

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

TECAN GENOMICS, INC.,

Plaintiff,

v.

INVITAE CORPORATION; ARCHERDX,
LLC; AND INTEGRATED DNA
TECHNOLOGIES, INC.,

Defendants.

C.A. No. 23-1114-GBW

**DEFENDANT INTEGRATED DNA TECHNOLOGIES’
INITIAL INVALIDITY CONTENTIONS REGARDING
U.S. PATENT NOS. 10,036,012, 10,876,108, 9,546,399, 11,098,357, AND 11,725,241**

Pursuant to the Court’s Scheduling Order, D.I. 45, the Parties’ Stipulation and Proposed Order to Extend Time, D.I. 49, and the United States District Court for the District of Delaware’s Default Standard for Discovery, Including Discovery of Electronically Stored Information (the “Default Standard”), Defendant Integrated DNA Technologies, Inc. (“IDT” or “Defendant”) provides the following initial invalidity contentions regarding U.S. Patent Nos. 10,036,012 (“the ’012 patent”), 10,876,108 (“the ’108 patent”), 9,546,399 (“the ’399 patent”), 11,098,357 (“the ’357 patent”), and 11,725,241 (“the ’241 patent”) (collectively, the “Asserted Patents”) to Plaintiff Tecan Genomics, Inc. (“Plaintiff” or “Tecan”). These initial contentions address claims 1–3 and 5–22 of the ’012 patent; claims 1–3, 5–12, and 14–19 of the ’108 patent; claims 1–3, 5–11, and 14–17 of the ’399 patent; claims 1–4, 6–7, and 9–10 of the ’357 patent; and claims 1–16 of the ’241 patent (collectively, “the Asserted Claims”) as identified in Plaintiff’s Initial Infringement Contentions, dated August 23, 2024. These contentions are responsive to, and based upon, Plaintiff’s Initial Infringement Contentions and should be understood in that context.

In accordance with the Court's Scheduling Order and the Default Standard, these invalidity contentions are necessarily preliminary. Defendant provides these Initial Invalidity Contentions in the absence of a claim construction order and based on information and discovery currently available, including publicly available information and information from Defendant's ongoing investigation of the facts. Defendant reserves the right to supplement or amend these invalidity contentions as discovery and the litigation progresses, and may do so as further information is obtained through discovery or after the Court issues a claim construction order.

Defendant's contentions are based in whole or in part on its present understanding of the Asserted Claims and Plaintiff's apparent construction of those claims in its Initial Infringement Contentions. Accordingly, Defendant's contentions may reflect alternative positions as to claim construction and scope. By providing these contentions based on Plaintiff's apparent claim constructions, Defendant is neither adopting Plaintiff's apparent claim constructions, nor suggesting the accuracy of any particular claim construction. Defendant reserves the right to present arguments and evidence, including expert evidence, regarding the proper scope and construction of all claim terms at issue.

Defendant reserves the right to amend, modify, or supplement these contentions pursuant to the Federal Rules of Civil Procedure, the Local Rules, or any other order or schedule entered by the Court, including as discovery progresses and the claims are construed. Defendant further reserves the right to supplement these contentions should Plaintiff amend, supplement, or expound upon Plaintiff's Initial Infringement Contentions, or based on other positions taken by Plaintiff during discovery, including regarding secondary considerations of nonobviousness or the claimed priority date of the patents.

I. THE ASSERTED CLAIMS ARE INVALID AS ANTICIPATED AND/OR OBVIOUS UNDER 35 U.S.C. § 102 AND/OR § 103

The Asserted Claims of all of the Asserted Patents are invalid as anticipated and/or obvious for the reasons provided in the petitions filed in the following *inter partes* review proceedings, which are fully incorporated herein by reference, including all exhibits and supporting materials.

- IPR2024-01502 (U.S. Patent No. 9,546,399)
- IPR2024-01504 (U.S. Patent No. 11,098,357)
- IPR2024-01506 (U.S. Patent No. 11,725,241)
- IPR2025-00015 (U.S. Patent No. 10,036,012)
- IPR2025-00016 (U.S. Patent No. 10,876,108)

IDT stipulates that if any of these *inter partes* review proceedings are instituted, it will not pursue any arguments in district court with respect to those patent(s) that could have been raised in such instituted proceeding(s) under 35 U.S.C. § 311(b).

II. THE ASSERTED CLAIMS OF THE '012 AND '108 PATENTS ARE INVALID UNDER 35 U.S.C. § 102(g) DUE TO PRIOR INVENTION

To the extent a patent is entitled to its claimed priority date, section 102(g)(2) provides that “a person shall be entitled to a patent unless . . . 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(g)(2). Thus, to the extent that prior inventors working in the United States had made and used methods within the scope of the Asserted Claims of the '012 and '108 patents, and did not abandon, suppress, or conceal that work, their work renders the Asserted Claims invalid as anticipated and/or obvious.

Because Defendant’s investigation of potentially invalidating prior art and other evidence relating to § 102(g) is ongoing, the contentions below are necessarily preliminary. In addition to

the evidence cited below, Defendant may rely on additional evidence, including materials that will be produced by any party as discovery progresses, including third parties, in this case or *Tecan Genomics, Inc. v. QIAGEN Sciences, LLC et al.*, Case No. 23-01115. Defendant reserves the right to amend, modify, or supplement its arguments relating to § 102(g) as discovery progresses, including third-party discovery relating to the prior work of the MGH inventors and the UT Austin inventors.

A. The Asserted Claims of the '012 and '108 Patents Are Invalid in Light of Prior Work by the MGH Inventors

The '012 and '108 patents are directed to a library preparation method for next generation sequencing (“NGS”) that selectively enriches for a sequence of interest. The claimed method comprises a single primer extension step followed by a separate PCR amplification step. IDT sells kits for library preparation for NGS (the “Archer products”) that incorporate a method that selectively enriches for multiple sequences of interest using anchored multiplex PCR technology. The Archer products incorporate technology that was originally developed by Drs. Anthony John Iafrate, Long Phi Le, and Zongli Zheng (“the MGH inventors”), pathologists at Massachusetts General Hospital (“MGH”) (the “MGH Method”), and commercialized by a company called ArcherDX. The MGH Method does not include a single primer extension step. Rather, it includes multiple rounds of PCR amplification.

In its infringement contentions, Tecan has applied a broad claim construction of the single primer extension step, under which it contends the “extension” step of a PCR reaction is equivalent to the single primer extension reaction claimed in the method of the '012 and '108 patents. Under its broad interpretation, Tecan asserts that the Archer products, which do not contain a “single primer extension” step, infringe the claimed method. To the extent Tecan intends to rely on this broad construction, it also sweeps in prior art inventions and work in the United States such as the

MGH Method and the Meyer Method described in Section II.A.B, which use multiple rounds of PCR rather than a single primer extension reaction followed by a PCR reaction, within the scope of the claims. See *Upsher-Smith Labs, Inc. v. Pamlab, LLC*, 412 F.3d 1319, 1322 (Fed Cir. 2005) (“A century-old axiom of patent law holds that a product ‘which would literally infringe if later in time anticipates if earlier’”) (cleaned up). The Asserted Claims of the ’012 and ’108 patents are therefore invalid because the method to which they are directed, under Tecan’s apparent claim constructions, was already invented and used prior to the earliest priority date of the ’012 and ’108 patents, January 26, 2012 (though Defendant contends that the Asserted Claims are not entitled to that priority date). Evidence relating to the MGH Method constitutes invalidating prior art under 35 U.S.C. § 102(g).

The Asserted Claims of the ’012 and ’108 patents are invalid over prior work by the MGH inventors. By at least December 18, 2011, prior to the earliest claimed priority date of the ’012 and ’108 patents, the MGH inventors had invented the MGH Method for creating selectively enriched libraries for NGS, which included all of the steps of the method claimed in the ’108 and ’012 patents, under Tecan’s apparent claim constructions.

The MGH Method is described in contemporaneous documentation from 2011 disclosing the MGH pathologists’ invention of the MGH Method at MGH in Massachusetts that will be produced during discovery. The contemporaneous documentation will show that, prior to the earliest claimed priority date of the ’012 and ’108 patents, the MGH inventors had developed and were using a method that included all of the steps of the method claimed in those patents under Tecan’s broad construction of primer extension, including ligating a partial duplex adaptor containing a “first adaptor sequence” to a nucleic acid fragment containing a sequence of interest, annealing an oligonucleotide tailed with a “second adaptor sequence” to the sequence of interest,

extending the tailed oligonucleotide (as part of a separate PCR reaction), amplifying the extension product using primers specific to the first and second adaptor sequences, annealing the amplification products at their 3' end to a complementary oligonucleotide on a surface, and sequencing the amplification products on a massively parallel sequencing machine.

The MGH Method was later disclosed to the public in the patents and printed publications that resulted from the MGH inventors' 2011 work, including Provisional Application No. 61/645,364, filed on May 10, 2012; Provisional Application No. 61/679,302, filed on August 3, 2012; U.S. Patent Application Publication No. 2013/0303461 ("the '461 application"), filed on March 11, 2013; and a paper published in *Nature Medicine* in 2014, entitled "Anchored multiplex PCR for targeted next-generation sequencing."

B. The Asserted Claims of the '012 And '108 Patents Are Invalid in Light of Prior Work by the UT Austin Inventors

To the extent Tecan contends that the claimed methods cover methods in which the claimed "single primer extension" step occurs as part of a separate PCR reaction, the Asserted Claims of the '012 and '108 patents are further invalid at least over prior work in the United States by scientists at the University of Texas at Austin, Eli Meyer and Mikhail V. Matz *et al.* ("the UT Austin Inventors"). At least by 2009, prior to the earliest claimed priority date of the '012 and '108 patents (though Defendant contends that the Asserted Claims are not entitled to that priority date), The UT Austin Inventors had invented and used in the United States a method ("the Meyer Method") for creating selectively enriched libraries for NGS that included all the steps of the method claimed in the '012 and '108 patents, under Tecan's apparent broad construction of those claims. Evidence relating to the Meyer Method constitutes invalidating prior art under 35 U.S.C. § 102(g).

The Meyer Method was disclosed to the public in a paper published in *BMC Genomics* on May 12, 2009, entitled “Sequencing and *de novo* analysis of a coral larval transcriptome using 454 GSFIx” and U.S. Patent Application No. 2010/0120097, filed on June 1, 2009. The *BMC Genomics* paper and corresponding patent application show that, prior to the earliest claimed priority date of the ’012 and ’108 patents, the UT Austin inventors had developed and were using a method that included all the steps of the method claimed in those patents, under Tecan’s apparent claim constructions, including ligating a partial duplex adaptor containing a “first adaptor sequence” to a nucleic acid fragment containing a sequence of interest, annealing an oligonucleotide tailed with a “second adaptor sequence” to the sequence of interest, extending the tailed oligonucleotide (as part of a separate PCR reaction), amplifying the extension product using primers specific to the first and second adaptor sequences, annealing the amplification products at their 3’ end to a complementary oligonucleotide on a surface, and sequencing the amplification products on a massively parallel sequencing machine.

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Discovery may reveal other instances of prior invention, in addition to those described herein. Defendant reserves the right to supplement these disclosures accordingly.

III. THE ASSERTED CLAIMS ARE INVALID UNDER 35 U.S.C. § 102(a) DUE TO PRIOR PUBLIC USE

Under 35 U.S.C. § 102(a), a patent is invalid if it was “in public use” or “otherwise available to the public” prior to the patent’s effective filing date.

A. The Asserted Claims of the ’399, ’357, and ’241 Patents Are Invalid Over Prior Public Use by the MGH Inventors

The Asserted Claims of the ’399, ’357 and ’241 patents are invalid over the prior work of the MGH inventors, which, discovery will show, constitutes a prior public use of the methods claimed in those patents. The ’461 application shows that prior to the earliest claimed priority date

of the '399, '357, and '241 patents, November 13, 2013 (though Defendant contends the Asserted Claims are not entitled to that priority date) the MGH inventors had invented and were using the MGH method, which employed an adaptor with all of the elements contained in the adaptor claimed in those patents, except for one: the molecular tag. It would have been obvious to add a molecular tag to the adaptor used in the MGH method to enable deduplication. The POSA would understand that molecular tags for deduplication were well-known in the art prior to the priority date of the '399, '357, and '241 patents, including for use with NGS, and including in the context of detecting mutations with oncological implications (the same application as the MGH method), as disclosed in the following publications:

- In 2010, Hiatt proposed randomized 20-nucleotide tags in adaptor-ligated fragments “to identify molecules that are clonally derived” from the same fragment following PCR. EX1023 to IPR2024-01502.
- In 2010, König incorporated random three-nucleotide tags in cDNA during reverse transcription to “discriminate between unique cDNA products and PCR duplicates.” EX1024 to IPR2024-01502.
- In 2011, Kinde added 12-14-nucleotide tags via PCR to identify PCR duplicates, enhance the accuracy of NGS, and detect rare mutations. EX1025 to IPR2024-01502.
- In 2011, Casbon ligated adaptors with partially random 12-nucleotide tags to fragments prior to PCR. The tags were “used to determine whether a putative variant is associated with a single template molecule or, alternatively, multiple template molecules and hence the probability that it derives from a polymerase error or true variant.” EX1026 to IPR2024-01502.

- In 2011, Fu ligated adaptors with 14-nucleotide tags to fragments prior to PCR to count the absolute number of original molecules in a sample. EX1027 to IPR2024-01502.
- In 2011, Jabara added 8-nucleotide tags to cDNA libraries of viral RNA to “directly remove error, correct for PCR resampling, and capture the fluctuation of minor variants in the viral population within a host.” EX1028 to IPR2024-01502.
- In 2011, Kivioja described a method of using random tags in combination with the sequences of the fragments to which they were attached as a “unique molecular identifier” associated with a particular original fragment to enable removal of copies from sequencing data and counting of original fragments. EX1012 to IPR2024-01502.
- In 2011, Tollervey used König’s protocol of random molecular tags prior to PCR to identify “3.7 million reads representing unique cDNA molecules.” EX1029 to IPR2024-01502.
- In 2012, Shiroguchi ligated adaptors containing 20-nucleotide pre-defined tags to cDNA prior to PCR in order to count the number of fragments in the original sample. EX1030 to IPR2024-01502.
- In 2012, Schmitt reported a method of ligating “standard Illumina sequencing adaptors” containing 12-nucleotide tags to fragments to detect and remove PCR errors and thereby discover rare genetic variants. EX1031 to IPR2024-01502.
- In 2013, Bielas filed a patent application disclosing a method of ligating adaptors with random molecular tags prior to PCR to differentiate “true mutations” in the original fragments from PCR artifacts. EX1013 to IPR2024-01502.

Based on the teachings of these publications, including that molecular tags can increase the accuracy of NGS, can be useful for the detection of mutations that could cause cancer, and can be added to existing adaptors for NGS, the POSA would have been motivated to modify the MGH method to include a molecular tag for deduplication, and would have had a reasonable expectation of success in doing so.

B. The Asserted Claims of the '399, '357, and '241 Patents Are Invalid Over Prior Public Use by the Fred Hutch Inventors

The Asserted Claims of the '399, '357, and '241 patents are further invalid at least over prior work by scientists at the Fred Hutchinson Cancer Research Center, Jason H. Bielas and Jessica A. Bertout (“the Fred Hutch Inventors”), which, discovery will show, constitutes a prior public use of the claimed methods. At least by 2009, prior to the earliest claimed priority date of the '012 and '108 patents (though Defendant contends that the Asserted Claims are not entitled to that priority date), the Fred Hutch inventors had invented a method of deduplication using a molecular tag (“the Bielas Method”) that included all the steps of the deduplication method claimed in the '399, '357, and '241 patents.

The Bielas Method was disclosed to the public in International Patent Publication No. WO 2013/123442 (“the Bielas Application”), filed on February 15, 2013, and published on August 22, 2013. The Bielas Application shows that, prior to the earliest claimed priority date of the '399, '357, and '241 patents, the Fred Hutch inventors had developed and were using a method that included all the steps of the deduplication method claimed in those patents. IPR2024-01502; IPR 2024-01504; IPR 2024-01506.

C. The Asserted Claims of the '399, '357, and '241 Patents Are Invalid Over Prior Public Use by the University of Helsinki Inventors

The Asserted Claims of the '399, '357, and '241 patents are further invalid at least over prior work by scientists at the University of Helsinki, Teemu Kivioja, Jussi Taipale, *et al.* (“the

University of Helsinki Inventors”), which, discovery will show, constitutes a prior public use of the claimed methods. At least by 2011, prior to the earliest claimed priority date of the ’012 and ’108 patents (though Defendant contends that the Asserted Claims are not entitled to that priority date), the University of Helsinki inventors had invented a method of deduplication using a molecular tag (“the Kivioja Method”) that disclosed all the steps of the deduplication method claimed in the ’241 patent, IPR 2024-01506, and rendered obvious the deduplication method claimed in the ’357 and ’399 patents, IPR2024-01502; IPR 2024-01504.

The Kivioja Method was disclosed to the public in a paper (“the Kivioja paper”) published in *Nature Methods*, “Counting absolute numbers of molecules using unique molecular identifiers,” which was available online by November 20, 2011. The Kivioja paper shows that, prior to the earliest claimed priority date of the ’399, ’357, and ’241 patents, the University of Helsinki inventors had developed and were using a method that disclosed or rendered obvious all the steps of the deduplication method claimed in those patents. IPR2024-01502; IPR 2024-01504; IPR 2024-01506.

D. The Asserted Claims Are Invalid Over Prior Public Use of Illumina, Ion Torrent, and 454 Systems

The Asserted Claims of all the Asserted Patents are further invalid over prior use by users of the Illumina, Ion Torrent, and Roche 454 Next Generation Sequencing platforms, all of which were commercially available prior to the claimed priority dates of the Asserted Patents.

Discovery will show that, prior to the effective filing date of the ’012 and ’108 patents, users of the Illumina, Ion Torrent, and Roche 454 sequencing platforms performed anchored PCR-based library preparation methods in conjunction with their use of those platforms that disclosed or rendered obvious the steps of the method claimed in those patents.

Discovery will further show that, prior to the effective filing date of the '399, '357, and '241 patents, users of the Illumina, Ion Torrent, and Roche 454 sequencing platforms performed deduplication methods in conjunction with their use of those platforms that disclosed or rendered obvious the steps of the method claimed in those patents.

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Discovery may reveal other instances of prior public use, in addition to those described herein. Defendant reserves the right to supplement these disclosures accordingly.

IV. THE ASSERTED CLAIMS ARE INVALID FOR LACK OF WRITTEN DESCRIPTION SUPPORT AND LACK OF ENABLEMENT UNDER 35 U.S.C. § 112.

The Asserted Claims are invalid for lack of written description support and for lack of enablement under 35 U.S.C. § 112(a).¹ “[T]he purpose of the written description requirement is to ‘ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor’s contribution to the field of art as described in the patent specification.’” *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 920 (Fed. Cir. 2004). “To show invention, a patentee must convey in its disclosure that it ‘had possession of the claimed subject matter as of the filing date.’” *Amgen, Inc. v. Sanofi*, 872 F.3d 1367, 1373 (Fed. Cir. 2017).

The enablement requirement “prevents both inadequate disclosure of an invention and overbroad claiming that might otherwise attempt to cover more than was actually invented.” *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1380–81 (Fed. Cir. 2012). To satisfy this requirement, the patent’s specification must teach the POSA how to make and use the claimed invention without undue experimentation. *Wyeth & Cordis Corp. v. Abbott Labs.*, 720

¹ To the extent the Asserted Patents’ validity is governed by the pre-AIA version of the Patent Act, analogous contentions are made pursuant to 35 U.S.C. § 112, first paragraph.

F.3d 1380, 1384 (Fed. Cir. 2013). “[A] patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage.” *Id.* at 1381.

Claims are not enabled when, at the effective filing date of the patent, the POSA could not practice the claims without undue experimentation. *Id.* Post-priority date evidence, such as evidence that the patentee engaged in lengthy and undue experimentation to enable the claims, can be used to demonstrate that the claims were not enabled as of the priority date. *Amgen*, 872 F.3d at 1375. A broad genus of compounds is not enabled on the basis of a small number of working examples absent evidence that the examples are representative of the entire genus. “[I]f the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid.” *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576–77 (Fed. Cir. 1984).

While the POSA may rely on background knowledge to fill gaps in the disclosure, a research plan or “mere germ of an idea” is not an enabling disclosure. *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). A genus comprising different types of species is not enabled by a disclosure of how to make only certain types of species. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213–14 (Fed. Cir. 1991).

A. The ’012 and ’108 Patents

The Asserted Claims of the ’012 and ’108 patents are invalid for lack of written description and lack of enablement. All Asserted Claims of the ’012 and ’108 patents require a “single primer extension” step, wherein an oligonucleotide is annealed to a “sequence of interest” within a nucleic acid fragment and then extended using a polymerase, followed by a separate, distinct PCR “amplification” step. To the extent Tecan attempts to argue that the scope of the method claimed

in the '012 and '108 patents includes methods in which the claimed single primer extension step takes place as part of a PCR reaction, such a broad scope is neither described nor enabled.

All of the patents'² examples and embodiments are consistent in their use of a single primer extension step separate from PCR amplification. In Example 1, the patents specify: "Ribosomal DNA fragments from the test library are selectively amplified with two distinct steps: 1) gene-specific primer extension, and 2) PCR with universal adaptor sequences." '012 patent at 32:2-5. The same is true of Examples 2 and 3, in which the patents refer to a "Primer Extension" reaction, *id.* at 33:7-43, 34:31-57, resulting in "primer extension products" followed by a distinct "Amplification" PCR reaction, *id.* at 33:44-56, 34:59-35:3, involving the primer extension products. All of the figures describing the selective enrichment method, including Figure 1, Figure 3, and Figure 4 likewise show a separate primer extension step outside of a PCR reaction. The same is true of the patents' general descriptions of the claimed method. For example, in the "Summary of the Invention" section, the patents separately describe first an "extending" step (d) (with no reference to amplification or PCR) and then a distinct "amplifying" step (e) with two opposing primers specific to the adaptor sequences. *Id.* at 2:34-53, 4:24-32, 11:47-12:14, 17:37-60. Moreover, the patents criticize the prior art use of PCR, further demonstrating the inventors were not in possession of methods wherein the extension step occurs as part of a separate PCR reaction. *Id.* at 1:39-63, Because there are no disclosures or examples of the claimed method in the patents' specification wherein the single primer extension step takes place as part of a PCR reaction, the specification does not show that the inventors were in possession of the alleged full scope of the claims.

² The '012 and '108 patents share a specification. While citations to the specification are to the '012 patent throughout this section, all of the same disclosures appear in the '108 patent.

Nor does the specification teach the POSA how to practice the alleged full scope of the claims. The POSA would not have been able to practice the full scope of the claims without engaging in undue experimentation to attempt to practice the method as part of a PCR reaction (which would require completely different reaction parameters and primer design, and would be contrary to the patents' stated goal of avoiding PCR) as a single primer extension reaction.

Therefore, to the extent Tecan argues the patents cover methods in which the single primer extension step takes place as part of a PCR reaction, the Asserted Claims are invalid for lack of written description and enablement.

To the extent Tecan argues that the "barcode" claimed in claims 7, 8, 9, or 10 of the '012 patent or claim 8 of the '108 patent refers to a molecular tag (also referred to as "unique molecular identifier") rather than a sample index, those claims are invalid for lack of written description and enablement. The '012 and '108 patents' specification never discloses or refers to a molecular tag, *i.e.*, a nucleic acid sequence used to deduplicate sequencing reads. To the contrary, the patents exclusively describe the barcode as a sample index, *i.e.*, a nucleic acid sequence used to identify the sample from which a sequence is derived:

- "In some embodiments, the feature of the polynucleotide to be identified is the sample from which the polynucleotide to be identified is the sample from which the polynucleotide is derived." '012 patent at 25:18-20.
- "In general, barcodes are of sufficient length and comprise sequences that are sufficiently different to allow the identification of samples based on barcodes with which they are associated." *Id.* at 25:29-33.

- “In some embodiments, the methods of the invention further comprise identifying the sample from which a target polynucleotide is derived based on the barcode sequence to which the target polynucleotide is joined.” *Id.* at 25:49-53.
- “In general, a barcode comprises a nucleic acid sequence that when joined to a target polynucleotide serves as an identifier of the sample from which the target polynucleotide was derived.” *Id.* at 25:53-56.

To the extent Tecan contends that the scope of the claimed “barcode” includes a molecular tag, the specification does not show that the inventors were in possession of the full scope of the claims. Likewise, the POSA would not have been able to practice the full scope of the claims without engaging in undue experimentation, as the patents nowhere explain how to incorporate a molecular tag sequence or use a molecular tag for deduplication or any other purpose. Therefore, to the extent Tecan argues that the “barcode” claimed in claims 7, 8, 9, or 10 of the ’012 patent or claim 8 of the ’108 patent refers to a molecular tag rather than a sample index, those claims are invalid for lack of written description and enablement.

All Asserted Claims of the ’012 and ’108 patents require attaching an adaptor to a nucleic acid fragment containing a sequence of interest (claim 1 of the ’012 patent specifically requires that this adaptor be a double-stranded “partial duplex adaptor”), and then “annealing one or more oligonucleotides” to the “sequence of interest in the nucleic acid fragment ligated to the partial duplex adaptor.” Claim 12 of the ’012 patent and claim 9 of the ’108 patent depend from their respective claims 1 and further require denaturing the nucleic acid fragment prior to the annealing step. These dependent claims necessarily require, therefore, that claim 1 of the ’012 patent and claim 1 of the ’108 patent encompass methods in which the annealing step takes place without first denaturing the double-stranded nucleic acid fragment. This process of annealing an

oligonucleotide to a double-stranded fragment is nowhere described or taught in the patents' specification or examples. Therefore, the specification does not show that the inventors were in possession of the full scope of the claims and the POSA would not have been able to practice the full scope of the claims without engaging in undue experimentation.

The Archer products further include several additional critical steps and features not disclosed in the '012 and '108 patents that are necessary for using the Archer products to successfully prepare an enriched library for NGS, including an entire additional round of PCR, the use of custom-designed nested gene-specific primers, a specific adaptor design that is unique to the Archer method, and other features. To the extent Tecan argues that the method practiced by the Archer products falls within the scope of the claims of the '012 and '108 patents, that broad scope is not adequately described or enabled. There are no disclosures in the specification or examples that show that the inventors of the '012 and '108 patents were in possession of a method that included two rounds of PCR, the use of custom nested gene-specific primers, the specific adaptor design used by the Archer products, or the other features of the method. In addition, the POSA would not have been able to practice the full scope of the claims, including methods involving multiple rounds of PCR, the use of custom nested gene-specific primers, and the specific adaptors used in the Archer products, without engaging in undue experimentation.

B. The '399, '357, and '241 Patents

All claims of the '399, '357, and '241 patents require identifying a duplicate sequencing read as a sequencing read comprising “the same,” in the case of the '399 patent, or “identical,” in the case of the '357 and '241 patents, identifier site and nucleic acid fragment as another sequencing read. The deduplication method employed by the accused Archer Products and Archer Analysis software does not require that duplicate sequencing reads have “the same” or “identical”

molecular tags and nucleic acid fragments. Indeed, the method would not be operable if it required “the same” or “identical” identifier and fragment sequences in order to call duplicates.

To the extent Tecan argues that the method claimed in the ’399, ’357, and ’241 patents is broad enough to encompass the deduplication method employed by the Archer Products and Archer Analysis software, the claimed method is not adequately described or enabled. Nowhere in the specification or examples do the ’399, ’357, or ’241 patents describe or enable deduplication based on anything other than the entire identifier and fragment sequence being the “same” or “identical” in duplicates. Therefore, to the extent that Tecan contends the claims are broad enough to encompass the Archer products and accompanying Archer Analysis software, the specification does not show that the inventors were in possession of the alleged full scope of the claims, and the POSA would therefore be unable to practice the full scope of the claims without undue experimentation.

Claim 1 of the ’241 patent is invalid as lacking written description and enablement in view of the language “an identifier site comprising a plurality of nucleotides unique to the amplified fragment” to the extent that this language requires that every fragment have an identifier that is unique as to every other fragment. As found by the Examiner during prosecution, there is no support in the specification for this claim limitation. The specification does not describe adaptors that provide identifiers capable of uniquely labeling every fragment in a sample. The specification does not show that the inventors were in possession of the alleged full scope of the claims and the POSA would therefore be unable to practice the full scope of the claims without undue experimentation. The claims depending from claim 1 are similarly invalid.

Claim 1 of the ’357 patent is invalid as lacking written description and enablement in view of the language “a unique identifier” to the extent that this language requires that every fragment

have an identifier that is unique as to every other fragment. The specification does not describe adaptors that provide identifiers capable of uniquely labeling every fragment in a sample. The specification does not show that the inventors were in possession of the alleged full scope of the claims and the POSA would therefore be unable to practice the full scope of the claims without undue experimentation. The claims depending from claim 1 are similarly invalid.

All asserted claims of the '399 patent require an adaptor comprising “an indexing primer binding site.” The patent defines an “indexing primer binding site” as “a nucleotide sequencing for binding a primer for an indexing site.” '399 patent at 4:33-34. It is not clear from the specification, the examples, or the claims whether the “indexing primer binding site” refers to a specific sequence on a single strand of a double-stranded fragment or two complementary sequences on both strands of a double-stranded fragment. If it is the former, it is not clear from the specification, the examples, or the claims, whether the “primer binding site” is located on the strand to which the primer actually binds, or its complementary strand. To the extent Tecan argues that the “indexing primer binding site” can comprise either the actual sequence of the indexing primer or a sequence complementary to the sequence of the indexing primer (or both), such a broad scope is not disclosed in the specification or examples. Therefore, the specification does not show that the inventors were in possession of the alleged full scope of the claims, and the POSA would be unable to practice the full scope of the claims without undue experimentation. The asserted claims of the '399 patent are therefore invalid.

All asserted claims of the '399 patent require an adaptor comprising a “target sequence primer binding site.” The '399 patent defines a “target sequence primer binding site” at 4:62-63: “A target sequence primer binding site nucleotide sequence for binding a primer for a target sequence [sic].” It is not clear from the specification, the examples, or the claims whether the

“target sequence primer binding site” refers to a specific sequence on a single strand of a double-stranded fragment or two complementary sequences on both strands of a double-stranded fragment. If it is the former, it is not clear from the specification, the examples, or the claims, whether the “primer binding site” is located on the strand to which the primer actually binds, or its complementary strand. To the extent Tecan argues that the “target sequence primer binding site” can comprise either the actual sequence of the sequencing primer or a sequence complementary to the sequence of the sequencing primer (or both), such a broad scope is not disclosed in the specification or examples. Therefore, the specification does not show that the inventors were in possession of the alleged full scope of the claims, and the POSA would be unable to practice the full scope of the claims without undue experimentation. The asserted claims of the ’399 patent are therefore invalid.

The Archer Analysis software further includes several additional critical steps not disclosed in the ’399, ’357, or ’241 patents that are necessary for “detecting a duplicate sequencing read from a population of sample sequencing reads,” *e.g.*, ’399 patent, claim 1, including entire modules relating to read cleaning, “molbar ID” creation, consensus sequence generation, and other analysis and processing necessary for detecting duplicate sequencing reads. To the extent Tecan argues that the Archer analysis software falls within the scope of the claims of the ’399, ’357, and ’241 patents, that broad scope is not adequately described or enabled. There are no disclosures in the specification or examples that show that the inventors of the ’399, ’357, and ’241 patents were in possession of a method that included any of these additional functions necessary for the proper functioning of the software. The POSA therefore would not have been able to practice the alleged full scope of the claims without engaging in undue experimentation.

V. THE ASSERTED CLAIMS OF THE '399, '357, AND '241 PATENTS ARE UNENFORCEABLE DUE TO INEQUITABLE CONDUCT.

A patent is unenforceable due to inequitable conduct if, during prosecution of the patent, the applicant misrepresents or omits information material to patentability with the specific intent to deceive the PTO. *Therasense, Inc. v. Becton, Dickinson and Co.*, 649 F.3d 1276, 1287, 1310 (Fed. Cir. 2011); *Am. Calcar, Inc. v. Am. Honda Motor Co., Inc.*, 768 F.3d 1185, 1187 (Fed. Cir. 2014). Specific intent to deceive can be inferred from indirect and circumstantial evidence. *Therasense*, 649 F.3d at 1290. Because during prosecution of the '399, '357, and '241 patents, Tecan's predecessor-in-interest, NuGEN, deliberately withheld prior art and evidence of prior invention that was material to the patentability of the patents, *see Am. Calcar, Inc.*, 768 F.3d at 1187, with the specific intent to deceive the patent office, the Asserted Claims of the '399, '357, and '241 patents are unenforceable due to inequitable conduct.

Tecan alleges that the method practiced by the Archer products (Archer's "Anchored Multiplex PCR" or "AMP" Technology") infringes the Asserted Claims of the '399, '357, and '241 patents. Archer's AMP Technology was originally developed by pathologists at MGH and later commercialized by ArcherDX. During the prosecution of the '399, '357, and '241 patents, including at least as of February 2014, *see D.I. 1* ¶ 78, Tecan's predecessor NuGEN was aware of ArcherDX, Inc.'s AMP Technology and numerous references disclosing and describing that technology ("the Archer references"), including:

- U.S. Patent App. No. 13/793,564, filed on March 11, 2013; claiming priority to U.S. provisional applications filed on May 10, 2012 (61/645,364) and August 3, 2012 (61/679,302); and published on November 14, 2013 as U.S. Patent Publication No. 2013/0303641.

- U.S. Patent App. No. 15/269,448, filed on September 19, 2016; claiming priority to the aforementioned May 10, 2012 and August 3, 2012 provisional applications; published on August 10, 2017 as U.S. Patent Publication No. 2017/0226575; and issued as U.S. Patent No. 10,017,810.
- U.S. Patent App. No. 15/984,612, filed on May 21, 2018; claiming priority to the aforementioned May 10, 2012 and August 3, 2012 provisional applications; published on May 9, 2019 as U.S. Patent Publication No. 2019/0136306; and issued as U.S. Patent No. 10,718,009.
- U.S. Patent App. No. 16/897,588, filed on June 10, 2020; claiming priority to the aforementioned May 10, 2012 and August 3, 2012 provisional applications; published on March 4, 2021 as U.S. Patent Publication No. 2021/0062253; and issued as U.S. Patent No. 11,781,179.

The Archer references, which are prior art to the '399, '357, and '241 patents, disclose and describe the technology that Tecan now accuses of infringing those patents. Indeed, the Archer AMP Technology, which is described in the Archer references, discloses an adaptor with all of the elements of the adaptor claimed in the '399, '357, and '241 patents except for the molecular tag, which would have been obvious to add for the purpose of deduplication. *See supra* § II.A.2; IPR2024-01502; IPR 2024-01504. Nevertheless, when prosecuting the claims of the '399, '357, and '241 patents, which issued on January 17, 2017; August 24, 2021; and August 15, 2023, respectively, NuGEN deliberately chose not to disclose any of the Archer references to the USPTO, despite NuGEN's awareness of the references during the prosecution of all three patents, and Tecan's current assertion that the technology described in those references infringes the claims of the '399, '357, and '241 patents. NuGEN's deliberate withholding of the Archer references

from the Patent Office during the prosecution of the '399, '357, and '241 patents indicates intent to deceive the Patent Office by hiding prior art that was material to patentability. The '399, '357, and '241 patents are therefore unenforceable due to inequitable conduct.

VI. THE ASSERTED CLAIMS OF THE '012 AND '108 PATENTS ARE NOT ENTITLED TO THE PRIORITY DATE OF JANUARY 26, 2012

On their face, the '012 and '108 patents claim priority to provisional application No. 61/591,241, filed on January 26, 2012. Defendant contends that the Asserted Claims are not entitled to that priority date. Based on the apparent claim constructions in Tecan's Infringement Contentions, the disclosures of the priority application cannot support the Asserted Claims, as required to effect a claim of priority pursuant to 35 U.S.C. § 120 for the reasons outlined above in § IV.A.

Because the Asserted Claims of the '012 and '108 patents are not entitled to their claimed priority date, to the extent Tecan contends they are infringed by the Archer products, they are invalid under pre-AIA 35 U.S.C. §§ 102(a)–(b) due to the prior public use and sale of the Archer products.

VII. THE ASSERTED CLAIMS OF THE '399, '357, AND '241 PATENTS ARE NOT ENTITLED TO THE PRIORITY DATE OF NOVEMBER 13, 2013

On their face, the '399, '357, and '241 patents claim priority to provisional application No. 61/903,826, filed on November 13, 2013. Defendant contends that the Asserted Claims are not entitled to that priority date. Based on the apparent claim constructions in Tecan's Infringement Contentions, the disclosures of the priority application cannot support the Asserted Claims, as required to effect a claim of priority pursuant to 35 U.S.C. § 120 for the reasons outlined above in § IV.B.

The '241 patent is further not entitled to the priority date of the provisional application due to the Examiner's statement during prosecution that the '241 patent could only claim priority to

July 21, 2021, the filing date of the '241 patent's non-provisional application, to which the applicant did not respond. '241 Patent, March 17, 2023 Notice of Allowance, at p. 3. For the same reasons, the claims of the '399 and '357 patents, which are very similar to the scope of the '241 patent, are likewise not entitled to any priority date earlier than the filing of those respective claim sets.

Because the Asserted Claims of the '399, '357, and '241 patents are not entitled to their claimed priority date, to the extent Tecan contends they are infringed by the Archer products, they are invalid under 35 U.S.C. § 102(a) due to the prior public use and sale of the Archer products.

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