'" (RIMB, Ex. 10 at 342 (emphasis added)).

Thus, the undersigned finds those dictionary definitions directed to "wild type" genes, or other macromolecules, to be of higher probative value than those directed to "wild type" organisms. As those gene-specific definitions do not link "wild type" to phenotype, a construction not limited to phenotype is warranted.

Regarding expert testimony as extrinsic evidence, the undersigned finds Glycosyn's expert to be completely conclusory on this issue, stating only "[a] person of ordinary skill in the art at the time of the invention would understand that 'wild type' as used in the claims and specifications of the Asserted Patents refers to the phenotype most commonly found in nature." (CIMB, Ex. 4 at ¶ 36.) Jennewein's expert provides a more persuasive and reasoned justification for his opinion to the contrary. (*See* RIMB, Ex. 4 at ¶¶ 55-66; RRMB, Ex. A at ¶¶ 16-19.) The undersigned also finds, however, no particular reason to use the word "form" in place of "type" as in Jennewein's construction either.

Accordingly, "wild-type" or "wild type" is hereby simply construed as "**the type most commonly found in nature.**"

SO ORDERED.

Charles E. Bullock
Chief Administrative Law Judge

CERTAIN HUMAN MILK OLIGOSACCHARIDES AND METHODS OF PRODUCING THE SAME

INV. NO. 337-TA-1120

PUBLIC CERTIFICATE OF SERVICE

I, Lisa R. Barton, hereby certify that the attached **Order No. 22** has been served by hand upon the Commission Investigative Attorney, **Lisa Murray, Esq.** and the following parties as indicated, on DEC 18 2018.

Lisa R. Barton, Secretary
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