PUBLIC VERSION

UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C.

In the Matter of **CERTAIN BIO-LAYER INTERFEROMETERS AND COMPONENTS THEREOF**	**Investigation No. 337-TA-1344**

COMMISSION OPINION

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I. INTRODUCTION

The Commission has determined to review in part the final initial determination ("FID") issued by the presiding Administrative Law Judge ("ALJ") on March 8, 2024, and, on review, to affirm with modification the FID's finding of no violation of section 337 of the Tariff Act of 1930, as amended, 19 U.S.C. § 1337 ("section 337"). Accordingly, the investigation is terminated with a finding of no violation of section 337.

This opinion sets forth the Commission's reasoning in support of its determinations. The Commission affirms all findings in the FID that are not inconsistent with this opinion.

II. BACKGROUND

A. Procedural History

On November 29, 2022, the Commission instituted this investigation under section 337 based on a complaint filed by complainant Sartorius Bioanalytical Instruments, Inc. ("Sartorius" or "Complainant") of Bohemia, New York. *See* 87 FR 73329-30 (Nov. 29, 2022). The complaint, as supplemented, alleges a violation 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 "bio-layer interferometers, biosensors, and kits containing biosensors and reagents" by reason of the infringement of certain claims of U.S. Patents Nos. 7,445,887 ("the '887 patent"); 7,394,547 ("the '547 patent"); 7,728,982 ("the '982 patent"); and 8,305,585 ("the '585 patent"). *Id.* The notice of investigation names Gator Bio, Inc. ("Gator Bio" or "Respondent") of Palo Alto, California as the respondent. *Id.* The Office of Unfair Import Investigations ("OUII") is also a party to the investigation. *Id.*

The Commission previously terminated the investigation as to the '547, '982, and '585 patents and claims 1-5, 7, 9-14, and 16-18 of the '887 patent based on the withdrawal of the complaint as to those patents and claims. *See* Order No. 14 (May 15, 2023), *unreviewed by*

Comm'n Notice (June 9, 2023); Order No. 26 (June 29, 2023), *unreviewed by* Comm'n Notice (July 20, 2023); Order No. 37 (Oct. 26, 2023), *unreviewed by* Comm'n Notice (Nov. 27, 2023). Claim 8 of the '887 patent ("asserted claim") remains pending in this investigation.

On May 31, 2023, the ALJ issued a claim construction order construing certain terms of the '887 patent. Order No. 16 (May 31, 2023). On June 26, 2023, the ALJ issued a supplemental claim construction order. Order No. 22 (June 26, 2023). In particular, the ALJ declined to correct the term "the layer of enzyme binding molecules," and found the remaining asserted claims to be indefinite on that basis. *See id*. Accordingly, on June 30, 2023, the ALJ issued an ID granting summary determination that the asserted claims are invalid for indefiniteness, thereby terminating the investigation with a finding of no violation of section 337. *See* Order No. 27 (June 30, 2023). On August 16, 2023, the Commission determined to reverse the ALJ's indefiniteness finding. *See* Comm'n Notice (Aug. 16, 2023). Specifically, the Commission corrected the term "the layer of enzyme binding molecules," which included an obvious and minor clerical error, and construed it as "the layer of *analyte* binding molecules." *Id.*[1] The Commission also remanded the investigation to the ALJ for further proceedings consistent with the Commission's determination. *See id.*

On September 16, 2022, the ALJ issued the FID finding no violation of section 337. Specifically, the FID finds the accused products do not infringe claim 8 of the '887 patent, and that the domestic industry products do not practice that claim, and thus Sartorius has failed to satisfy the technical prong of the domestic industry requirement. *See* FID at 59-88, 97-110.

[1] Commissioner Johanson dissented from the majority's decision to reverse the ALJ's indefiniteness finding and to construe the term "the layer of enzyme binding molecules" to mean "the layer of analyte binding molecules." *See* Comm'n Op. at 2 n.1 (Aug. 24, 2023) (public version).

Additionally, the FID finds that the importation requirement is satisfied regarding the accused Gator Bio instruments but is not satisfied with respect to the accused probes and kits, and that the Commission lacks *in rem* jurisdiction over those probes and kits. *See id.* at 16-17. The FID does not address whether the accused instruments are "articles that infringe" under section 337(a)(1)(B) reasoning that "the record on this issue is undeveloped and because [the ALJ] ha[s] found that the use of Gator Bio's GatorPrime instruments with one of its HRP probes does not practice claim 8." *Id.* at 89. The FID further finds that claim 8 of the '887 patent is not invalid based on obviousness-type double patenting and that assignor estoppel bars Gator Bio's assertions of invalidity based on obviousness and obviousness-type double patenting. *See id.* at 114-22. The FID also rejects as moot Gator Bio's assertions of invalidity based on patent ineligibility, indefiniteness, lack of written description, and lack of enablement, which are premised on Sartorius's construction for the term "air gap," which the FID does not adopt. *See id.* at 122. Lastly, should the Commission find that the technical prong of the domestic industry requirement is in fact satisfied, the FID finds that the economic prong of the domestic industry requirement is also satisfied with respect to the '887 patent. *See id.* at 122-58.

The FID includes a Recommended Determination ("RD") recommending, should the Commission find a violation of section 337, that the Commission issue: (1) a limited exclusion order against certain bio-layer interferometers and components thereof that are imported into the United States, sold for importation, or sold within the United States after importation by or on behalf of Gator Bio; and (2) a cease and desist order against Gator Bio. The RD recommends no (zero percent) bond during the period of Presidential review against Gator Bio's infringing probes/kits but recommends that the Commission set a bond of 100 percent with respect to the

infringing GatorPrime instruments, 54.6 percent bond with respect to the infringing GatorPlus instruments, and 100 percent with respect to infringing GatorPro instruments.

On March 22, 2024, Sartorius petitioned for Commission review of certain FID findings, including with respect to: (1) importation and *in rem* jurisdiction; (2) whether the accused instruments are "articles that infringe"; (3) claim construction; (4) infringement; (5) the technical prong of the domestic industry requirement; and (6) assignor estoppel.[2] On the same day, Gator Bio filed a contingent petition for review of certain FID findings, including with respect to: (1) infringement; (2) invalidity; and (3) the domestic industry requirement (economic prong and technical prong).[3] On April 3, 2024, the parties and OUII filed responses to the petitions.[4]

On April 8 and 9, 2024, respectively, Sartorius and Gator Bio filed statements on the public interest pursuant to Commission Rule 210.50 (19 C.F.R. § 210.50). On April 5, 2024, the Commission received public interest submissions from Paul Yu, Jordon Wang, and Zucai Suo in response to its post-RD *Federal Register* notice. *See* 89 Fed. Reg. 18667 (Mar. 14, 2024).

B. The Asserted Patent

The '887 patent relates to measurements of enzyme activity using bio-layer interferometry ("BLI").[5] The specification of the '887 patent explains that enzyme assays of the

[2] *See* Complainant's Combined Petition for Review and Contingent Petition for Review of the Final Initial Determination (Mar. 22, 2024) ("Complainant's Pet.").

[3] *See* Respondent Gator Bio Inc.'s Contingent Petition for Review (Mar. 22, 2024) ("Respondent's Pet.").

[4] *See* Complainant's Response to Respondent Gator Bio, Inc.'s Contingent Petition for Review of the Initial Determination Finding of No Violation of Section 337 (Apr. 3, 2024) ("Complainant's Resp."); Respondent Gator Bio, Inc.'s Response to Complainant's Petition for Review and Contingent Petition for Review of Initial Determination (Apr. 3, 2024) ("Respondent's Resp."); The Commission Investigative Staff Combined Response (Apr. 3, 2024) ("OUII's Resp.").

[5] The earliest effective filing date for the '887 patent is January 7, 2005, and therefore the patent is subject to the pre-AIA ("America Invents Act") patentability provisions of the Patent Act.

prior art "typically require labeling the substrate in such a way that the enzyme acting on the substrate produces a detectable change in signal." *See* JX-2, '887 patent at 1:34-36. Labeled enzyme substrates, however, are often not commercially available and add to the time, expense, and inconvenience of enzyme activity measurements. *See id.* at 1:36-44. The present invention "can be carried out using unlabeled substrates" and allows for "simple, fiber based, real-time enzyme activity assays, capable of providing specific activity measurements, [and] suitable for low-volume samples." *See id.* at 1:48-54.

The claimed invention relies on the BLI sensor's ability to detect sub-nanometer changes in the thickness of its optical layer detection surface. *See* JX-2, '887 patent at 4:31-33. As recited in claim 8 of the '887 patent, the optical element of the BLI apparatus includes a layer of analyte[6] binding molecules. *See id.* at 10:48-67 (claim 8). When an enzyme substrate binds to the layer of analyte binding molecules, the thickness of that layer changes and can be detected by the BLI sensor. *See id.* at 4:33-36. Thus, the activity of an enzyme can be measured by reacting an enzyme with an enzyme substrate in the presence of the BLI sensor, which affects the thickness of the optical layer of the BLI sensor. *See id.* at 4:36-43.

Figure 4 of the '547 patent (which is incorporated by reference in the '887 patent) shows an example of the BLI apparatus. *See* JX-1, '547 patent, Figure 4 (reproduced below).

[6] "Analyte" refers to a chemical substance that is being identified or measured. For instance, in the context of the '887 patent, the analyte can be the "enzyme substrate."

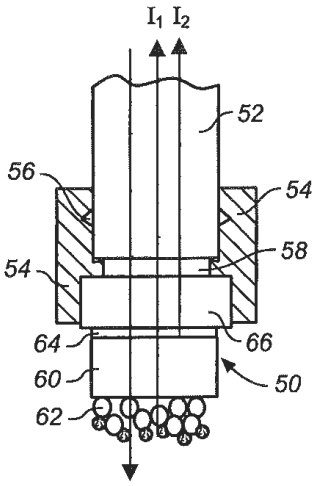


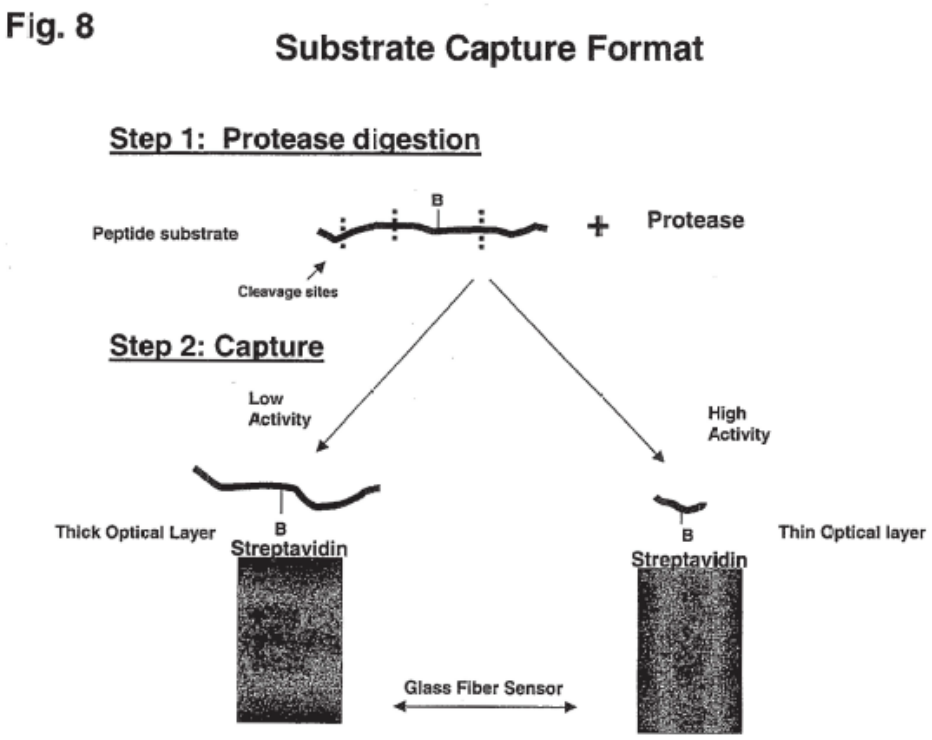
FIG. _4

The specification of the '547 patent explains that the optical assembly **50** of Figure 4 includes a first optical element **60** and having first and second reflective layers **62**, **64**. *See* JX-1, '547 patent at 9:38-42. The optical assembly of Figure 4 can further include a second optical element **66**. *See id.* at 9:42-43. The optical assembly **50** can be "removably carried on the distal end of an optical fiber **52**" and can include "a plurality of flexible gripping arms such as arms **54** that are designed to slide over the end of the fiber [**52**] and grip the fiber by engagement of an annular rim or detente **56** on the fiber." *See id.* at 9:23-29. The specification explains that "[t]his attachment serves to position the optical assembly **50** on the fiber **52** to provide an air gap **58** between the distal end of the fiber **52** and the upper surface of the assembly. *See id.* at 9:29-33.

In operation, "[t]he lower surface of the assembly is then exposed to a sample of analyte, under conditions that favor binding of sample analyte to the analyte-binding molecules forming reflective layer **62**." JX-1, '547 patent at 9:52-56. "As analyte molecules bind to this layer, the thickness of the layer increases, increasing the distance 'd' between reflective surfaces **62** and **64**." *Id.* at 9:56-59. "This produces a shift in the extrema of the interference wave produced by

reflection from the two layers, . . . [which] is used to determine the change in thickness at the lower (distal-most) reflecting layer." *Id.* at 9:59-64.

Figure 8 of the '887 patent illustrates the use of a BLI sensor to measure enzyme activity. *See* '887 patent, Figure 8 (reproduced below). The specification of the '887 patent discloses an assay of protease activity using the substrate capture format, *i.e.*, using a BLI sensor including a layer of analyte binding molecules (*e.g.*, streptavidin) that bind with the enzyme substrate (*e.g.*, biotinylated cytochrome C).[7] *See* JX-2, '887 patent at 7:50-55 (Example 3), Figure 8.



The assay of Example 3 and Figure 8 consists of adding a trypsin (enzyme) sample to a biotinylated cytochrome C solution. *See* JX-2, '887 patent at 7:50-53. "After a digestion time period, a streptavidin coated sensor is placed in the enzyme/substrate mixture for substrate

[7] In Example 3, the biotin in the biotinylated cytochrome C (the "enzyme substrate" or "analyte") binds with streptavidin which is the molecule in the layer of analyte binding molecules that binds with the biotinylated cytochrome C.

capture." *See id.* at 7:53-55. The specification explains that the "BLI sensor can assess the change in substrate size by a measuring the optical layer thickness upon binding the biotinylated peptide" as "protease activity produces smaller peptides with a thinner optical layer." *See id.* at 7:59-63, Figure 8.

Complainant asserts infringement of claim 8 of the '887 patent, which recites as follows:

> **8.** **[8Pre]** A method for ***assaying enzyme activity***, comprising:
>
> **[8A]** providing an optical element coupled to a light source via a mechanical coupling that engages the first optical element with a fiber and **[8B]** ***provides an air gap*** between the first optical element and the fiber, **[8C]** the optical element including (a) a proximal reflecting surface and a distal reflecting surface **[8D]** separated by at least 50 nm, and **[8E]** (b) a layer of analyte binding molecules;
>
> **[8F1]** exposing the optical element to an enzyme substrate reacted or reacting with an enzyme, **[8F2]** whereby the enzyme substrate or a portion of the enzyme substrate binds to the layer of analyte binding molecules, and **[8F3]** wherein interference between a reflected beam from the proximal reflecting surface and a reflected beam from the distal reflecting surface varies as the enzyme substrate or portion thereof binds to the layer of [analyte] binding molecules, **[8G]** the reflected beams coupled into the fiber; and
>
> [**8H**] detecting a change in optical thickness of the first reflecting surface, wherein the change is ***indicative of enzyme activity***.

See JX-2, '887 patent (claim 8) (emphasis added for disputed limitations).

C. Accused Products

The notice of investigation defines the scope of the investigation as "biolayer interferometers, biosensors, and kits containing biosensors and reagents." 87 Fed. Reg. at 73330.

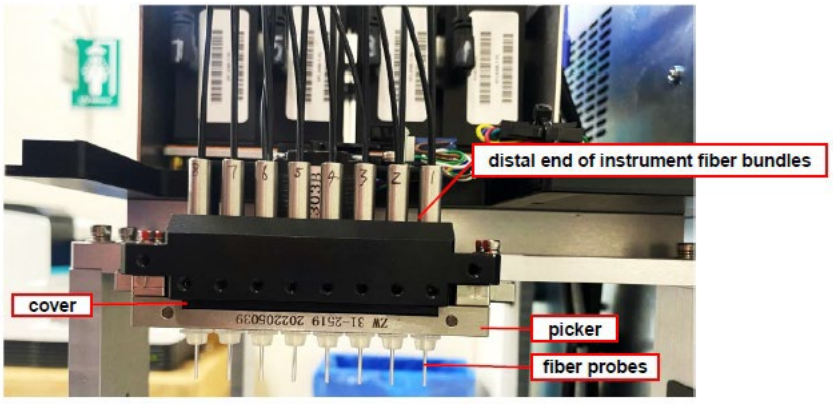
The accused products are GatorPrime (shown below), GatorPlus, and GatorPro interferometers (referred to as instruments) and HRP (horseradish peroxidase) probes (*i.e.*, biosensors) and kits (*i.e.*, biosensors and reagents) used with those instruments. FID at 10-14.

GatorPrime Instrument

Probe

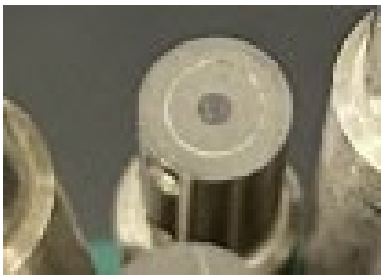
See FID at 10 (citing CDX-1.12 (GatorPrime Instrument reproduced above); CDX-1.14 (Gator Bio probe)).

As explained in the FID, Gator Bio's accused instrument is a bio-layer interferometer which operates with one or more fiber bundles and a number of probes to perform bio-layer interferometry. FID at 11 (citing RDX-2.3 (reproduced below)).



Gator Bio redesigned its fiber bundles in an attempt to provide physical contact between the fiber and the probe and to eliminate any air gap between them. FID at 63-75; CDX-1.13 (Gator Bio's first and second redesigned fiber bundles).

First Redesigned Fiber Bundle



Second Redesigned Fiber Bundle

D. Domestic Industry Products

The domestic industry products are certain Octet BLI instruments (shown below) and probes marketed by Sartorius in the United States. *See* FID at 14-15 (citing CX-190C.15).

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The FID finds that the Octet R8 instrument, which is representative of the domestic industry instruments, includes a lamp, an optical fiber, a fiber bundle, and a probe. FID at 92-95 (citing CX-187C.3 (reproduced below)). In asserting a domestic industry, Sartorius relies on its Anti-CHO HCP detection kit,[8] which also uses HRP (enzyme). *Id.* at 96.

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[8] "CHO" refers to "Chinese hamster ovary," and HCP refers to "host cell protein." FID at 94.

III. STANDARD FOR REVIEW

The Commission may review an ID either upon petition by one of the parties or on its own motion. *See* 19 C.F.R. §§ 210.43, 210.44. The Commission will grant a petition for review, in whole or in part, where it appears:

> (i) that a finding or conclusion of material fact is clearly erroneous;
>
> (ii) that a legal conclusion is erroneous, without governing precedent, rule or law, or constitutes an abuse of discretion; or
>
> (iii) that the determination is one affecting Commission policy.

19 C.F.R. § 210.43(b)(1), (d)(2). The Commission's review will encompass those issues for which at least one participating Commissioner has voted for review. *See id.* at § 210.43(d)(3).

When the Commission reviews an initial determination, in whole or in part, it reviews the determination *de novo*. *Certain Soft-Edged Trampolines and Components Thereof*, Inv. No. 337-TA-908, Comm'n Op. at 4 (May 1, 2015). Upon review, the "Commission has 'all the powers which it would have in making the initial determination,' except where the issues are limited on notice or by rule." *Certain Flash Memory Circuits & Prods. Containing Same*, Inv. No. 337-TA-382, USITC Pub. No. 3046, Comm'n Op. at 9-10 (July 1997) (quoting *Certain Acid-Washed Denim Garments & Accessories*, Inv. No. 337-TA-324, Comm'n Op. at 5 (Nov. 1992)). With respect to the issues under 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." 19 C.F.R. § 210.45(c). The Commission also "may take no position on specific issues or portions of the initial determination," and "may make any finding or conclusions that in its judgment are proper based on the record in the proceeding." *Id.*; *see also Beloit Corp. v. Valmet Oy*, 742 F.2d 1421, 1423 (Fed. Cir. 1984).

IV. DISCUSSION

For the reasons set forth below, the Commission has determined to review the FID in part and, on review, to affirm with modification the FID's finding of no violation of section 337. More specifically, the Commission has determined to review and, on review, to: (1) take no position on the FID's findings of no importation with respect to Gator Bio's probes and kits; (2) vacate the FID's findings of no *in rem* jurisdiction with respect to Gator Bio's probes and kits; (3) find that Gator Bio's instruments are not "articles that infringe" because the accused articles do not infringe the asserted claim; (4) modify the claim construction of the preamble of claim 8, "assaying enzyme activity," and the claim term "air gap"; (5) affirm with modification the FID's finding that the accused products do not infringe claim 8 of the '887 patent; (6) affirm with modification the FID's finding that the domestic industry products do not practice claim 8 of the '887 patent, and thus Sartorius does not satisfy the technical prong of the domestic industry requirement; and (7) take no position as to the FID's finding that Sartorius satisfies the economic prong of the domestic industry requirement.

The Commission has determined not to review of the remainder of the FID's findings including with respect to induced infringement, invalidity, and assignor estoppel issues.

A. *In Rem* Jurisdiction and Importation

The FID finds that the Commission has *in rem* jurisdiction over Gator Bio's accused instruments because they have been imported into the United States. FID at 16-17. The FID notes that Gator Bio has stipulated that its accused instruments have been imported into the United States. *Id*. at 18. The FID also finds, however, that the Commission does not have *in rem* jurisdiction over the accused probes and kits because they are not imported into the United States. *Id.* at 17-19.

Sartorius petitions for review of the ALJ's findings with respect to the probes and kits. Sartorius argues that "importing components of accused products into the U.S. is 'sufficient to establish the requirement that there be an 'importation into the United States' as provided in section 337(a)(1)(B).'" Complainant's Pet. at 93-94 (quoting *Certain High-Density Fiber Optic Equipment & Components Thereof*, Inv. No. 337-TA-1194, Comm'n Op., 2021 WL 3809088, *11 (Aug. 23, 2021) ("*High-Density Fiber Optic Equip.*")). According to Sartorius' petition, it is "irrelevant . . . that the Accused Probes are completed in the U.S." because they are "manufactured using admittedly imported components." Complainant's Pet. at 94. In response, Gator Bio admits that components of the accused probes are imported into the United States, but argues that the importation requirement is not satisfied because "the uncoated optical fiber (that is used to make the domestically manufactured probes) has substantial non-infringing uses." *See* Respondent's Resp. at 69-70; *see also* FID at 18 (citing Tr. (Zuk) at 440:13-18 ("The raw material optical fiber is imported from China.")). OUII agrees with Sartorius that the Commission does not lack *in rem* jurisdiction over the accused probes/kits. OUII's Resp. at 26.

The Commission uses "*in rem* jurisdiction" as a shorthand to refer to its statutory authority to investigate accused articles that are imported, sold for importation, or sold in the United States after importation. Based on the particular facts and allegations in this investigation, we reject Gator Bio's contention that the Commission lacks statutory authority over the accused articles due to a supposed failure to satisfy the importation requirement. As the ID correctly stated: "To prove a violation of section 337 by a respondent, the complainant must show that the respondent engaged in '[t]he importation into the United States, the sale for importation, or the sale within the United States after importation by the owner, importer, or consignee' of products accused of infringement." FID at 17 (citing 19 U.S.C. § 1337(a)(1)(B)).

Here, Sartorius alleges, *inter alia*, a violation of section 337 based on induced infringement by the post-importation use of the accused instruments to practice claim 8. *See* Complainant's Initial Post Hr'g Br. at 38 ("Respondent has committed induced infringement under 35 U.S.C. § 271(b) by: (i) importing the Accused Instruments; and (ii) using them to practice claim 8 of the '887 patent."). Under Sartorius' theory of induced infringement, the accused instruments are used with the accused probes in the United States to practice claim 8. *See id.* at 15-19, 37 (arguing that the accused instruments satisfy, *inter alia*, the detecting limitation and the accused probes constitute the claimed optical element). The importation requirement as set forth in section 337(a)(1)(B) requires that there be an "importation into the United States, the sale for importation, or the sale within the United States after importation . . . of articles" that infringe. There is no dispute that the accused instruments are imported, and Sartorius alleges a violation of section 337 based on induced infringement through the use of those imported instruments. Therefore, in the context of the allegations in this investigation, importation of the accused instruments is sufficient to meet the importation requirement and it is unnecessary for the Commission to reach the issue of whether Gator Bio's probes and kits are also imported.

Accordingly, the Commission has determined to review the FID's findings that the accused probes and kits are not imported and that the Commission has no *in rem* jurisdiction over those probes and kits. On review, the Commission takes no position on the FID's findings of no importation with respect to the accused Gator Bio probes and kits. The Commission also vacates the FID's findings of no *in rem* jurisdiction with respect to Gator Bio's probes and kits.

B. Articles that Infringe

Gator Bio submitted a two-sentence argument in its Responsive Post-Hearing Brief ("RRB") before the ALJ arguing that the accused Gator Bio instruments, although imported, do

not constitute "articles that infringe" under section 337(a)(1)(B) because, at the time of importation, the accused instruments "cannot themselves 'perform the recited steps of method claim 8 and have countless noninfringing uses; it is the non-imported U.S.-made probes that are alleged to be the claimed optical element and that are used to carry out any allegedly infringing methods.'" FID at 88-89 (citing RRB at 3-4). Neither Sartorius nor OUII address this issue. *See id.* at 89.

The FID declines to decide whether Gator Bio's instruments are "articles that infringe" under section 337 because "the record on this issue is undeveloped" and "the use of Gator Bio's GatorPrime instruments with one of its HRP probes does not practice claim 8." *Id*. at 88-89; *see* 19 U.S.C. § 1337(a)(1)(B). The FID notes Gator Bio's contention in a footnote in its Responsive Post-Hearing Brief that "the Commission misreads *Suprema* as disavowing either a nexus requirement or all consideration of the state of imported articles at the time of importation." *Id.* The FID finds, however, that Gator Bio abandoned this latter argument by failing to raise it in its pre-hearing brief. *Id.* at 89 (citing RRB at 4 n.1).

Sartorius argues in its petition that "should the Accused Products be found to practice claim 8, the Accused Products are 'articles that infringe.'" Complainant's Pet. at 80-81. Gator Bio responds that "[n]either *Suprema* nor *Comcast* disavowed all consideration of the state of imported articles at the time of importation or the requirement of some connection between importation and the accused infringement." *See* Respondent's Resp. at 55-56. OUII argues that the FID correctly declines to reach the issue of whether Gator Bio's accused products are articles that infringe, arguing that both Sartorius and Gator Bio waived the issue and that the record was underdeveloped. *See* OUII's Resp. at 23-24.

Because, as discussed *infra* section IV.D, the Commission has determined to affirm the FID's finding that the Gator Bio accused products do not practice claim 8 of the '887 patent, the Commission finds that Gator Bio's accused instruments are not "articles that infringe" based on that non-infringement determination.[9] The Commission therefore need not address Gator Bio's arguments regarding the state of imported articles at time of importation. However, the Commission notes that *Suprema* and *Comcast*, in addressing allegations of induced infringement, found that there is no requirement that articles infringe at the time of importation.

C. Claim Construction

1. Preamble: "Assaying Enzyme Activity"

The preamble of claim 8 of the '887 patent recites "[a] method for assaying enzyme activity." JX-2, '887 patent at 10:48-67 (claim 8). The parties disagree as to whether the preamble is limiting, and they disagree on the construction of the term "assaying" as follows:

Claim Term	Sartorius's Construction	Gator Bio's Construction	OUII's Construction
Assaying	No construction needed because "assaying" is not a claim limitation. In the event that the ALJ finds "assaying" to be a claim limitation, "assaying" should be given its plain and ordinary meaning (*i.e.*, "detecting, measuring, or monitoring").	Measuring	Measuring

FID at 33.

[9] As discussed *infra* note 15, Commissioner Johanson declines to join the majority's non-infringement analysis as to claim limitations [8Pre], [8H], [8F2], and [8F3]. To the extent the majority's finding that Gator Bio's accused instruments are not "articles that infringe" is based on that analysis, Commissioner Johanson respectfully declines to join that finding.

The FID finds that the preamble is limiting and construes "assaying" as "measuring." *See id.* at 32-37. In Order No. 16, the ALJ provisionally concluded based on the *Markman* briefing that the preamble was not limiting, but the ALJ noted that whether the construction of the term "assaying" was "relevant to any argument that the preamble is limiting" and "[t]o the extent such an argument is properly raised later, [the ALJ] [would] consider it at that time." Order No. 16 at 24-25; FID at 33 (citing Order No. 16). In the FID, the ALJ noted that a dispute remains as to the "assaying" limitation, and accordingly, revisited the construction of that term and whether the preamble was limiting. FID at 33. Thus, contrary to Sartorius's contention (Complainant's Pet. at 14-15), the ALJ did not violate the Administrative Procedure Act ("APA") (5 U.S.C. §§ 551 *et seq.*) because Sartorius was on notice that the ALJ could revisit this issue, and Sartorius had a full opportunity to be heard on this issue since it presented alternative arguments on whether the preamble is limiting in its post-hearing briefing. *See Genzyme Therapeutic Prods. Ltd. P'ship v. Biomarin Pharm. Inc.*, 825 F.3d 1360, 1366-67 (Fed. Cir. 2016) ("The critical question for compliance with the APA and due process is whether [appellant] received 'adequate notice of the issues that would be considered, and ultimately resolved, at that hearing.'") (citation omitted); *see also O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1362 (Fed. Cir. 2008) ("When the parties present a fundamental dispute regarding the scope of a claim term, it is the court's duty to resolve it."). Accordingly, there is no prejudice to Sartorius, and the FID does not err in revisiting the issue as to whether the preamble is limiting. *Accord* Respondent's Resp. at 3-5; OUII's Resp. at 4-5.

The FID finds that the preamble of claim 8 is limiting in view of the body of the claim, particularly, the phrase "detecting a change in optical thickness of the first reflecting surface, wherein the change is indicative of enzyme activity." FID at 36-37. The FID explains that the

preamble is "tied" to the detecting step. *Id.* at 37. In addition, the FID construes the preamble, *i.e.*, "assaying enzyme activity" as "measuring enzyme activity." *Id.* at 34-36. The FID reasons that the "detecting a change" limitation shows that "what is assessed is enzyme activity." *Id.*

The FID further finds that the specification supports its construction. *Id.* The FID explains that the specification states that "[t]he invention is useful for measuring enzyme activity" and the examples consistently describe enzyme activity measurements. *Id.* at 34-35 (citing JX-2, '887 patent at 1:20-22, 1:26-28, 3:27-33, 4:44-49, 5:40-63, 6:5-29, 7:19-8:13, 8:32-52, 8:54-9:43). The FID dismisses Sartorius's argument that "assaying" includes "monitoring," explaining that "Sartorius fails to explain how enzyme activity can be monitored without being measured and that monitoring enzyme activity suggests taking measurements over time." *Id.* at 35. The FID declines to rely on the parties' expert testimony finding that it does not negate that "the specification clearly and consistently discloses measuring enzyme activity." *Id.* at 36.

In its petition, Sartorius argues that the preamble is not limiting because the body of the claim describes a structurally complete invention. Complainant's Pet. at 17-18. Sartorius also argues that the FID construes the claim term "assaying" too narrowly because the claim language does not exclude detecting and monitoring which can provide a qualitative rather than a quantitative measurement of enzyme activity. *Id.* at 19-20. For instance, Sartorius argues, claim 8 encompasses a binary detection without quantification of enzyme activity, *i.e.*, the presence of enzyme activity or lack of such activity. *Id.* at 23-24. Sartorius also argues that the specification describes Figures 9 to 13 as "detect[ing]" enzyme activity, thereby confirming that "assaying" includes "detecting." *Id.* at 22-24. Sartorius further argues that the specification discloses that "[i]n the development and manufacture of enzyme or enzyme inhibitor based products for

therapeutic or industrial applications, it is critical to monitor the activity of the enzyme throughout the process." *Id.* at 26 (quoting JX-2, '887 patent at 1:30-34).

Gator Bio and OUII respond that the preamble is limiting because it provides antecedent basis for the body of claim 8. *See* Respondent's Resp. at 7-8; OUII's Resp. at 7-8. Gator Bio also argues that the FID correctly construed the term "assaying" as "measuring" and that "detecting" and "monitoring" are each a form of measurement. Respondent's Resp. at 11-13.

The Commission has determined to review the FID's construction of the term "assaying." On review, the Commission affirms the FID's finding that the preamble is limiting but construes the term "assaying" as "detecting, measuring, or monitoring."

A preamble is limiting when other limitations in the body of the claim rely on the preamble for antecedent basis. *See Bio-Rad Labs., Inc. v. 10X Genomics Inc.*, 967 F.3d 1353, 1369 (Fed. Cir. 2020) ("Reliance on a preamble phrase for antecedent basis . . . may limit claim scope.") (citation omitted). Indeed, the term "detecting . . . indicative of enzyme activity" depends for antecedent basis on the preamble "assaying enzyme activity" because enzyme activity is measured by detecting changes in the thickness of the optical layer. Thus, "enzyme activity" appears both in the preamble and in the body of the claim, demonstrating a dependence on the preamble for antecedent basis, which supports a finding that the preamble is limiting.

In addition, the preamble is also limiting because it is "essential to understand limitations or terms in the claim body." *Catalina Marketing Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002) (citing *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1306 (Fed. Cir. 1999)). Here, the claim language shows that the "detecting" step is conducted in the context of "assaying enzyme activity." Thus, the preamble is "necessary to give life, meaning, and vitality" to claim 8. *Id.* ("A preamble limits the claimed invention if it recites

essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim.") (citing *Pitney Bowes*, 182 F.3d at 1305).

As to the FID's construction of the preamble, the Commission agrees with Sartorius that the FID construes "assaying" too narrowly. While the claim language recites detecting a change in optical thickness and that such change is indicative of enzyme activity, there is no requirement in the claim that the enzyme activity be quantitatively measured.

The specification of the '887 patent describes the invention as "address[ing] the[] . . . shortcomings of the prior art by providing simple, fiber based, real-time enzyme activity assays, *capable of* providing specific activity measurements, suitable for low volume samples, that are highly multiplexable and in some embodiments can be carried out using unlabeled substrates." JX-2, '887 patent at 1:48-54 (emphasis added). Even if the claimed invention is capable of providing specific activity measurements, the claim language does not require such quantitative measurements of enzyme activity. *See Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004) ("Even when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using 'words or expressions of manifest exclusion or restriction.'").

Although the examples disclosed in the specification consistently refer to measuring enzyme activity, the claim language does not, and the '887 patent specification does not evidence statements of "manifest exclusion or restriction" or clear disavowal to support narrowing the claim language. *Id*. The specification also describes shortcomings associated with prior art methods of "[q]uantitation as by, *e.g.*, enzyme-linked immunosorbant (ELISA)-based assays" which "adds to the time and expense of specific activity measurements and requires additional sample," but it does not support limiting the scope of the claimed invention, contrary to Gator

Bio's suggestion. Respondent's Resp. at 8; JX-2, '887 patent at 1:45-48. Gator Bio also appears to agree that quantitative measurements are not required, stating that "nothing in the FID's construction of the preamble limits it to quantitative or numerical measurements." *Id*. at 13.

As such, the Commission finds that the "assaying" may be either qualitative or quantitative in nature, and thus, the Commission finds no support in the record for narrowing the plain meaning of the term "assaying." Accordingly, the Commission construes the term "assaying" as "detecting, measuring, or monitoring."

2. <u>Air Gap</u>

Claim 8 of the '887 patent recites "[a] method for assaying enzyme activity, comprising: providing an optical element coupled to a light source via a mechanical coupling that engages the first optical element with a fiber and provides an ***air gap*** between the first optical element and the fiber." JX-2, '887 patent at 10:48-67 (claim 8). The parties dispute the construction of the term "air gap" as follows:

Claim Term	Sartorius's Construction	Gator Bio's Construction	OUII's Construction
Air gap	plain and ordinary meaning—a gap filled with air	controlled spacing between surfaces that avoids undesired interference fringes	a designed separation between two non-contacting elements

FID at 24.

The FID construes the term "air gap" as a designed separation, *i.e.*, an intentional design feature. *Id.* at 23-32. The FID rejects Sartorius's construction that "air gap" means "a gap filled with air." *Id.* at 24. The FID further finds that neither OUII nor Gator Bio waived their proposed constructions, and that they raised them in their pre-hearing briefs. *See id.* at 23. In addition, the FID states that it has the duty to resolve a claim construction dispute even if it arises

after the claim construction phase of the investigation. *Id.* (citing *O2 Micro*, 521 F.3d at 1362; *Certain Laparoscopic Surgical Staplers, Reload Cartridges, & Components Thereof*, Inv. No. 337-TA-1167, Comm'n Op., 2021 WL 6071753, *13 (Dec. 20, 2021)).

The FID relies on the intrinsic evidence, including the claim language, the specification, and the prosecution history, and finds that the intrinsic evidence supports construing "air gap" as an intentional design feature. *See id.* at 24-25. Specifically, the FID reasons that "[t]he claim language itself thus instructs what provides the air gap (the mechanical coupling) and where it is (between the first optical element and the fiber)." *Id.* The FID notes that the '887 patent specification does not mention an "air gap," but that the '547 patent specification (which is incorporated by reference in the '887 patent specification), and more specifically Figures 4 and 5 of that patent, "show an air gap as a design feature between an optical element and the optical fiber." *Id.* at 25-28 (citing JX-1, '547 patent at Figures 4, 5, 9:22-64, 10:1-30; JX-2, '887 patent at 4:1-10 (incorporating Application Serial No. 10/981,901, which issued as the '547 patent)). The FID, however, agrees with Complainant that "the specification does not mandate that all contact [between the optical element and the fiber] is precluded via the air gap." *Id.* at 30. As to the prosecution history, the FID finds that "[t]he claim amendments made by applicant to introduce the claimed air gap and applicant's arguments distinguishing the prior art on this basis, support that the claimed air gap is a designed separation between the optical element and the fiber." *Id.* at 30-32 (citing JX-6.221, 224, 225, 228).

Sartorius argues that the FID errs in construing the term "air gap" for the first time after the evidentiary hearing. Complainant' Pet. at 63-64. Sartorius contends that the ALJ violated the APA by failing to give Complainant timely notice of that construction. *See id.* at 65. Sartorius also argues that construing "air gap" as requiring an intentional design feature is

erroneous because claim construction and infringement cannot turn on the intent of the accused infringer. *See id.* at 66-67 (citing *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1353 (Fed. Cir. 2001); also citing *Cochlear Bone Anchored Sols., AB, v. Oticon Med., AB*, 958 F.3d 1348, 1355 (Fed. Cir. 2020)). Sartorius further contends that the intrinsic evidence "does not justify importing an intent requirement into a structural element." *See id.* at 67-69.

Gator Bio responds that Sartorius was on notice of Gator Bio's non-infringement positions during both fact and expert discovery and the issue was briefed in the parties' pre-hearing and post-hearing briefs. *See* Respondent's Resp. at 37-39; *accord* OUII's Resp. at 14-15. Gator Bio also argues that Sartorius incorrectly "conflates an intent to infringe with an intent to assemble an invention in a certain manner." *Id.* at 45-46 (citing, *inter alia*, *Koito Mfg. Co. v. Turn-Key-Tech, LLC*, 381 F.3d 1142, 1150 n.2 (Fed. Cir. 2004); *Combined Sys., Inc. v. Def. Tech. Corp. of Am.*, 350 F.3d 1207, 1210-14 (Fed. Cir. 2003); *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003)). Alternatively, Gator Bio argues that construing "air gap" as a "controlled separation" does not require any intent but implies that the separation is controlled to ensure that it has certain size or properties. *See id.* at 46.

The Commission has determined to review the FID's construction of the term "air gap." On review, the Commission affirms that "air gap" is not any "gap filled with air" as proposed by Sartorius. Rather, the Commission construes the term "air gap" as a structural separation that is distinct from a physical contact structure and does not encompass surface roughness as would typically exist in a physical contact structure.

The Commission finds that Sartorius was on notice that there was both a claim construction and an infringement dispute relating to the term "air gap." Indeed, during fact and expert discovery, Gator Bio expressly disputed Sartorius's infringement contentions with respect

to Gator Bio's second redesigned product, which were based on the theory that surface roughness can provide the claimed air gap. *See* Respondent's Resp. at 36-37 (citing CX-619C.48 ("[N]or would such roughness create an 'air gap.'"); Sartorius Motion for Summary Determination of No Invalidity, Ex. 10 (Schaafsma[10] Expert Report at ¶ 216-17) (opining that "there is no 'air gap' between a fiber and probe when they are in physical contact" and that an "air gap" is "not merely nanoscale surface 'roughness'")). Sartorius does not contend that it had no notice of Gator Bio's non-infringement arguments. Thus, at a minimum, the Commission must resolve whether the scope of the term "air gap" can extend to cover surface roughness, and therefore, the Commission is required to resolve the parties' claim construction dispute and to construe the term "air gap." *See O2 Micro*, 521 F.3d at 1362 ("When the parties present a fundamental dispute regarding the scope of a claim term, it is the court's duty to resolve it."). Thus, Sartorius received adequate notice that the scope of the term "air gap" was in dispute and had a full opportunity to be heard on this issue. *See Genzyme*, 825 F.3d at 1366-67 ("The critical question for compliance with the APA and due process is whether Genzyme received 'adequate notice of the issues that would be considered, and ultimately resolved, at that hearing.'") (quotation omitted).

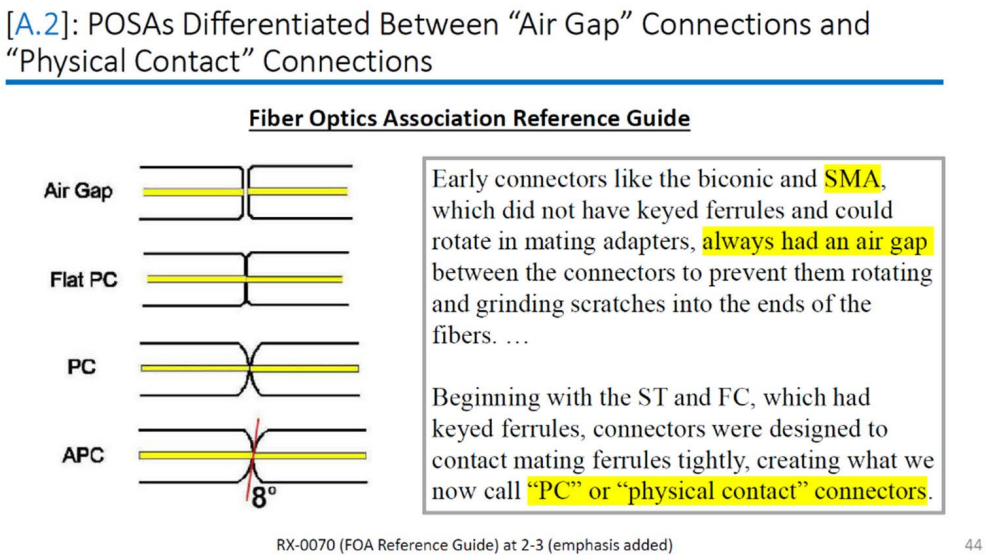
The Commission need not adopt or apply the FID's construction of "air gap" as a "designed separation" or Gator Bio's proposed construction of a "controlled separation." To resolve the parties' claim construction and infringement disputes, it is sufficient for the Commission to find that the scope of the claimed "air gap" term does not encompass physical contact structures or surface roughness which is typically found on all solid surfaces. The Commission also finds that the FID correctly rejects Sartorius's proposed construction for "air

[10] Dr. David Schaafsma is one of Gator Bio's technical experts in this investigation.

gap" as "a gap filled with air" as this construction is contrary to the intrinsic evidence, including the claim language and patent specification. *See* FID at 24-32; *see also Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005) (*en banc*) ("The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.") (quotation omitted).

The Commission finds that the intrinsic and extrinsic evidence support construing the term "air gap" as a structural separation that is distinct from a physical contact structure. The Commission also finds that the claimed air gap does not encompass any void due to surface roughness as is typically present in a physical contact configuration. The claim language provides that the air gap is a specific structure that results from the arrangement of other structural elements. Indeed, the claim language recites that the air gap is specifically provided by the mechanical coupling at a specific location between the optical element and the fiber. *See* JX-2, '887 patent at 10:48-67 (claim 8). Gator Bio's expert testified that such a structure is consistent with certain connectors (*e.g.*, Sub Miniature A "SMA" connectors) which were known to provide a separation between optical fibers so they can freely rotate. *See* Tr. (Schaafsma) at 906:18-907:14; Tr. (Tan[11]) 370:10-371:12; RX-70.2-3 (FOA Reference Guide). In contrast, Dr. Schaafsma distinguished connectors that are in physical contact with the fiber (PC connectors) from those providing an air gap and testified that they would not be considered by persons of ordinary skill in the art at the time of the invention to provide the claimed "air gap." *See* Tr. (Schaafsma) at 906:18-907:14; *see also* Respondent's Resp. at 44 (citing RDX-6C.44 (reproduced below)).

[11] Dr. Hong Tan is one of the inventors of the '547 patent and is the Chief Executive Officer of Gator Bio.



Thus, the term "air gap" does not merely refer to a gap filled with air but had a specific meaning to persons of ordinary skill in the art at the time of the invention. Tr. (Schaafsma) at 906:1-17. Importantly, there is no evidence that skilled artisans, including Sartorius's own experts, ever measured surface roughness or considered such surface roughness as an air gap outside the context of the present investigation. *See* Tr. (Bailey[12]) at 679:11-21; Tr. (Sailor[13]) at 1159:15-20; *see also* Respondent's Resp. at 44 (citing Tr. (Schaafsma) at 907:17-908:8)).

The specification also supports Gator Bio's arguments and confirms that the "air gap" does not include surface roughness but refers to a specific structural design feature of the optical assembly having a specific function. *See* JX-1, '547 patent at 9:23-33 & Figure 4. For instance, the specification explains that the air gap has a dimension of "less than 100 nm or greater than 2 μm" to prevent "undesirable fringes that can adversely impact the detection accuracy." *Id.* at 9:33-37; *see also* Tr. (Schaafsma) 904:8-19. Nowhere does the specification suggest that any void due to surface roughness can provide the claimed "air gap."

[12] Dr. Ryan Bailey is one of Sartorius's technical experts in this investigation.

[13] Dr. Michael Sailor is one of Sartorius's technical experts in this investigation.

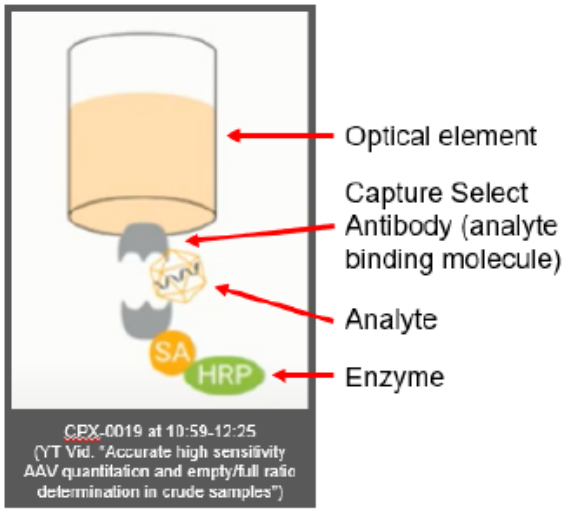
Similarly, the prosecution history confirms that the claimed "air gap" is a structural separation, not the surface roughness that exists on virtually any surface. Specifically, the patentee considered the air gap as a specific structural separation and distinguished the prior art without regard to any surface roughness that would almost inevitably exist on any surface. *See* JX-6.225 ("Cunningham does not disclose the coupling providing an air gap between the first optical element and the fiber."), 228 ("Garini also does not disclose the air gap provided between the optical element and the fiber."); *see also* Tr. (Schaafsma) at 915:17-25, 917:16-918:2, 941:8-22 (testifying that nanoscale surface roughness is a natural phenomenon that exists on the surface of any solid material). There is also no evidence that the surfaces of the fibers or the probes in the prior art were polished or that an index-matching liquid was used, as would be necessary to eliminate surface roughness according to Sartorius. *See* Complainant's Pet. at 76 ("Respondent was well aware that using rough fibers alone would not remove the air gap, and that other methods such as using an index-matching liquid between the probe and the fiber, would need to be employed to eliminate the gap."); *see also* Respondent's Resp. at 43 ("[I]f haphazard, nanoscale surface roughness of the sort that exists on nearly every solid surface sufficed as an 'air gap,' as Sartorius now asserts, then the cited prior art likewise would have disclosed an 'air gap.'").

Thus, the Commission construes the term "air gap" as a structural separation that is distinct from a physical contact structure and does not encompass surface roughness as would exist in a physical contact structure.

D. Infringement

Sartorius asserts infringement against Gator Bio's instruments, when used with HRP probes, infringe claim 8 of the '887 patent. The accused probe includes a layer of analyte

binding molecules, namely, a layer of CaptureSelect anti-AAV[14] capsid antibodies. FID at 78 (citing CPX-19 at 10:59-12:25) (reproduced below).



The probe is dipped in a sample that may or may not include AAV capsid, *i.e.*, the analyte. FID at 78. Additional detection reagents are exposed to the probe, including streptavidin (SA) linked to the enzyme HRP, such that the streptavidin binds to the analyte AAV capsid, if the analyte is present in the sample. *Id.* The probe is then exposed to a "substrate solution" containing chloronaphthol, which reacts with HRP, thereby causing the reacted chloronaphthol to precipitate out of the solution. *Id.* at 79, 81.

The FID finds no infringement of claim 8 of the '887 patent. FID at 59. Specifically, the FID finds that the accused products do not satisfy elements [8Pre] ("assaying enzyme activity"), [8F2] ("whereby the enzyme substrate or a portion of the enzyme substrate binds to the layer of analyte binding molecules"), [8F3] ("wherein interference between a reflected beam from the proximal reflecting surface and a reflected beam from the distal reflecting surface varies as the enzyme substrate or portion thereof binds to the layer of [analyte] binding molecules"), or [8H]

[14] "AAV" refers to "adeno-associated virus." Tr. (Bailey) at 619:25-620:2.

("detecting a change in optical thickness of the first reflecting surface, wherein the change is indicative of enzyme activity"). *See id.* at 77-88. The FID also finds that Gator Bio's first redesigned product satisfies element [8B] ("air gap"), but that the second redesigned product does not. *See id.* at 63-75.

The Commission has determined to review the FID's infringement findings with respect to claim limitations [8Pre], [8B], [8F], and [8H]. On review, the Commission reverses the FID's findings with respect to limitations [8Pre] and [8H], and affirms with modification the FID's findings with respect to limitations [8B] and [8F]. The Commission thus affirms with modification the FID's determination of no infringement.[15]

1. Claim Limitations [8Pre] and [8H]

Before the ALJ, Sartorius argued that, in the accused instruments and probes, enzyme activity is assayed because enzyme activity causes precipitation of the enzyme substrate and a change in the interference pattern associated with the probe. *Id*. at 87. Gator Bio argued that no information about the concentration or activity of the enzyme is provided. *Id.*

The FID finds that the accused instruments do not satisfy limitations [8Pre] ("assaying enzyme activity") and [8H] ("detecting a change in optical thickness of the first reflecting surface, wherein the change is indicative of enzyme activity"). *Id*. at 87-88. The FID explains that "[t]he evidence persuasively demonstrates that the change in optical thickness [of the optical layer] is indicative of the concentration of [the analyte] AAV capsids or the ratio of empty-to-full

[15] As described *supra* note 1, Commissioner Johanson disagrees with the majority's construction of the term "the layer of enzyme binding molecules" in claim limitation [8F3]. Because this claim construction is integral to review of the FID's infringement findings, Commissioner Johanson respectfully declines to join the majority's analysis below regarding claim limitations [8Pre], [8H], [8F2], and [8F3].

AAV capsids and is not indicative of enzyme activity." *Id.* at 88 (citing Tr. (Forrest[16]) at 1024:1-1027:2; Tr. (Zuk) at 387:25-389:7, 404:5-405:19). Thus, the FID finds that, while the HRP enzyme causes precipitation of chloronaphthol, what is measured is not enzyme activity but "the concentration of AAV capsids or the ratio of empty-to-full AAV capsids." *Id.*

Sartorius argues that Gator Bio's HRP Kits are "assaying enzyme activity" because they are "measuring whether or not the enzyme has enzyme activity." Complainant's Pet. at 31-32. Sartorius reasons that "th[e] change in optical thickness is due to the catalytic action of the enzyme on the substrate" and, as such, "it is indicative of the enzyme's activity." *Id.* at 31. Sartorius analogizes the accused instruments and probes to Example 5 of the '887 patent in which the enzyme reacts with its substrate (mitogen-activated protein kinase or MAPK) to add a phosphate group, and "[t]he phosphorylated substrate then binds to the optical layer of the probe, as illustrated in Figure 13, thereby increasing the thickness of the optical layer." *See id.* at 32 (citing JX-2, '887 patent at Figure 13). Gator Bio responds that "[t]he role of HRP [enzyme] is merely to serve as a label that amplifies the signal developed from binding of the [analyte] AAV capsids, and the strength of the signal is proportional to the concentration of AAV capsids, not the degree of activity of the HRP." Respondent's Resp. at 18; *accord* OUII's Resp. at 11-12.

The Commission has determined to review the FID's findings that Gator Bio's accused instruments and probes do not satisfy elements [8Pre] and [8H] of the '887 patent and, on review, reverses those findings. The Commission agrees with Sartorius that the change in optical thickness of the first reflective surface in Gator Bio's accused instrument and probe is indicative of enzyme activity. The claim language requires assaying enzyme activity not determining the quantitative level or degree of such activity. As discussed *supra* section IV.C.1, the Commission

[16] Dr. Laird Forrest is one of Gator Bio's technical experts in this investigation.

construes "assaying enzyme activity" as "detecting, measuring, or monitoring enzyme activity," which encompasses detecting enzyme activity on a qualitative basis. In this case, the change in optical thickness is directly related to enzyme activity and is indicative of such enzyme activity. *See, e.g.*, Tr. (Bailey) at 625:25-627:9; *see also* JX-2, '887 patent at claim 8 (reciting that "a change in optical thickness of the first reflecting surface . . . is indicative of enzyme activity"). That something else (AAV capsid concentration) is assayed in the same experiment does not negate that enzyme activity is also assayed. Thus, the Commission finds that Gator Bio's instruments and HRP probes satisfy claim elements [8Pre] and [8H].

2. Claim Limitations [8F2] and [8F3]

Before the ALJ, the parties disputed whether "the enzyme substrate or a portion of the enzyme substrate binds to the layer of analyte binding molecules" in the accused instruments and probes. *See* FID at 81-86. Sartorius argued that the enzyme substrate (chloronaphthol) binds "indiscriminately" to any available surface, including the layer of analyte binding molecules (CaptureSelect antibodies). *Id.* at 82. Gator Bio argued that Sartorius provided insufficient evidence to establish that chloronaphthol binds to the layer of CaptureSelect antibodies. *Id.*[17]

The FID finds no evidence that the chloronaphthol (enzyme substrate) binds to the layer of analyte binding molecules, and therefore that Gator Bio's accused instruments and probes do not satisfy limitations [8F2] and [8F3]. *See* FID at 81-85. The FID rejects the testimony of Sartorius's expert, Dr. Bailey, as equivocal, conclusory, and unsupported by the evidence. *See id.* at 82-83. In particular, Dr. Bailey testified that the chloronaphthol binds indiscriminately to any available surface, but the FID finds that Dr. Bailey's testimony was not supported by "any

[17] OUII takes no position with respect to whether Gator Bio's accused instruments and probes satisfy element [8F]. *See* OUII's Resp. at 36.

examination or testing of Gator Bio's HRP probes." *Id.* at 83 (citing Tr. (Bailey) at 694:1-696:9). The FID also finds that Dr. Bailey's testimony was contrary to evidence showing that the precipitated chloronaphthol was hydrophobic and would bind to the surface of the probe, which is also hydrophobic, rather than binding to the CaptureSelect antibodies (analyte binding molecules), which are hydrophilic. *See id.* (citing Tr. (Zuk) at 421:1-422:25, 467:12-24; Tr. (Bailey) at 622:24-623:1).

The Commission has determined to review the FID's findings with respect to limitation [8F] and, on review, affirms these findings with supplemental analysis, as discussed below.

Sartorius argues that the FID errs in finding that the accused instruments do not satisfy limitations [8F2] and [8F3]. *See* Complainant's Pet. at 41. Sartorius again relies on Dr. Bailey's conclusory testimony that the chloronaphthol binds "indiscriminate[ly]" to all available surfaces. *Id.* at 42. Sartorius also conflates and equates binding to the optical layer with binding to the layer of analyte binding molecules. *See id.* at 43-44. The optical layer, however, is not the same as the layer of analyte binding molecules, and it is not sufficient for Sartorius to argue that the chloronaphthol binds to the optical layer. *Accord* Respondent's Rep. at 21-22, 29-30. Rather, the claim requires that "the enzyme substrate or a portion of the enzyme substrate binds to the layer of analyte binding molecules," not to the optical layer or any portion thereof. *See* JX-2, '887 patent at 10:48-67 (claim 8).

Sartorius also argues that Mr. Zuk admitted that "[s]ome hydrophobic compounds can bind to some antibodies." Complainant's Pet. at 43. That is insufficient to satisfy Sartorius's burden to establish that the particular compound at issue here, *i.e.*, chloronaphthol, binds to the particular layer of analyte binding molecules, *i.e.*, the CaptureSelect anti-AAV capsid antibodies. In addition, Sartorius misapprehends Mr. Zuk's testimony. As Mr. Zuk explained, antibodies

include amino acid chains that typically have hydrophilic and hydrophobic domains, but the hydrophobic domains are not exposed in an aqueous environment because they are repelled by water. *See* FID at 83 (citing Tr. (Zuk) at 421:1-422:25, 467:12-24). In other words, the tertiary structure of the antibody (i.e., its three-dimensional arrangement) is such that the hydrophobic amino acid residues are oriented inside and the hydrophilic amino acid residues are oriented outside. *See* Tr. (Zuk) at 473:15-22. Sartorius presented no evidence establishing that chloronaphthol binds to the layer of analyte binding molecules, *i.e.*, the anti-AAV capsid antibodies, particularly where the exposed hydrophilic domains of the antibodies will similarly repel the hydrophobic chloronaphthol. Thus, while the hydrophobic domains may be used to bind the antibodies to the hydrophobic polystyrene layer of the probe, they are not exposed in the aqueous environment of the reaction and therefore unavailable for binding with the precipitated chloronaphthol. *See* Tr. (Zuk) at 467:18-468:24; *see also* Respondent's Resp. at 29 (citing Tr. (Zuk) at 473:25-474:4).

In addition, while admitting that Gator Bio's expert, Dr. Forrest, agreed with Mr. Zuk's testimony that the chloronaphthol substrate would be expected to bind only to hydrophobic portions of the probe, Sartorius contends that Dr. Forrest did not testify as to the hydrophobic nature of chloronaphthol and the hydrophilic nature of the CaptureSelect anti-AAV capsid antibodies. Complainant's Pet. at 42-43 (citing Tr. (Forrest) at 1029:20-25); *see also* Tr. (Forrest) at 1030 (quoting Dr. Forrest's deposition testimony that the precipitant, *i.e.*, chloronaphthol, "does adsorb to the tip of the probe"). Sartorius's expert, however, Dr. Bailey, did not dispute these properties, and testified that the enzyme substrate (chloronaphthol) "goes from being soluble in water to being insoluble in water." *See* FID at 83 (citing Tr. (Bailey) at 622:24-623:1). Thus, the Commission agrees with the FID that Dr. Bailey's testimony that the

enzyme substrate binds indiscriminately to the optical layer, including the layer of analyte binding molecules, was conclusory and contrary to the evidence. *Accord* Respondent's Resp. at 22-25. Sartorius further argues that "Dr. Bailey thoroughly examined the product literature for Gator Bio's kits [and] Gator Bio's presentations explaining how its kits function with HRP," but Sartorius fails to show how any of these exhibits supports Dr. Bailey's conclusory testimony. *See* Complainant's Pet. at 41 (citing CX-132C; CX-100; CX-104; CX-109). Accordingly, the Commission finds that Sartorius failed to meet its burden to prove infringement as to elements [8F2] and [8F3] by a preponderance of the evidence.

The Commission also notes that Gator Bio's accused method is not similar to Example 5 of the '887 patent. *See id.* at 32-33. In Example 5, the layer of analyte binding molecules includes "anti phospho MAPK" bound to the BLI sensor. *See* JX-2, '887 patent at 9:44-52. Thus, the patent discloses that the enzyme substrate MAPK (which is also the analyte in Example 5) binds to the layer of analyte binding molecules, as required by element [8F2] and [8F3]. The '887 patent thus exemplifies enzyme substrates binding to a layer of analyte binding molecules based on the affinity of an antigen and its corresponding antibody thereby forming an antigen/antibody type of bond. In contrast, Sartorius has not established by a preponderance of the evidence that the enzyme substrate in Gator Bio's accused method, *i.e.,* chloronaphthol, which is distinct from the analyte (AAV capsid), binds to the layer of analyte binding molecules (CaptureSelect anti-AAV capsid antibodies). While there is no question that AAV capsid binds to anti-AAV capsid antibodies, the AAV capsid is not alleged to be the enzyme substrate in the accused method.[18] Sartorius presented insufficient evidence to establish that the hydrophobic

[18] While the "enzyme substrate" is the same as the "analyte" in Example 5 of the '887 patent, that is not the case with respect to Gator's accused method.

chloronaphthol would also bind to the hydrophilic layer of anti-AAV capsid antibodies. Nor did Sartorius explain what affinity the chloronaphthol would have with the layer of CaptureSelect anti-AAV capsid antibodies and what type of bond would be involved. Rather, the evidence shows that the hydrophobic chloronaphthol would bind to the surface of the probe which is also hydrophobic. *See* FID at 83-84 (citing Tr. (Zuk) at 421:11-14; Tr. (Bailey) at 622:24-623:1; Tr. (Forrest) at 1029:8-25); *accord* Respondent's Resp. at 20.[19] As the FID notes, "hydrophobic molecules will bind to each other in an aqueous environment such that the chloronaphthol will bind to the surface of the probe," while "any exposed residues of the CaptureSelect antibodies (the analyte binding molecules) are hydrophilic, such that the chloronaphthol will not bind to them. FID at 83 (citing Tr. (Zuk) at 421:1-422:25, 467:12-24); *see also generally* FID at 83-85.

Thus, the Commission agrees with the FID that Gator Bio's accused instruments and probes do not satisfy claim elements [8F2] and [8F3] of the '887 patent. Accordingly, the Commission affirms the FID's findings with respect to limitation [8F] with the supplemental analysis discussed above.

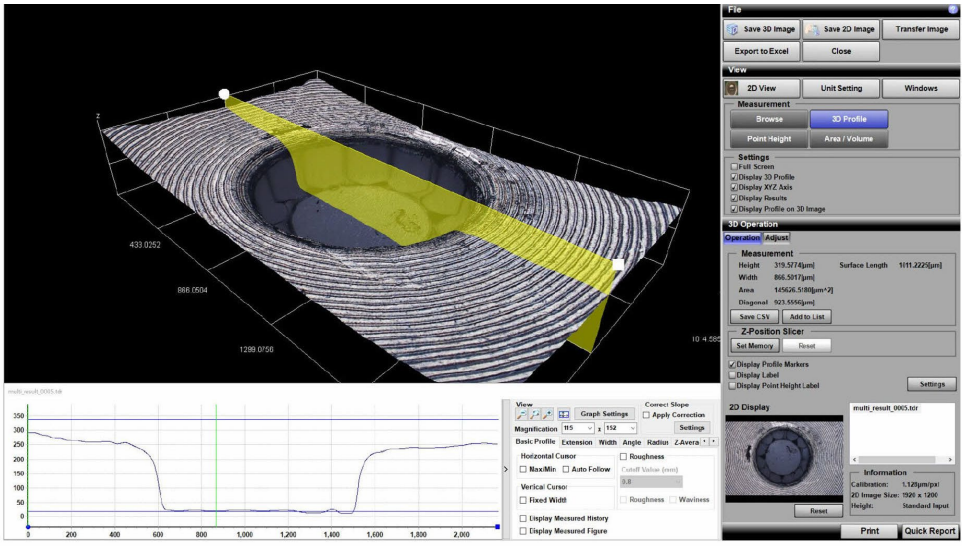
3. Claim Limitation [8B]

Before the ALJ, Sartorius argued that Gator Bio's accused products satisfy the "air gap" limitation. FID at 63. Specifically, Sartorius argued that a depression or recess in the first and

[19] The ALJ rejected Sartorius's objection at the hearing to Dr. Forrest's testimony agreeing with Mr. Zuk that "the enzyme substrate would be expected actually just to bind to certain portions of the biosensor," but gave Sartorius an opportunity to file a motion to strike the testimony, which Sartorius did not file. *See* Tr. at 1029:20-1031:7; Respondent's Resp. at 25. Sartorius further objects to Mr. Zuk's testimony, but those objections are also waived and without merit. *See* Complainant's Pet. at 42. As the FID finds, Sartorius waived such objections because they were not timely raised during the hearing. *See* FID at 83-84. In addition, the FID finds that "Mr. Zuk was competent to testify on the nature of enzyme substrates and analyte binding molecules" and "he has personal knowledge of the chemistry at the tip of Gator Bio's probes." *Id.* at 84 (citing Tr. (Zuk) at 381:12-13, 383:15-19, 390:1-5); *accord* Respondent's Resp. at 25-28.

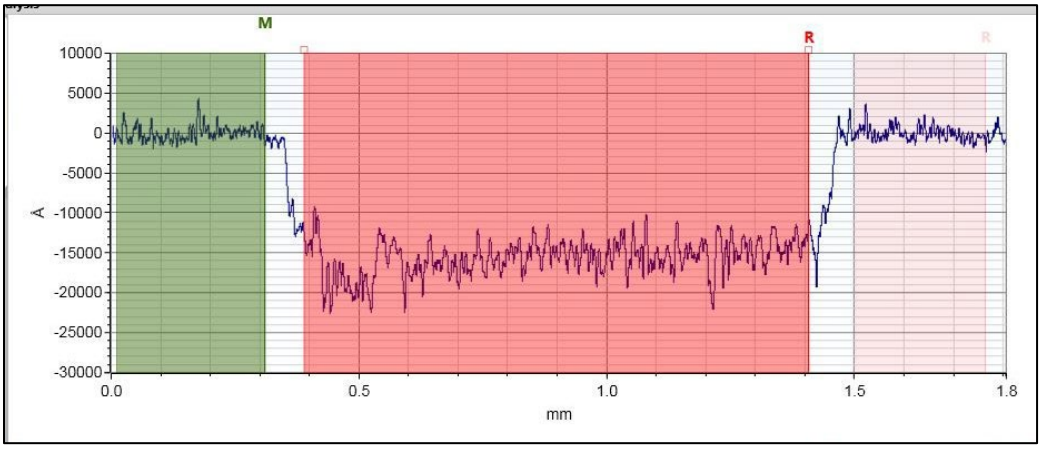
second redesign of a fiber bundle created the claimed air gap between the fiber and the probe. *Id.* at 68. Sartorius also argued that surface roughness of the fiber bundle created the claimed "air gap" in Gator Bio's second redesign. *See id.* at 70-72. Gator Bio responds that "[t]he alleged recess in the First Redesign . . . [is] neither designed nor controlled" and that "any recess in its first redesign fiber bundle is an undesigned 'manufacturing defect.'" *See id.* at 67. As to the second redesign, Gator Bio argues that there is no claimed gap because "the probe and the optical fiber are in physical contact." *Id.* at 69.

The FID finds that the "air gap" limitation is satisfied by Gator Bio's first redesign but not the second redesign. *See id.* at 65-75. The FID explains that the first redesign includes "a depression in the metal casing," and that "the probe cannot fit within the metal casing" such that, "when the probe contacts the fiber bundle, there is an air gap with a depth of 204±9 µm between the optical element and the optical fiber." *Id.* at 66-67 (citing CX-279C.20 (reproduced below); CX-286C.3).



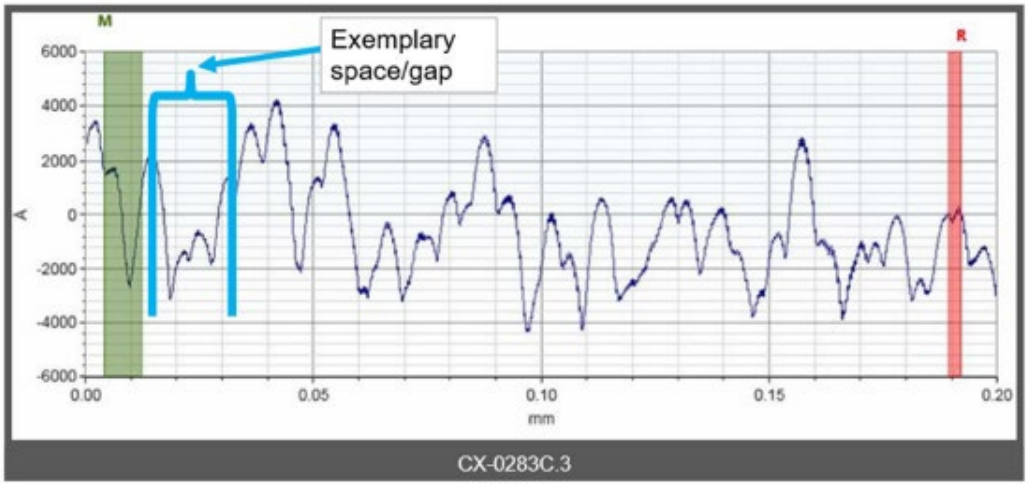
As to the second redesign, the FID explains that the fiber and the probe are in physical contact and that surface roughness is not a designed or controlled separation. *See id.* at 68-75. Specifically, the FID notes that Dr. Bailey's profilometry measurements show "a recess (*i.e.*, a

depression) in the middle of the fiber." *Id*. at 68-69 (citing CX-282C.2 (reproduced below); CX-286C.4).



The FID finds that the diameter of the recess is 1146±2 µm, and that it is "greater than the average diameter of Gator Bio's representative probes," which is 999±2 µm or 1000±3 µm. *Id*. at 69 (citing Tr. (Bailey) at 605:24-606:16, 609:18-25; CX-286C.2, 4). Thus, the FID finds that the probe could fit within the recess in the fiber, and as such, the fiber and the probe are in physical contact. *Id.* at 69-70 (citing Tr. (Tan) at 307:9-15; (Schaafsma) at 910:17–912:10); Tr. (Bailey) at 672:10-14); *accord* OUII's Resp. at 20-21. The FID also finds no evidence of "misalignment," as would be required to prevent the probe from fitting within the recess in the fiber. *Id*. at 70.

The FID also rejects Sartorius's contention that surface roughness creates the claimed "air gap." *See* FID at 70-72. The FID notes that "Sartorius identifies with a blue bracket what it contends is an exemplary air gap in Gator Bio's second redesign caused by surface roughness." *Id.* at 71-72 (citing CX-283C.3 (reproduced below)).



The FID finds, however, that "surface roughness is present on virtually all materials" and that "[s]uch unavoidable and undesigned imperfections cannot be the claimed air gap." *Id.* at 72 (citing Tr. (Schaafsma) at 915:17-25).

In its petition for review, Sartorius no longer appears to dispute that the probe fits within the recess in the accused second redesign. Nor does Sartorius address or dispute the FID's finding that the fiber and the probe are in physical contact. Sartorius, however, again argues that surface roughness creates the claimed "air gap." *See* Complainant's Pet. at 73-74. Sartorius also argues that such surface roughness is an intentional design feature because Gator Bio failed to use a laser, fling-polishing, or an index-matching liquid to remove the air gap. *See id.* at 76-77. Gator Bio responds that there is no air gap because the fiber and the probe are in physical contact. *See* Respondent's Resp. at 47-48. Gator Bio further argues that surface roughness is not an air gap because it is not a controlled or designed separation. *See id.* at 49-50.

The Commission has determined to review the FID's findings that Gator Bio's second redesigned instruments and probes do not satisfy the claimed "air gap" and, on review, affirms the FID with modification.

As discussed *supra* section IV.C.2, the Commission agrees with the FID that the term "air gap" does not encompass a physical contact structure or configuration. Nor does it encompass a void or space due to surface roughness. Thus, the Commission finds that the FID correctly determined that Gator Bio's second redesigned fiber bundle does not satisfy limitation [8B]. However, as discussed *supra* section IV.C.2, to resolve the parties' infringement dispute, the Commission need not adopt or apply the FID's construction of "air gap" as a "designed separation." Rather, it is sufficient for the Commission to find that Gator Bio's fiber is in physical contact with the probe and, thus, such configuration does not fall within the scope of the term "air gap." Additionally, the scope of the term "air gap" does not encompass surface roughness that may create a void in such "physical contact" configuration.

The Commission also finds that the FID correctly credited Dr. Schaafsma's opinion that one of ordinary skill of the art would not have considered spaces containing air caused by the surface roughness as the claimed air gap. *See* FID at 74 (citing Tr. (Schaafsma) at 907:22-914:1). As discussed *supra* section IV.C.2, there is no evidence that any skilled artisan, including Sartorius's own experts, ever measured or considered surface roughness as an air gap outside the context of the present investigation. *See* Tr. (Bailey) at 679:11-21; Tr. (Sailor) at 1159:15-20. Sartorius's position that "atomically flat" surfaces are required to avoid infringement and that any *de minimis* number of air molecules would create an air gap is not credible and inconsistent with the intrinsic and extrinsic records. *See* Complainant's Pet. at 77; *see supra* section IV.C.2.

Rather, the evidence shows that the fiber and the probes are in physical contact, and thus do not satisfy the claimed air gap, *i.e.*, a structural separation between the optical element and the fiber, which does not encompass void created by surface roughness as is present on virtually all

solid surfaces. *See* FID at 69-70 (citing Tr. (Tan) at 307:9-15; (Schaafsma) at 910:17–912:10); *see also* Respondent's Resp. at 47 ("As Dr. Tan testified, during the operation of the Gator instruments, the fiber probes are placed in a tray on a motorized platform, and the platform is raised so that the fiber probes are brought into physical contact with the fibers of the corresponding instrument fiber bundles.") (citing Tr. (Tan) at 299:16-300:25; Tr. (Schaafsma) at 908:1-18).

Thus, the Commission affirms, with the modified analysis discussed above, the FID's finding that Gator Bio's accused instruments and probes, when used with the second redesigned fibers, do not satisfy the claimed "air gap."

E. Domestic Industry

Sartorius asserts that its Octet R8 instrument when used with its Anti-CHO (Chinese hamster ovary cells) HCP (host cell protein) detection kit practices claim 8 of the '887 patent. *See* FID at 90-97. The accused probe includes a layer of analyte binding molecules, namely, a layer of Cygnus 3G anti-HCP antibody. *Id.* at 104-05. The probe is then exposed to HCP (analyte), a fluorescein-tagged anti-HCP antibody, and HRP (enzyme) with anti-tag conjugate. *Id.* at 105-06 (citing CX-0201.2 (reproduced below)).

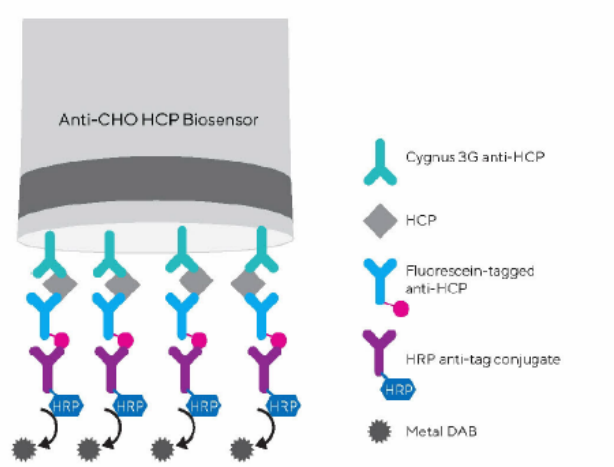


Figure 1: Biosensor-based assay format for the detection of CHO HCP.

The FID explains that "once this sequence of proteins is formed on the tip of the probe, the probe is exposed to an enzyme substrate called metal DAB," which reacts with HRP (enzyme) thereby causing DAB to precipitate and to bind to the optical layer. *Id*. at 106; Complainant's Pet. at 54. The thickness of the optical layer increases as DAB precipitates out of the solution. *Id*. at 109.

1. Technical Prong

The FID finds that Sartorius's domestic industry products do not practice claim 8 of the '887 patent. In particular, the FID finds that Sartorius's Octet R8 instrument when used with Sartorius's Anti-CHO HCP detection kit does not satisfy claim limitations [8Pre], [8H], and [8F] for essentially the same reasons as Gator Bio's accused products. *See* FID at 107-10.

The Commission has determined to review the FID's technical prong findings with respect to claim limitations [8Pre], [8F], and [8H]. On review, for reasons similar to the infringement analysis discussed above, the Commission reverses the FID's findings with respect to [8Pre] and [8H], and affirms with modification the FID's findings with respect to [8F]. The Commission thus affirms with modification the FID's determination of no technical prong of the domestic industry requirement.[20]

a. Claim Limitations [8Pre] and [8H]

The FID finds that, for the same reasons as stated with respect to infringement, "the evidence does not show that us[ing] the Sartorius Octet R8 instrument with the probe of its Anti-CHO HCP detection kit meets element [8pre] or element [8H]." *See* FID at 109-10. Sartorius argues that the domestic industry instruments and probes are assaying enzyme activity because

[20] For reasons similar to those described *supra* note 15, Commissioner Johanson respectfully declines to join the majority's technical prong analysis regarding claim limitations [8Pre], [8H], [8F2], and [8F3].

the change in optical thickness and interference pattern is "due to the catalytic action of the enzyme on the substrate" and "it is indicative of the enzyme's activity." *See* Complainant's Pet. at 54-55. Gator Bio responds that Sartorius's "kit measures or assays binding of host cell proteins (HCP)" (*i.e.*, analyte), "not the activity of HRP" (*i.e.*, enzyme). *See* Respondent's Resp. at 32, 35; *accord* OUII's Resp. at 13-14 ("Dr. Forrest testified that the DI Products use an enzyme as a label, but do not "measure anything having to do with enzyme activity.") (citing Tr. (Forrest) at 1038:18-1040:3).

As discussed *supra* section IV.C.1 (claim construction) and IV.D.1 (infringement by Gator Bio's accused products), claim limitations [8Pre] and [8H] do not require quantitatively measuring enzyme activity. Thus, the Commission agrees with Sartorius that using the assay with the Anti-CHO detection kit and HRP detects enzyme activity, and that the change in the thickness of the optical layer and in the interference pattern is a direct result of enzymatic activity.

Accordingly, the Commission has determined to review the FID's findings that Sartorius's domestic industry instruments and probes do not satisfy claim elements [8Pre] and [8H] of the '887 patent and, on review, reverses those findings.

b. Claim Limitations [8F2] and [8F3]

The FID finds that, for similar reasons as stated with respect to infringement, Sartorius failed to prove that the enzyme substrate (metal DAB) will bind to the layer of analyte binding molecules (Cygnus 3G anti-HCP antibody). *See* FID at 107-08. Specifically, the FID finds that "Dr. Bailey's conclusory testimony does not support that the metal DAB or a portion of the metal DAB binds to the layer of Cygnus 3G anti-HCP antibodies and Dr. Bailey did no testing to support his assertion." *See id.*

Sartorius argues that "Dr. Bailey's testimony was not conclusory or unsupported." Complainant's Pet. at 57-58. Specifically, Sartorius contends that "Dr. Bailey explained that when the probes . . . are exposed to the metal DAB substrate the 'enzyme catalytically oxidizes' it and renders it insoluble," such that DAB will bind indiscriminately to all available surfaces. *See id.* at 58 (citing Tr. (Bailey) at 645:15-23, 645:20-646:2). Gator Bio responds that Sartorius provided no evidence "regarding the disputed question of whether the precipitated substrate (in this case metal DAB) binds to the capture antibody (in this case an Anti-HCP antibody, shown at CX-201.2) that Sartorius identified as the analyte binding molecule. Respondent's Resp. at 33.[21]

The Commission has determined to review the FID's finding that Sartorius's domestic industry instruments and probes do not satisfy elements [8F2] and [8F3] and, on review, affirms that finding with modification. The Commission finds that Sartorius has failed to satisfy its burden to prove by a preponderance of the evidence that the enzyme substrate (metal DAB) binds to the layer of analyte binding molecules (Cygnus 3G anti-HCP antibody). As it did in connection with Gator Bio's accused products, Sartorius equates the optical layer with the layer of analyte binding molecules without regard to the affinity of metal DAB with the various components of the optical layer or the tip of the probe. Complainant's Pet. at 61. Sartorius argues that "once the [DAB] substrate reacts with the enzyme, it becomes insoluble and binds to the tip of the probe" (Complainant's Pet. at 61). Binding to the tip of the probe, however, is not the same as binding to the layer of analyte binding molecules as required by claim 8.

Sartorius also argues that "Dr. Bailey cited to Complainant's technical literature to support his opinion that the metal DAB substrate will react with HRP and bind to every

[21] OUII takes no position with respect to whether Sartorius's domestic industry instrument and probe satisfy element [8F]. *See* OUII's Resp. at 36.

constituent of the optical layer, including the analyte binding molecules." Complainant's Pet. at 58 (citing Tr. (Bailey) at 646:6-653:14; CX-201; CX-202; CX-502). Neither Dr. Bailey nor Sartorius, however, explain how the technical literature supports Dr. Bailey's testimony that the metal DAB binds to the layer of Cygnus 3G anti-HCP antibody. *Accord* Respondent's Resp. at 33 ("[N]one of the documents that Sartorius cites (CX-0201, CX-0202, or CX-0502) describes or depicts anything about the metal DAB substrate binding to the anti-HCP antibody.").

Thus, the Commission agrees with the FID that Sartorius's domestic industry instruments and probes do not satisfy elements [8F2] and [8F3] of the '887 patent. Accordingly, the Commission affirms with the modified analysis discussed above the FID's determination that Sartorius has failed to satisfy the technical prong of the domestic industry requirement with respect to claim 8 of the '887 patent.

2. Economic Prong

The FID finds that the economic prong of the domestic industry requirement is satisfied. *See* FID at 123-58. Because the domestic industry products are not protected by the asserted patent, however, Sartorius cannot satisfy the domestic industry requirement. *See* 19 U.S.C. § 1337(a)(2) (requiring in relevant part "an industry in the United States[] relating to the articles protected by the patent"); *see Certain Filament Light-Emitting Diodes*, Inv. No. 337-TA-1220, Comm'n Op., 2022 WL 766226, *46 (March 8, 2022) (finding that "Complainant cannot satisfy the domestic industry requirement" where "the domestic industry products are not protected by their respective patents"). The Commission has determined to review the FID's findings that Sartorius has satisfied the economic prong of the domestic industry requirement and, on review, takes no position on those findings. *See Beloit*, 742 F.2d at 1423.

V. CONCLUSION

The Commission has determined to review in part the FID and, on review, affirms with modification the FID's finding of no violation of section 337. Accordingly, the investigation is terminated with a finding of no violation of section 337.

By order of the Commission.

Lisa R. Barton
Secretary to the Commission

Issued: July 16, 2024