Nos. 2018-2198, -2303, -2305, -2306, -2317

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

VERINATA HEALTH, INC., ILLUMINA, INC.,

Plaintiffs – Appellants,

v.

ARIOSA DIAGNOSTICS, INC., ROCHE MOLECULAR SYSTEMS, INC.,

Defendants – Cross-Appellants.

Appeal from the United States District Court for the Northern District of California, Case Nos. 3:12-cv-05501-SI, 3:14-cv-01921-SI, and 3:15-cv-02216-SI, Judge Susan Illston

NON-CONFIDENTIAL BRIEF FOR DEFENDANTS – CROSS-APPELLANTS ARIOSA DIAGNOSTICS, INC. AND ROCHE MOLECULAR SYSTEMS, INC.

THOMAS G. SAUNDERS
CHRISTOPHER ASTA
WILMER CUTLER PICKERING
HALE AND DORR LLP
1875 Pennsylvania Avenue, NW
Washington, DC 20006
(202) 663-6000

DAVID I. GINDLER
ALAN J. HEINRICH
LISA GLASSER
IRELL & MANELLA LLP
1800 Avenue of the Stars
Suite 900
Los Angeles, CA 90067

MARK C. FLEMING
TIMOTHY A. COOK
KATHERINE P. KIECKHAFER
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

ROBERT J. GUNTHER, JR.
OMAR KHAN
CHRISTOPHER R. NOYES
WILMER CUTLER PICKERING
HALE AND DORR LLP
7 World Trade Center
250 Greenwich Street
New York, NY 10007
(212) 230-8800

February 28, 2019

CERTIFICATE OF INTEREST

Counsel for Defendants/Cross-Appellants Ariosa Diagnostics, Inc. and Roche Molecular Systems, Inc. certifies the following:

1. The full name of every party or amicus represented by us is:

Ariosa Diagnostics, Inc.

Roche Molecular Systems, Inc.

2. The names of the real party in interest represented by us is:

N/A

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

Roche Molecular Systems, Inc.

Roche Holdings, Inc.

Roche Holding Ltd.

Novartis AG

4. The names of all law firms and the partners or associates that appeared for Ariosa Diagnostics, Inc. or Roche Molecular Systems, Inc. in proceedings before the United States District Court or in this court and who are not already listed on the docket for the current case are:

For Ariosa Diagnostics, Inc.
IRELL & MANELLA LLP: Casey M. Curran, Lauren N. Drake, Joshua B. Gordon, Molly J. Russell, David A. Schwarz, S. Adina Stohl, Arka Chatterjee (former), Sandra L. Haberny (former), Andrei Iancu (former), Cathy T. Moses (former), Amir A. Naini (former)

For Roche Molecular Systems, Inc.
WILMER CUTLER PICKERING HALE AND DORR LLP: Keith L. Slenkovich (former), Aaron S. Thompson, Elaine Zhong (former)

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal.

Ariosa Diagnostics, Inc. v. Sequenom, Inc., No. 3:11-cv-06391-SI (N.D. Cal.)

Natera, Inc. v. Sequenom, Inc., No. 3:12-cv-00132-SI (N.D. Cal.)

Verinata Health, Inc. v. Sequenom, Inc., No. 3:12-cv-00865-SI (N.D. Cal.)

Verinata Health, Inc. v. Ariosa Diagnostics Inc., No. 3:12-cv-5501-SI (N.D. Cal.)

Illumina, Inc. v. Ariosa Diagnostics Inc., No. 3:14-cv-1921-SI (N.D. Cal.)

Illumina, Inc. v. Ariosa Diagnostics Inc., No. 3:15-cv-2216-SI (N.D. Cal.)

Illumina, Inc. v. Natera, Inc., No. 3:18-cv-01662-SI (N.D. Cal.)

Illumina, Inc. v. Ariosa Diagnostics, Inc., No. 3:18-cv-02847-SI (N.D. Cal.)

Ariosa Diagnostics, Inc. v. Illumina, Inc., No. 18-109 (U.S.)

Dated: February 28, 2019

/s/ Mark C. Fleming

MARK C. FLEMING
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

TABLE OF CONTENTS

CONFIDENTIAL MATERIAL OMITTED

The first omission on page 71 reflects Roche's confidential marketing strategy. The remaining omissions on page 71 reflect information regarding Illumina's third-party customers and customer relationships that Illumina has designated as confidential.

TABLE OF AUTHORITIES

CASES

STATUTES AND RULES

OTHER AUTHORITIES

STATEMENT OF RELATED CASES

Plaintiff-Appellant and Cross-Appellee Illumina, Inc. previously sought review of its request to compel arbitration in this Court, but its appeal was terminated to allow it to move to compel arbitration and cure a jurisdictional defect. *Illumina, Inc. v. Ariosa Diagnostics, Inc.*, No. 2014-1815 (Fed. Cir. June 23, 2015) (Clerk's order, before Wallach, Clevenger & Taranto, JJ.). Illumina, Inc. then appealed the district court's denial of an order to compel arbitration, and this Court affirmed the district court. *Verinata Health, Inc. v. Ariosa Diagnostics, Inc.*, 830 F.3d 1335 (Fed. Cir. 2016) (Reyna, J., joined by Clevenger & Wallach, JJ.). Illumina, Inc. and Verinata Health, Inc.—the two Plaintiffs-Appellants in this appeal (collectively, "Illumina")—also filed a petition for a writ of mandamus in this Court seeking review of the district court's denial of its motion to strike portions of the invalidity contentions served by Ariosa Diagnostics, Inc. ("Ariosa") and Roche Molecular Systems, Inc. ("Roche") (together with Ariosa, "Defendants"); that petition was denied. *In re Verinata Health Inc.*, No. 2017-109 (Fed. Cir. Mar. 9, 2017) (per curiam, before Prost, C.J., Newman & Hughes, JJ.).

Ariosa separately challenged the validity of certain claims of one of Illumina, Inc.'s patents that is involved in this appeal, U.S. Patent No. 7,955,794 (the "'794 patent"), in an *inter partes* review. The Patent Trial and Appeal Board concluded that the challenged claims were not unpatentable, and this Court

affirmed in an unpublished opinion. *Ariosa Diagnostics, Inc. v. Illumina, Inc.*, Nos. 2016-2388, 2017-1020, 705 F. App'x 1002 (Fed. Cir. Dec. 11, 2017) (Moore, J., joined by Bryson & Hughes, JJ.). Ariosa has filed a petition for a writ of certiorari seeking review of that decision, and on October 29, 2018, the Supreme Court invited the Solicitor General to file a brief expressing the views of the United States. *Ariosa Diagnostics, Inc. v. Illumina, Inc.*, No. 18-109, 139 S. Ct. 445 (Oct. 29, 2018) (mem.). Counsel for Defendants are unaware of any other case pending in this or any other court or agency that will directly affect or be directly affected by this Court's decision in the pending appeal.

JURISDICTIONAL STATEMENT

The district court had jurisdiction under 28 U.S.C. §§ 1331, 1338. It entered judgment on January 29, 2018, Appx15257, and resolved the parties' post-trial motions on July 19, 2018. Appx1-64. Illumina appealed on July 23, 2018, and Defendants timely cross-appealed on August 17, 2018. Appx15380-15392. The district court clarified its July 19 order on October 4, 2018, Appx226-229, and the parties filed amended notices of appeal on October 10 and 26, 2018. Appx15393-15410. This Court has jurisdiction under 28 U.S.C. § 1295(a)(1).

INTRODUCTION

Based primarily on a patent that neither it nor any of its licensees uses, Illumina sought tens of millions in damages and an injunction excluding Ariosa

from a market that Illumina exited years ago. But Illumina's case was fatally flawed. Not only were the asserted claims invalid, but Ariosa had specifically designed its Harmony V2 product to avoid them. Illumina was forced to concoct a theory that cannot support a judgment of infringement. Among other flaws, Illumina relied on a chemical reaction that nobody has ever observed and that Illumina's expert admitted was based on only a "guess." Appx2005.

Illumina nonetheless demands that this Court direct entry of a permanent injunction—a request as bewildering as it is extraordinary. Illumina has not even briefed (and has therefore waived any argument regarding) the requirement that it prove a "causal nexus" between Ariosa's Harmony V2 sales and the imaginary act of infringement that Illumina's expert first hypothesized in this litigation. That is no wonder, as Illumina did not prove that Ariosa's customers even ***know about*** the hypothetical infringing reaction, let alone factor it into purchasing decisions. That suffices to affirm the denial of an injunction; Illumina's failure to show any abuse of discretion in the district court's analysis of the relevant factors is icing on the cake.

The judgment of liability should be reversed or vacated, and the order denying a permanent injunction should be affirmed.

STATEMENT OF ISSUES

Defendants' Cross-Appeal[1]

1. Whether the infringement judgment regarding Ariosa's Harmony V2 test should be reversed because no reasonable jury could find that Harmony V2 satisfies the "immobilizing" and "detecting" limitations of the '794 patent's asserted claims.

2. Whether the Harmony V2 infringement judgment should be reversed because no reasonable jury could find that Harmony V2 satisfies the "providing" and "contacting" limitations of the '794 patent's asserted claims.

3. Whether the judgment of liability on the '794 patent should be reversed because the '794 patent is anticipated by Straus and assignor estoppel does not prevent Defendants from challenging the patent's validity.

4. Whether the judgment of liability on U.S. Patent No. 8,318,430 (the "'430 patent") should be reversed for lack of enablement.

[1] Ariosa's parent, Roche Molecular Systems, Inc., was dismissed before trial by stipulation providing that, although Roche would be deemed a party to any judgment, "Ariosa will be deemed the [Defendant] responsible for the conduct that Illumina has accused of infringing." Appx11606. After Illumina unexpectedly listed Roche as a party to its permanent-injunction appeal, Roche filed a protective notice joining Ariosa's cross-appeal to preclude any argument that Roche could not benefit from a favorable appellate decision.

Illumina's Appeal

5. Whether the district court's denial of a permanent injunction was within its discretion.

6. Whether the district court's decisions regarding supplemental damages and prejudgment interest were within its discretion.

STATEMENT OF THE CASE

I. TECHNOLOGY BACKGROUND AND PRIOR ART

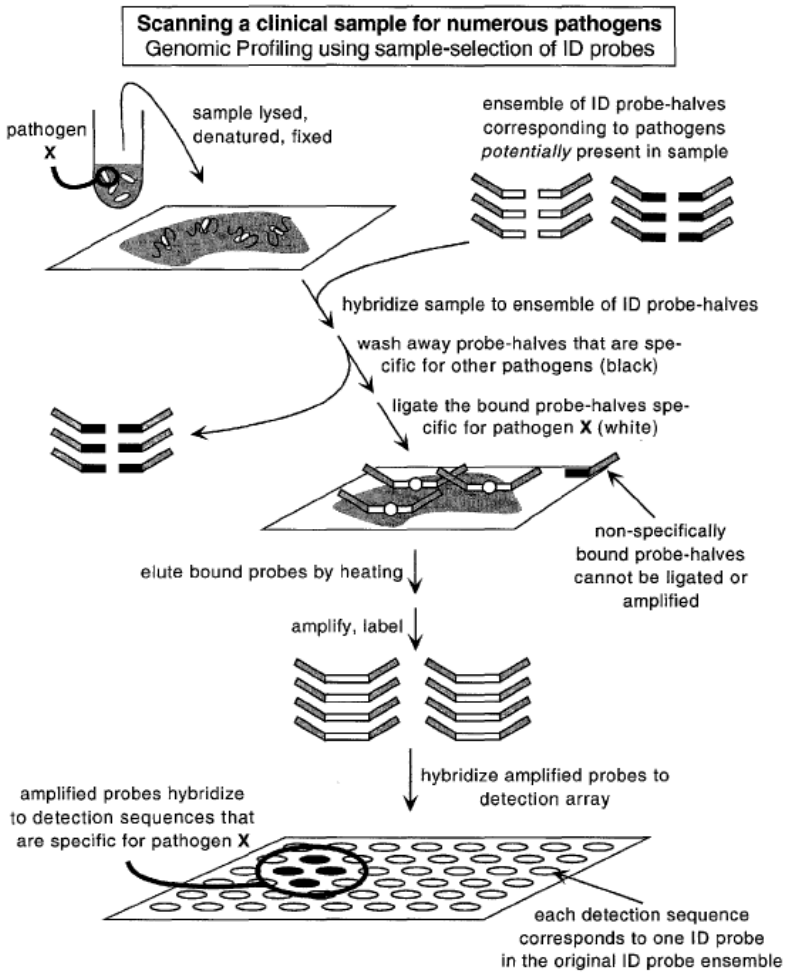
The body's cells contain most of a person's unique DNA, but some DNA fragments circulate in the blood. This type of DNA is called cell-free DNA, or cfDNA. Appx1368. A tiny fraction of the cfDNA in a pregnant woman's blood belongs to her fetus and has the fetus's DNA sequence. Appx1196-1198. Modern tests allow healthcare professionals to predict genetic abnormalities using fetal cfDNA, reducing the need for invasive tests like amniocentesis. Appx2407-2408.

Assays that test for the presence of many different genes at the same time, known as "multiplex" assays, have long been known. Appx190(1:27-57) (describing background of gene probe assays, the use of amplification technologies as part of such assays, and the use of biochip detectors, and citing references from as early as 1993). For example, the Straus prior-art reference[2] discloses multiplex methods for detecting more than 250 nucleic-acid sequences, such as the signature

[2] U.S. Patent Application No. 2002/0086289 (Appx5395-5441).

sequences of pathogens in a blood sample, using DNA probes. Straus's Figure 5 illustrates such a method:

Figure 5



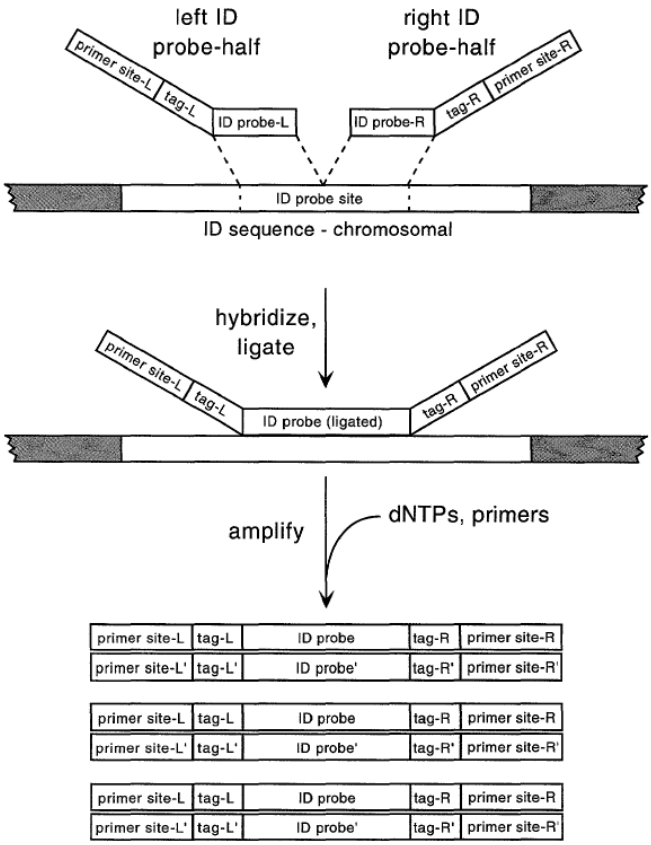
Appx5400.

In Straus's method, single-stranded DNA is first attached to a solid support. Appx5423. Next, short single-stranded DNA molecules called oligonucleotides are added. Appx5425. These oligonucleotides contain part of a DNA sequence that complements targeted DNA sequences in the sample. Appx5420. If the

sample contains those targets, the oligonucleotides will bind to—or "hybridize" with—the corresponding DNA in the sample. Appx5425.

Because each oligonucleotide used in Straus's method contains DNA corresponding to only half of a pathogen target sequence, Straus calls its oligonucleotides "probe-halves." Appx5422. If a target sequence is present in a sample, both probe-halves corresponding to the target sequence will hybridize to it. *Id.* Any unhybridized probe-halves are then washed away, and the probe-halves that are bound to target sequences are chemically joined together by a process called "ligation." *Id.*; Appx5425.

The ligated probe-halves are then separated from the solid support and "amplified" using polymerase chain reaction ("PCR") to create many copies of the probe corresponding to each target sequence present in the sample. Appx5425-5426; *see Board of Trustees of Leland Stanford Junior Univ. v. Roche Molecular Sys., Inc.*, 583 F.3d 832, 837 (Fed. Cir. 2009) ("PCR is a biochemical technique that enables measurement of relatively small quantities of nucleic acids by iteratively and exponentially 'amplifying' a sample to detectable levels."), *aff'd*, 563 U.S. 776 (2011). The amplification relies on sequences called "primers" that bind to an "amplification" or "primer binding" site on the probes. Appx5422; Appx5426. Only full probes (with both halves ligated together) are copied. Straus's Figure 3 summarizes this process:



Appx5398. The probes depicted have a "common pair of primer binding sites" across all probes. Appx5422.

After amplification, Straus binds the amplified probes to an array and detects which probes (and therefore which pathogens or other sequences of interest) are present. Appx5426.

II. ARIOSA'S HARMONY TESTS

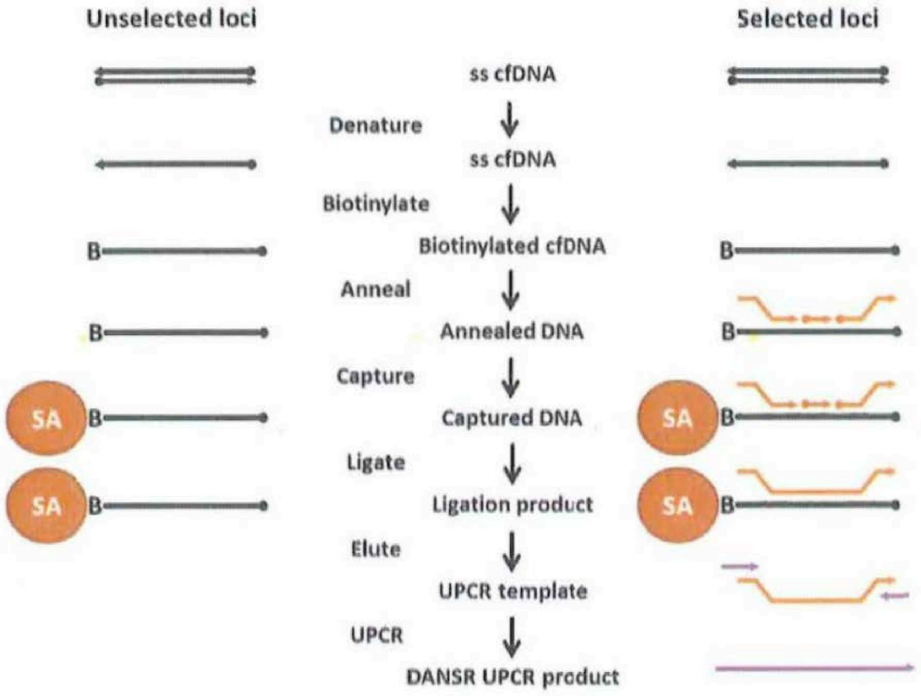
After substantial investment and innovation, Ariosa developed a testing product called Harmony. Harmony, like Straus, is a multiplex method that analyzes DNA—in Harmony's case, fetal cfDNA. After Illumina sued Ariosa for infringing its patents with the original Harmony test (Harmony version 1, or "V1"),

Ariosa designed Harmony V2 and discontinued Harmony V1. Harmony V2 differs from Harmony V1 in each of its three main steps. Harmony V2 is Ariosa's current test method and is the method that Illumina seeks to enjoin.

A. Harmony V2

1. Probe Binding and Amplification

Harmony V2 tests a sample of isolated fetal cfDNA for the presence of about 6800 gene sequences by using a laboratory robot to perform the steps summarized in the following figure. Appx3100-3101; Appx2067-2068.



Appx3101.

First, the sample's double-stranded fetal cfDNA is separated, or "denatured," into individual strands. Appx3100-3101; Appx3110; Appx2064-

2066. Next, a molecule called biotin is added to the end of each cfDNA strand (represented by "B" in the figure above). Appx3101; Appx3110-3111; Appx1951. The robot then adds a solution containing a mixture of single-stranded oligonucleotides that are complementary to the 6800 sequences Harmony V2 detects (orange lines in the figure above, which are analogous to Straus's probe-halves). Appx3101; Appx3111; Appx2066-2070; Appx1952-1953. The mixture contains three different oligonucleotides for each of the 6800 target sequences: (1) a first oligonucleotide complementary to the target sequence's beginning; (2) a second oligonucleotide complementary to the target sequence's middle; and (3) a third oligonucleotide complementary to the target sequence's end. Appx1971; Appx2066-2070; Appx2399-2400. The first oligonucleotide contains a "Readout Cassette," which is a short, artificial DNA segment designed to have a sequence that does not occur in the human genome. There is a unique Readout Cassette for each of the 6800 sequences tested in Harmony V2.

After the oligonucleotides are added to the cfDNA at room temperature, the mixture is heated to 70 ˚C and allowed to cool to about 30 ˚C. Appx2066-2070. If the cfDNA sample contains one of the 6800 target sequences, each of the three oligonucleotides corresponding to that target sequence will hybridize to it, creating a section of double-stranded DNA with two gaps (between the first and second and between the second and third oligonucleotides). *Id.* If the cfDNA does not contain

a certain target sequence, the oligonucleotides corresponding to that sequence will remain unbound in solution. *Id.*

The test allows the oligonucleotides two hours to bind to target sequences. After the two hours elapse, the robot adds magnetic beads coated with a protein called streptavidin, which binds strongly with the biotin on the cfDNA and links it to the beads. The robot then immobilizes the magnetic beads (and therefore the sample DNA and any bound oligonucleotides) and washes away anything that is left in solution, including any unbound oligonucleotides. Appx3100-3101; Appx3111; Appx1964; Appx1972.

Next, the robot adds an enzyme that ligates (i.e., connects) the three oligonucleotides, creating a single DNA strand. Appx3101; Appx3111; Appx1987. This only happens if all three oligonucleotides corresponding to the target sequence are bound to the sample cfDNA. Appx2388. The robot then denatures (i.e., separates) the newly-joined oligonucleotides from the sample cfDNA and amplifies them. Universal primer sequences on the first and third oligonucleotides enable this amplification. Appx2011.

2. Processing

The copies that result from the amplification step (called "amplicons") are large molecules—too large for Ariosa to reliably sort and identify. Appx2076-2078. To solve this problem, Ariosa developed a special processing method. First,

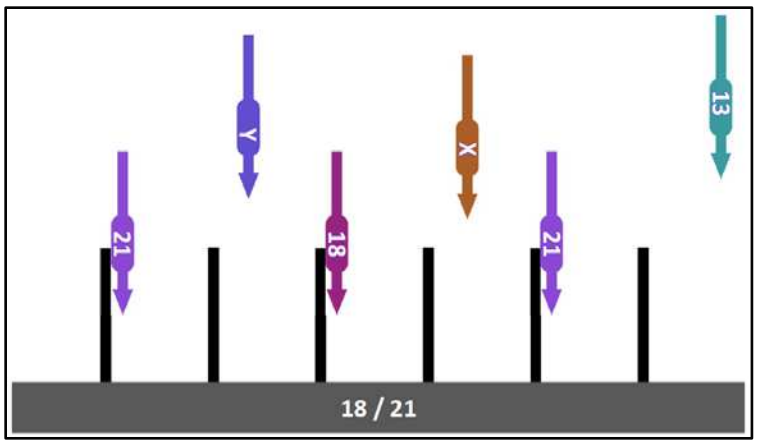
the amplicons are purified and added to a mixture that cuts ("digests") them into fragments. Appx3101; Appx3111-3112; Appx2074-2076.

Readout Cassettes contain none of the sample cfDNA sequence. Appx2402. Instead, they are artificial sequences, not matching DNA in the human genome. *Id.* Readout Cassettes are much smaller than the amplicons, thus solving the size problem that prevents Ariosa from analyzing the amplicons directly. Appx2076-2078; Appx2401.

3. Detection

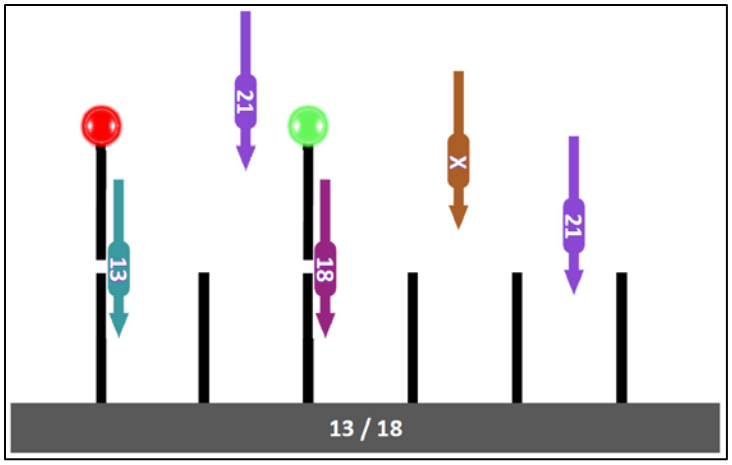
Harmony V2 performs its final step, detection, on an array, which is a chip containing thousands of short DNA sequences attached to a solid support. Harmony V2's array is manufactured by another company, Affymetrix. Appx3100.

The detection step begins by applying the digested reaction mixture, including the Readout Cassettes, to the Affymetrix array. Appx3101-3102. If a Readout Cassette corresponding to one of the 6800 target sequences is present, part of the Readout Cassette will bind to a DNA sequence on the array. *Id.* The other part of the Readout Cassette remains unbound, hanging like a single-stranded tail off the double-stranded sequence attached to the solid support. *Id.* The following figure shows how Readout Cassettes indicating target sequences on chromosomes 18 and 21 bind to the array while other Readout Cassettes remain unbound.

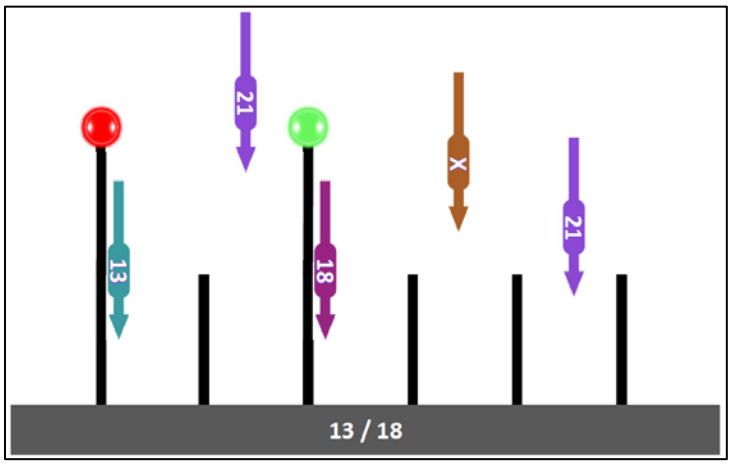


Next, any materials that do not bind to the array are washed away. Appx3101-3102; Appx3112. Only Readout Cassettes—which are made of artificial DNA, not cfDNA fragments—remain bound to the array. Appx3101-3102.

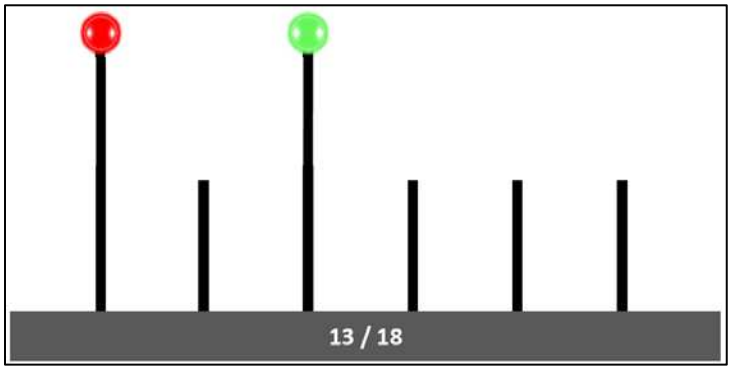
Fluorescently labeled oligonucleotides that are complementary to the Readout Cassettes' free single-stranded tails are then added. Appx3101-3102; Appx3112. After the labeled oligonucleotides are given time to bind to the single-stranded tails on the Readout Cassettes, they are chemically joined or ligated to the DNA strand attached to the chip. Appx3101-3102; Appx3112. The array is then heated up to separate the Readout Cassettes from the fluorescently tagged chip. The Readout Cassettes are then washed away, leaving only the labeled oligonucleotides attached to the DNA strands. Appx3101-3102; Appx3112.



Ligation



Heat & Remove Readout Cassettes



An Affymetrix machine then analyzes the array and detects the different colors of the fluorescent tags and their positions. Appx3101-3102; Appx3112-3113. From these data, and using sophisticated algorithms and analyses that it developed, Ariosa can calculate the probability that each of the 6800 sequences was present in the cfDNA sample. Appx3102. Notably, no part of the original sample, target sequence, amplicon, or Readout Cassette is present on the array when this detection is performed; they have all been washed away by this point. Appx1982.

B. Harmony V1

Ariosa designed the Harmony V2 method after this litigation began by making three main changes to its original Harmony V1 process.

First, Harmony V1 mixed the biotin-tagged sample DNA, the streptavidin-coated beads, and the oligonucleotides in a single step. Appx3081-3082; Appx3090. In Harmony V2, the sample DNA is mixed with the biotinylated oligonucleotides for two hours before the streptavidin-coated beads are added. Appx3101; Appx3111. This is the opposite of Illumina's '794 patent claims, in which the sample DNA first binds to the beads, and the oligonucleotides then bind to the sample–bead complex. Appx3110-3111; *infra* pp. 40-47.

Second, Harmony V1 used Illumina DNA sequencers—not Affymetrix arrays—for its detection step. Appx3082-3083.

Third, Harmony V1 did not use Readout Cassettes; it directly detected whether specific amplicons were present after the amplification step. Appx3082. Ariosa implemented the Readout Cassette methodology because the amplicons are too big to be detected on the Affymetrix array. Appx2076-2078. The processing step (i.e., the digestion of the amplicon to generate Readout Cassettes) is unique to Harmony V2.

III. ILLUMINA'S PATENTS

A. '794 Patent

Like the Straus reference, the '794 patent describes a technique for detecting the presence of certain DNA sequences, or "target sequences," in a sample. Appx190-191(1:61-3:40). Today, the '794 patent is old technology—Illumina no longer manufactures products that practice it, and "virtually every other provider of DNA sequencing-based non-invasive prenatal testing" uses different technology from that claimed in the '794 patent. Appx15343.

The sole independent claim recites:

> 1. A multiplex method for determining whether a sample contains at least 100 different target sequences, comprising:
>
> a) providing a sample which may contain at least 100 different single-stranded target sequences attached to a first solid support;
>
> b) contacting said target sequences with a probe set comprising more than 100 different single-stranded probes, wherein each of said more than 100 different probes comprises:

> i) a first universal priming site, wherein each of said more than 100 different probes has identical universal priming sites, and
>
> ii) a target specific domain, such that different double-stranded hybridization complexes are formed, each of the different hybridization complexes comprising one of said more than 100 different single-stranded probes and one of the different single-stranded target sequences from the sample;
>
> c) removing unhybridized probes;
>
> d) contacting said probes of the hybridization complexes with a first enzyme and forming different modified probes;
>
> e) contacting said modified probes with:
>
> i) at least a first primer that hybridizes to said universal priming site;
>
> ii) NTPs; and
>
> iii) an extension enzyme;
>
> wherein said different modified probes are amplified and forming different amplicons;
>
> f) immobilizing said different amplicons to a second solid support, and
>
> g) detecting said different amplicons immobilized to said second solid support, thereby determining whether the sample contains at least 100 different target sequences.

Appx223-224(68:44-69:12).

The asserted dependent claims (2, 3, 9, and 13) add limitations that do not affect the issues in this appeal. If Ariosa's tests do not infringe claim 1, they necessarily do not infringe the dependent claims. Likewise, the limitations in the

dependent claims do not affect the invalidity issues in this appeal because Illumina did not dispute that Straus discloses them. *See infra* p. 50.

The '794 patent lists seven inventors, including Drs. Arnold Oliphant and John Stuelpnagel, who once worked at Illumina but later became Ariosa executives. Drs. Oliphant and Stuelpnagel left Illumina years before the '794 patent issued and dispute that the '794 patent claims their inventions. Appx2269-2270 (both at Ariosa in 2009); Appx172 ('794 patent issued in 2011).

B. '430 Patent

The Harmony V1 test was separately found to infringe independent claim 1 and dependent claims 4 and 7 of the '430 patent. The asserted claims recite a method for determining the presence or absence of a fetal aneuploidy (i.e., an abnormal number of chromosomes) using "enumerated sequence reads." Appx293. In the claimed method, targeted sequences of cfDNA are enriched (e.g., amplified), indexed, pooled together, and sequenced. Counts of the number of times a sequence appears ("enumerated sequence reads") are then made and used to determine whether the fetus has aneuploidy.

The '430 patent's method is "non-random" because it isolates particular DNA sequences in a sample prior to sequencing. This generates data about a smaller portion of the genome than the more common method of "shotgun" sequencing, which generates data about the whole genome. Appx2479-2480.

Ariosa succeeded in developing a reliable non-random method, but Illumina did not. Illumina never commercialized a product based on the '430 patent's claimed invention; Verinata—the Illumina subsidiary that owned the '430 patent—opted to pursue whole-genome "shotgun" sequencing instead. Appx1262; Appx1273.

Of relevance here, the last two steps of the claimed method are:

> (e) based on the indexing nucleotide sequence, for each of the plurality of maternal blood samples, enumerating sequence reads corresponding to enriched and indexed fetal and maternal ***non-random polynucleotide sequences*** selected from the first chromosome tested for being aneuploid and sequence reads corresponding to enriched and indexed fetal and maternal ***non-random polynucleotide sequences*** selected from the reference chromosome; and
>
> (f) for each of the plurality of maternal blood samples, ***determining the presence or absence of a fetal aneuploidy*** comprising using a number of enumerated sequence reads corresponding to the first chromosome and a number of enumerated sequence reads corresponding to the reference chromosome of (e).

Appx4810.[3]

Step (f) purports to cover ***all ways*** of determining the presence or absence of a fetal aneuploidy using enumerated sequence reads from ***non-random*** polynucleotide sequences, but the patent "does not explicitly disclose" ***any*** algorithm for detecting fetal aneuploidy based on ***non-random*** sequencing. Appx15.

[3] Emphases added except where noted.

IV. DISTRICT COURT PROCEEDINGS

Illumina, Inc. and its subsidiary Verinata Health filed three suits against Ariosa and/or its parent company Roche. The suits, which were later consolidated, asserted that Harmony V2 infringed the '794 patent and that Harmony V1 infringed the '794 and '430 patents. Illumina did not assert the '794 patent until two years after Harmony V1's launch and did not move for injunctive relief until six years after. Appx4354-4362; Appx15411-15415; Appx10001-10018. Ariosa responded, *inter alia*, that neither Harmony test infringes, that Straus anticipates the '794 patent, and that the '430 patent is not enabled.

A. Claim Construction, Summary Judgment, And Trial

As relevant here, the district court's claim-construction order construed two terms of the '794 patent. Appx15001-15011. First, the court construed "modified probe," as used in claim 1's steps (d) and (e), as "an enzymatically altered polynucleotide which contains a universal priming site and is capable of substantially hybridizing to a target sequence." Appx15009. Second, the court construed step (e)'s term "wherein said different modified probes are amplified and forming ***different amplicons***" to mean "wherein the different modified probes are replicated, in whole or in part, to yield ***amplification products of*** each of the different ***modified probes***." Appx15011.

The court denied the parties' cross-motions for summary judgment as they related to infringement and invalidity, Appx15117-15158, but its order construed additional claim terms. First, it determined that "'attachment' of the single-stranded target sequences to a first solid support can occur during step (a)." Appx15148-15149. Second, it concluded that "step (b) cannot be performed before step (a)." Appx15149-15153. Third, it construed "detecting said amplicons immobilized to said solid support" in step (g) to encompass any methods that "detect[] the presence of immobilized amplicons," ***even if the detection does not occur "while the amplicon is immobilized."*** Appx15156-15158.

On the merits, the court—relying entirely on opinions of Illumina's expert Dr. Cooper—found a factual dispute about whether the cfDNA samples in the Harmony V2 process are attached to a solid support before they are hybridized with probes. Appx15154. The court also found a dispute about whether Harmony V2's Readout Cassettes qualified as the claimed "amplicons" under the doctrine of equivalents. Appx15156. Finally, even though Harmony V2's detection undisputedly happens after the Readout Cassettes are washed away, the court denied summary judgment of non-infringement because it construed "detecting said amplicons immobilized to said solid support" to encompass detection when the amplicons are not "immobilized to said support." Appx15157-15158.

The jury found infringement by both Harmony tests and no invalidity. Appx11552-11559. It found no willful infringement but awarded approximately $15.7 million for the '794 patent (for both tests) and approximately $11 million for the '430 patent (for Harmony V1). *Id.*

B. Post-Trial Motions

The district court denied Ariosa's post-trial motions. Appx3-49. The court granted Illumina's post-trial motion that assignor estoppel barred Ariosa from challenging the '794 patent's validity, Appx49-56, but it denied Illumina's motion for an accounting and supplemental damages pending appeal, Appx64. The court also denied Illumina's request to permanently enjoin Harmony V2, finding that Ariosa and Illumina are not in direct competition; that Illumina offered to license the '794 patent to Ariosa; that legal remedies could adequately compensate Illumina; that the balance of hardships was neutral; and that the public interest would not be served by an injunction. Appx56-63.

After this Court requested clarification, the district court awarded pre- and post-judgment interest to Illumina. Appx226-229.

SUMMARY OF ARGUMENT

1. No reasonable factfinder could have found that Harmony V2 immobilizes and detects "amplicons," as the '794 patent requires. In Harmony V2, it is only the Readout Cassettes that are attached to the Affymetrix array; because

they are not the product of any amplification process, they are not "amplicons," either literally or by equivalents. Separately, the Harmony V2 process does not practice the claimed "detecting" step because even the Readout Cassettes are washed away from the solid support—and therefore are not "immobilized" to it—before any detection is performed.

2. The '794 patent's claims separately require that a cfDNA sample first be attached to a solid support before being mixed with probes. But Ariosa designed Harmony V2 precisely so the oligonucleotide probes bind to the cfDNA ***before*** the cfDNA is attached to a solid support. Illumina's infringement theory turned on its expert's speculation that some cfDNA would remain unbound to probes during a two-hour mixing period but then rapidly bind to three probes in the short period after the cfDNA is attached to the solid supports. No one has ever observed this hypothetical reaction happening. Mere speculation by Illumina's expert cannot constitute substantial evidence.

3. Straus's Figure 5 undisputedly discloses nearly every element of the '794 patent's asserted claims, and a skilled artisan would immediately envisage the only two disputed elements: (1) the use of more than 100 probes in a sample containing at least 100 targets, and (2) a universal priming site on the probes. Illumina's attempts to distort the legal test for anticipation, and the disclosure of

Straus provided no basis on which a reasonable jury could have found the claims not invalid.

Additionally, the district court erred in holding that assignor estoppel barred Ariosa from challenging the '794 patent's validity. Besides resting on tenuous grounds, the assignor-estoppel doctrine does not apply here. Indeed, the court never decided whether Drs. Oliphant and Stuelpnagel are properly listed as inventors on the '794 patent—and they are not. And even if they did invent certain aspects of the '794 patent, Ariosa is not challenging the validity of their invention, but rather the validity of claims to different matter added after their assignment of the patent application. Assignor estoppel does not apply in this context.

4. The '430 patent's claims, asserted only against Harmony V1, are invalid for lack of enablement. Although the '430 patent broadly covers all ways of determining the presence or absence of fetal aneuploidy using counts of ***non-random*** sequences, it discloses no way to make that determination, let alone enable the claims' full scope. Illumina pointed only to the '430 patent's incorporation by reference of prior art methods using ***random*** sequences. But the patent does not teach how to modify random sequencing methods to enable the '430 patent's non-random method, which required undue experimentation. Nor does any limited disclosure enable the full scope of Illumina's broad claims.

5. On Illumina's appeal, Illumina has not shown any reason to reverse the district court's refusal to enjoin Harmony V2. Illumina has not even briefed—and has therefore waived—any argument of a "causal nexus" between the '794 patent's specific claimed method and any of Illumina's alleged harm. Moreover, the court's finding that Illumina failed to prove irreparable injury and inadequacy of damages was well within its discretion, not least because Illumina admitted at trial that it does not compete against Ariosa and that its stated objective was to license Ariosa, not exclude it from the market. The court's findings that the balance of hardships and the public interest do not favor an injunction were also within its discretion.

6. The district court was entitled to defer a decision on pre-verdict supplemental damages and an accounting on post-verdict supplemental damages until after this appeal. Illumina likewise shows no abuse of discretion in the court's choice of a prejudgment interest rate.

STANDARDS OF REVIEW

This Court reviews the denial of JMOL *de novo*, reversing "'when a party has been fully heard on an issue and there is no legally sufficient evidentiary basis for a reasonable jury to find for that party on that issue.'" *Integrated Tech. Corp. v. Rudolph Techs., Inc.*, 734 F.3d 1352, 1356 (Fed. Cir. 2013) (quoting *Hangarter v. Provident Life & Accident Ins. Co.*, 373 F.3d 998, 1005 (9th Cir. 2004)). Claim

construction is reviewed *de novo* and any underlying factual findings for clear error. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 841 (2015).

Anticipation is a question of fact reviewed for substantial evidence. *Blue Calypso, LLC v. Groupon, Inc.*, 815 F.3d 1331, 1341 (Fed. Cir. 2016). The district court's application of assignor estoppel is reviewed for an abuse of discretion. *Carroll Touch, Inc. v. Electro Mechanical Sys. Inc.*, 15 F.3d 1573, 1579 (Fed. Cir. 1993). Enablement is a question of law reviewed *de novo* with underlying factual findings reviewed for substantial evidence. *Trustees of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1361 (Fed. Cir. 2018).

The district court's order denying a permanent injunction is reviewed for abuse of discretion. *Apple Inc. v. Samsung Elecs. Co.*, 809 F.3d 633, 639 (Fed. Cir. 2015) ("*Apple IV*"). Its decision to award pre-verdict supplemental damages is reviewed for abuse of discretion, *Telcordia Techs., Inc. v. Cisco Sys., Inc.*, 612 F.3d 1365, 1377-1378 (Fed. Cir. 2010), as is its choice of prejudgment-interest rate, *Laitram Corp. v. NEC Corp.*, 115 F.3d 947, 955 (Fed. Cir. 1997).

ARGUMENT

I. THE HARMONY V2 INFRINGEMENT JUDGMENT SHOULD BE REVERSED BASED ON THE '794 PATENT'S "IMMOBILIZING" AND "DETECTING" LIMITATIONS

A. No Reasonable Jury Could Find That Readout Cassettes Are The "Amplicons" Produced By Harmony V2, Either Literally Or By Equivalents

The '794 patent claims "forming different amplicons" by amplifying modified probes and then "immobilizing … and … detecting said different amplicons." Appx224(69:6-13). Harmony V2 does not do that; Ariosa developed a superior method because it is impossible to reliably immobilize and detect the amplicons produced in Harmony V2's amplification step on the Affymetrix array. No reasonable jury could have found that Harmony V2 immobilizes or detects the amplicons produced in the amplification step (i.e., the "said … amplicons" in steps (f) and (g) of claim 1) either literally or by equivalents. Indeed, because the Readout Cassettes are not the same as the amplicons produced in Harmony V2's amplification step—which are the only amplicons produced in the entire Harmony V2 process—Harmony V2 does not immobilize or detect an "amplicon" at all.

1. Harmony V2 does not literally infringe because it immobilizes and detects Readout Cassettes, which are not the "amplicons" produced in the amplification step.

The undisputed evidence shows that Harmony V2 amplifies ***full ligated probes***—each including a target sequence, two universal primers, and a Readout Cassette. These amplicons are then digested, and only the Readout Cassettes produced by the digestion bind to the Affymetrix array. All the amplified cfDNA is discarded. *See supra* pp. 11-12. Illumina's literal infringement argument therefore depended on a malleable and inconsistent understanding of an "amplicon"—under Illumina's theory, the ***full ligated probes*** were the "amplicons" produced in step (e), but the ***Readout Cassettes*** were the "***said*** … amplicons" in steps (f) and (g). That is contrary to both the district court's construction of "amplicons" and the term's plain meaning. Because the Readout Cassettes are different from Harmony V2's amplification products—and not the "said … amplicons" produced by Harmony V2's amplification step—no reasonable jury could find that Harmony V2 literally practices the asserted claims' "immobilizing" and "detecting" limitations.

Claim 1's plain meaning precluding Illumina's theory. The claim refers to "amplicons" three times, each of which plainly refers only to the full sequences produced by amplifying the modified probes. First, step (e)—the amplification step—recites "contacting [the] modified probes" with a primer, nucleotides, and an

extension enzyme "wherein said different modified probes are amplified and forming ***different amplicons***." Appx224(69:1-7). Step (f) then recites "immobilizing ***said different amplicons***" to a solid support. Appx224(69:8-9). The "said … amplicons" in step (f) are the "said" copies of the modified probes produced in step (e). Finally, step (g) recites "detecting ***said different amplicons***" immobilized to the solid support. Appx224(69:10-12). At no point does claim 1 recite any step allowing "said … amplicons" to be anything other than the complete copies of the modified probes, which are the "amplicons" formed in step (e).

The district court's claim construction likewise permits no other conclusion. The court construed step (e)'s term "wherein said different modified probes are amplified and forming different amplicons" to mean "wherein the different modified probes are replicated, in whole or in part, to yield ***amplification products of each of the different modified probes***"—a construction that implicitly construed "amplicons" as "amplification products of each of the different modified probes." Appx15011; *see also* Appx15154-15158 (summary judgment order referring to "the Court's claim construction" of "amplicons"). This construction is consistent with the '794 patent's specification, which defines an "amplicon" as a "PCR amplification product." Appx193(8:22-23). Indeed, no example in the '794 patent contemplates immobilization or detection of anything other than amplification

products (copies) of modified probes. Illumina's expert Dr. Cooper testified on direct examination that "amplicons are just a word for ***DNA, that you've amplified***." Appx1974. Dr. Oliphant, who developed Harmony V2, voiced a similar understanding. Appx2073 ("[A] thing that is amplified is called an 'amplicon.'").

"Literal infringement requires that each and every limitation set forth in a claim appear in an accused product." *V-Formation, Inc. v. Benetton Group SpA*, 401 F.3d 1307, 1312 (Fed. Cir. 2005). The asserted claims therefore require that "said … amplicons"—i.e., the complete amplification products formed in step (e), not some remnant of them—be immobilized and detected in steps (f) and (g).

In its JMOL order, the district court identified no substantial evidence that could support a finding of literal infringement of the "said … amplicon" limitations in steps (f) and (g). Appx25 (upholding infringement verdict "at least under the doctrine of equivalents," but not addressing literal infringement). Indeed, at summary judgment, the only issue identified "for the fact finder to resolve" was "whether the Readout Cassettes are 'amplicons' under a doctrine of equivalents theory." Appx15156. Illumina presented no evidence of literal infringement at trial, and its expert Dr. Cooper even conceded that a Readout Cassette is merely "***part*** of the amplicon"—i.e., "a cleaved amplicon." Appx1976; *see also* Appx1980 ("[T]hey're using the Readout Cassette, which is part of the

amplicon …."); Appx2030. Because the Readout Cassette is the only thing that Harmony V2 immobilizes in preparation for detection, Harmony V2 does not immobilize or detect an "amplicon" at all—let alone "said … amplicon" produced from the amplification step, as required by the '794 patent's claims. Based on this record, no reasonable jury could have found literal infringement.

2. Harmony V2 does not infringe by equivalents because immobilizing and detecting Readout Cassettes leads to substantially different results from immobilizing and detecting "amplicons."

Unable to prove that Harmony V2 literally infringes, Illumina resorted to the doctrine of equivalents. That required Illumina to show an insubstantial difference between Readout Cassettes and the claimed "amplicons" and to provide "particularized testimony and linking argument as to the 'insubstantiality of the differences' between the claimed invention and the accused device or process … on a limitation by limitation basis." *Texas Instruments Inc. v. Cypress Semiconductor Corp.*, 90 F.3d 1558, 1567 (Fed. Cir. 1996). Ariosa offered extensive evidence that the differences ***are*** substantial; Illumina offered handwaving.

Ariosa offered detailed and unrebutted evidence that Harmony V2 would not work if the full amplicons were immobilized on the Affymetrix array. Because the use of full amplicons versus Readout Cassettes determines whether the method will work for its intended purpose, the difference between the two is substantial. *Cf.*

Genentech, Inc. v. Wellcome Found. Ltd., 29 F.3d 1555, 1568-1569 (Fed. Cir. 1994) (reversing denial of JMOL of non-infringement under the doctrine of equivalents because "the results achieved [by the alleged equivalent versus the claimed composition] are hardly substantially the same").

Dr. Oliphant, Ariosa's Chief Scientific Officer, testified that Ariosa tried using full amplicons for detection when designing Harmony V2. Those attempts failed. Asked if Ariosa would "get data or any useful information at all" if Harmony V2 "immobilized the amplicons rather than the cassettes," Dr. Oliphant testified, "No, it's not useful. We tried it. It doesn't work." Appx2078. Harmony V2's Readout-Cassette-based method and the claimed amplicon-based method therefore gave substantially different results.

Ariosa also explained the reason for these different results. Dr. Oliphant testified that there are significant—and undisputed—size differences between the Readout Cassettes and the amplicons, and that these differences limited the amplicons' ability to interact with the Affymetrix array. Appx2076-2077. The DNA sequences attached to the Affymetrix array are densely packed, leaving only small spaces for other DNA molecules to bind. Appx2077. The Readout Cassettes "are small and can float around easily and can find the appropriate place to bind on the array," but the much larger amplicons are "flapping around in the solution" and "bothering each other," which is "more significant than [the] interaction" between

the amplicons and the array. *Id.* So even though Harmony V2's processing step requires an "expensive" enzyme and "costs [Ariosa] time," *id.*, Ariosa had to use this step because binding amplicons to the array "doesn't work." *Id.*

Illumina's expert Dr. Cooper did not dispute Dr. Oliphant's account. Appx2625; Appx2678. In fact, he admitted that an oligonucleotide's size would "be[] one important factor among a variety of factors that ultimately dictate how" immobilization works, and that one would "want to optimize" for this effect. Appx2033-2035. Dr. Cooper did not explain, much less provide "particularized testimony and linking arguments," why the size difference between the small Readout Cassette and much larger amplicons would be insubstantial. *Texas Instruments*, 90 F.3d at 1567. On the contrary, he admitted that he "did not explicitly explain or account for size difference in [his] doctrine of equivalents argument," other than to baldly call it "insubstantial." Appx2035. And when asked whether there is "any similarity … between a full amplicon and a cleaved amplicon," Dr. Cooper asserted only: "they're both amplicons," Appx2683—an answer that incorrectly assumed literal infringement by equating Readout Cassettes with "amplicons." Nor did this assertion implicitly show that amplicons and Readout Cassettes are insubstantially different, particularly given that the latter work in Harmony V2 while the former do not. Dr. Cooper's unelaborated assertion that Readout Cassettes and the claimed "amplicons" hybridize with

"similar kinds of properties," *id.*, also does not help, as he did not identify those "properties" or explain how the differences in those properties were insubstantial. Dr. Cooper's doctrine-of-equivalents theory withered on cross-examination, and he had only adverbs to prop it up on redirect:

> Q. Does immobilization of a Readout Cassette perform that same function in substantially the same way as immobilizing an uncleaved amplicon?
>
> A. Yes, ***it's clearly performing in substantially the same way***, because it's via hybridization of this DNA molecule.
>
> Q. And does it lead to substantially the same result?
>
> A. ***Clearly the result is substantially the same***, because it leads to detection of the amplicons, which -- which then leads to detection of the target sequences that were in the original mixture.

Appx2683-2684. The only evidence that Dr. Cooper cited was Ariosa's statements describing the Readout Cassettes as "surrogates" for the amplicons. Appx2679. But those statements at most suggest that Harmony V2's Readout Cassettes perform the same function as the amplicons; they do not establish that the Readout Cassettes work in the same way, achieve the same result, or are insubstantially different.

The district court's discussion on this point amounted to a single sentence quoting Dr. Cooper's testimony, Appx25; it did not explain how his conclusory assertions amounted to the "particularized testimony and linking argument" required to prove infringement by equivalents. *Texas Instruments*, 90 F.3d at

1567. But as this Court has repeatedly held, Illumina cannot rebut (and the district court cannot discard) Ariosa's detailed testimony simply because Dr. Cooper disagreed, citing no evidence. *See MobileMedia Ideas LLC v. Apple Inc.*, 780 F.3d 1159, 1172 (Fed. Cir. 2015) ("MobileMedia's expert did not rebut this testimony, offering only the conclusory statement that 'I don't see evidence for that.' Conclusory statements by an expert, however, are insufficient to sustain a jury's verdict." (citation omitted)); *see also Augme Techs., Inc. v. Yahoo! Inc.*, 755 F.3d 1326, 1336 (Fed. Cir. 2014) (rejecting doctrine-of-equivalents argument based on conclusory expert testimony); *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1188 (Fed. Cir. 1998) (same). In the face of Ariosa's specific, credible, and unrebutted fact testimony, no reasonable juror could find that Illumina's conclusory expert opinions proved that Harmony V2's Readout Cassettes are equivalent to the "amplicons" recited in claim steps (f) and (g). The Court should therefore reverse the district court's denial of JMOL of non-infringement for Harmony V2. *Cf. Cordis Corp. v. Boston Sci. Corp.*, 658 F.3d 1347, 1357-1358 (Fed. Cir. 2011).

B. No Reasonable Jury Could Find That Harmony V2 Detects Amplicons Immobilized To A Solid Support

Separately, even if Harmony V2's Readout Cassettes were the "amplicons" produced in Harmony V2's amplification step (though plainly they are not), no

reasonable jury could conclude that Harmony V2 detects the Readout Cassettes "immobilized to a second solid support," as step (g) requires.

To shoehorn Harmony V2 into the '794 patent's claims, Illumina argued that Harmony V2 could still "detect[] said different amplicons immobilized to said second solid support" even when the Readout Cassettes were ***not actually*** "immobilized" to the support. In Illumina's overly broad view, this limitation could be satisfied if the asserted amplicons were ***at some point*** immobilized to the solid support. Appx15090-15093; Appx15302-15305. The district court agreed and construed step (g)'s "immobilizing" term to encompass any method that "detect[s] the presence of immobilized amplicons," even if the detection does not occur "while the amplicon is immobilized." Appx15157-15158. But apparently recognizing this construction's vulnerability, Illumina did not seek a jury instruction on it. Appx2851-2853; Appx15171-15172; Appx15247-15248. The jury therefore applied plain meaning. Appx2848.

1. Under step (g)'s plain meaning, no reasonable jury could conclude that Harmony V2 detects amplicons "immobilized" to a solid support.

Harmony V2 does not literally practice step (g) under the term's plain meaning.[4] As Dr. Cooper admitted, the Readout Cassettes are "no longer

[4] At JMOL, the district court ignored Illumina's literal infringement arguments and addressed only the doctrine of equivalents. Appx24.

need[ed]" and are "wash[ed] away" after the fluorescent probes are ligated to the array. Appx1982. Only then, after the Readout Cassettes are gone, is a "picture of this image" taken. Illumina mapped this picture to the claimed "detecting" limitation. *Id.* The Readout Cassettes are therefore not literally "immobilized" to the array during the detecting step under the plain meaning of the claim.

The doctrine of equivalents cannot extend the "detecting" step to encompass detection done after the Readout Cassettes are washed away. Such an interpretation would include detection of supposed amplicons that are ***not*** "immobilized to said second support," which vitiates the claim element that the amplicons be "immobilized to said second solid support." *See Conopco, Inc. v. May Dep't Stores Co.*, 46 F.3d 1556, 1562 (Fed. Cir. 1994); *Athletic Alternatives, Inc. v. Prince Mfg., Inc.*, 73 F.3d 1573, 1582 (Fed. Cir. 1996). The vitiation doctrine has its clearest application "where the accused device contain[s] the antithesis of the claimed structure." *Planet Bingo, LLC v. GameTech Int'l, Inc.*, 472 F.3d 1338, 1345 (Fed. Cir. 2006); *see also Asyst Techs., Inc. v. Emtrak, Inc.*, 402 F.3d 1188, 1195 (Fed. Cir. 2005) (refusing to apply doctrine of equivalents where the proposed application would change "mounted" to "unmounted"). What happens in Harmony V2 ("detecting" only when Readout Cassettes are no longer immobilized to the array) and what is recited in the claim (detecting "amplicons" immobilized to the second solid support) cannot be insubstantially different; they

are the opposite of one another. Thus, no reasonable jury could have concluded that Harmony V2 practices step (g) under its plain meaning.

2. Alternatively, a new trial is warranted employing the proper construction of step (g).

Although JMOL is appropriate under step (g)'s plain meaning, to the extent there was ambiguity in step (g) that required clarification, the district court should have construed the term to require that the amplicons be immobilized at the time of detection. Ariosa presented that argument at summary judgment after Illumina first raised the theory that immobilization during detection was not required. Appx15027-15030; Appx15113-15115. But the court "agree[d] with" Illumina's reading of the claims and rejected what it characterized as "Ariosa's narrowing of the claim to require detection while the amplicon is immobilized." Appx15156-15157.

Defendants expressly sought reconsideration of the district court's construction of step (g) in their post-trial motions. Appx15275. The court acknowledged that request but failed to rule on it. Appx24-25. Reviewing the issue of claim construction *de novo*, *Teva*, 135 S. Ct. at 841, this Court should correct the district court's error and, at minimum, order a new trial under the correct construction.

Step (g) requires the amplicons to be immobilized ***while*** detecting is performed. Step (g) recites "detecting said different amplicons immobilized to

said second solid support." "Immobilized to said second solid support" is an adjectival phrase that describes the state of the "amplicons" during the "detecting" step—it modifies the things subject to detection.

This understanding is consistent with the prosecution history. As filed, claim 1's "detecting" step simply read "detecting said amplicons." In response to the examiner's obviousness rejections, Illumina added the "immobilizing" limitation as step (f) and amended the then-pending "detecting" step to read "detecting said amplicons immobilized to said solid support, thereby detecting at least 100 target sequences." Appx15047 (emphasis in original indicating newly added claim language). Construing the "detecting" step to allow detection when the amplicon is not immobilized to the solid support improperly reads out the language added to overcome the rejection. *See Computer Docking Station Corp. v. Dell, Inc.*, 519 F.3d 1366, 1375 (Fed. Cir. 2008) ("Claims should not be construed one way in order to obtain their allowance and in a different way against accused infringers." (internal quotation marks omitted)).

The Court should reverse the district court's denial of JMOL of non-infringement for Harmony V2 under step (g)'s plain meaning. *See supra* § I.D.1. But if it does not, the Court should remand for a new trial before a jury that is instructed on the term's proper construction.

II. THE HARMONY V2 INFRINGEMENT JUDGMENT SHOULD BE REVERSED BASED ON THE '794 PATENT'S "PROVIDING" AND "CONTACTING" STEPS BECAUSE NO REASONABLE JURY COULD FIND THAT THE PROBES HYBRIDIZE TO 100 TARGET SEQUENCES THAT ARE ATTACHED TO SOLID SUPPORTS

Throughout the case, Illumina struggled with an inconvenient fact: its claims require ***first*** "providing a sample [of] at least 100 different single-stranded target sequences attached to a first solid support" (step (a)) and ***then*** "contacting said target sequences with a probe set" (step (b)). But Harmony V2 does the exact opposite: it mixes ***unbound*** single-stranded DNA with oligonucleotide probes and only adds a solid support (the beads) after double-stranded complexes are formed. That is intentional, as Ariosa redesigned its process after this litigation began.

The order of operations in Harmony V2 was undisputed at trial. *See supra* pp. 9-15. Indeed, Dr. Cooper admitted that Harmony V2's "goal" is to "allow hybridization to occur ***before*** the solid support" is attached. Appx2003. Only after two hours of hybridization—in which the cfDNA is mixed with a vast excess of probes, between a million and 10 million probes per cfDNA molecule, Appx2019-2020, Appx2069-2070—are the beads added to attach the cfDNA to a solid support. Excess probes that did not bind to the cfDNA are then washed away. Appx3111; Appx1972.

Illumina first argued at summary judgment that steps (a) and (b) can be performed in any order. Appx15076-15085. The district court rightly rejected that

argument based on the claims' plain language. Appx15149-15153. Faced with the court's rejection of its infringement theory after the close of expert discovery, Illumina attempted to retrofit its evidence by focusing not on the steps Harmony V2 was designed to perform, but on a hypothetical process that Illumina's expert guessed might happen inside the Harmony V2 reaction vessel. Illumina's new theory had three parts. First, Illumina asserted that at least 100 different single-stranded target sequences would remain unbound to ***any*** of the three oligonucleotide probes (the left, right, or middle probes) after the two-hour period. Next, Illumina speculated that, although those 100 different single-stranded cfDNA sequences did not bind to any probe during the two-hour hybridization period, they would ***immediately*** bind to the newly-added streptavidin beads. Finally, Illumina theorized that those single-stranded cfDNA sequences—now weighed down by a bead—would find and bind with ***each*** of their three corresponding probes in the short time between when the beads are added and the unbound probes are washed away. Appx1963-1970.

No Illumina witness claimed to have observed this reaction or conducted any experiment to confirm its occurrence in ***any*** circumstance, much less in the reaction vessel for ***each*** Harmony V2 test. *See NTP, Inc. v. Research in Motion, Ltd.*, 418 F.3d 1282, 1318 (Fed. Cir. 2005) ("[T]he use of a process necessarily involves doing or performing each of the steps recited."). For example, if any of

the "at least 100 different target sequences" bound to any one of the three probes ***before*** the beads were added, it would not meet step (a)'s requirement of being "single-stranded." And if any of the three probes failed to bind to the bead-bound single-stranded cfDNA in the few minutes before the probes were washed away, the targeted sequence would not proceed through the rest of the claimed method (because the incomplete probe could not be amplified).

Illumina's only evidence for its theory was Dr. Cooper's testimony, but that was speculative, conclusory, and internally inconsistent, and thus cannot sustain the verdict. *See Cordis*, 658 F.3d at 1358 ("find[ing] very little evidence to support the jury's verdict" of infringement and thus affirming JMOL of non-infringement); *see also Brooke Grp. Ltd. v. Brown & Williamson Tobacco Corp.*, 509 U.S. 209, 242 (1993) ("When an expert opinion is not supported by sufficient facts to validate it in the eyes of the law, or when indisputable record facts contradict or otherwise render the opinion unreasonable, it cannot support a jury's verdict."); *InTouch Techs., Inc. v. VGo Commc'ns, Inc.*, 751 F.3d 1327, 1351 (Fed. Cir. 2014); *SkinMedica, Inc. v. Histogen Inc.*, 727 F.3d 1187, 1195 (Fed. Cir. 2013). Dr. Cooper's conclusory assertion of an unobserved reaction is precisely the sort of speculation that cannot support a verdict. *See Lucent Techs., Inc. v. Gateway, Inc.*, 543 F.3d 710, 722-724 (Fed. Cir. 2008) (affirming finding of no infringement as a matter of law where patentee's infringement evidence "established only

uncertainty and speculation," expert "did not know at what rates" infringement occurred and "did not ever observe" infringement).

At least two of the three elements of Dr. Cooper's infringement theory were supported by nothing more than his say-so. ***First***, Dr. Cooper offered no evidence that at least 100 different single-stranded target sequences remain completely unbound from any probe after the two-hour hybridization period. Instead, he ventured only "the complexity of this reaction." Appx2675; Appx2674. In Dr. Cooper's telling, multiple conditions conspire against hybridization: "incorrect interactions," "random collisions," and an "overwhelm[ing] … concentration of the wrong probe[s]." Appx1968; Appx1966; Appx2012-2013. These alleged conditions led Dr. Cooper to assert that the reaction would be "relatively slow." Appx2676. But Dr. Cooper did not explain what "relatively slow" meant, and he did not offer any data or test results to support his theories. Appx1967 (describing his theory as "***an estimate*** that approximately one percent of the fragments would" remain unhybridized after two hours); Appx2007 (admitting that he cannot give an error rate for his "one percent guess"). Nor did he explain how these qualitative factors proved that at least 100 ***different*** single-stranded sequences would remain unbound in ***every*** Harmony V2 reaction after ***two hours***.

Second, Dr. Cooper presented no evidence that any unbound single-stranded target sequences would bind to ***all three probes*** during the short period between

the addition of the streptavidin beads and the washing-away of the probes. Dr. Cooper simply stated, without support: "And then they allow continued time to proceed. And that would, in fact, allow those now—those single-stranded fragments that are now attached to a solid support to contact and hybridize with their oligos." Appx1965.

Dr. Cooper's assertion left at least three gaping holes: (1) he never explained why ***any*** target sequence—having failed to hybridize to even ***one*** probe during the ***two-hour*** hybridization step—would then hybridize with ***all three*** probes in the ***minutes*** between the addition of the beads and the probes being washed away;[5] (2) he did not identify how many unbound target sequences would hybridize with all three probes after attaching to a bead; and (3) he did not testify that such post-attachment hybridization happens in ***every*** sample that Ariosa runs in Harmony V2. He could only speculate that the conditions "would … allow" these reactions, Appx1965; he could not say that they actually occurred. *See* Appx2009 (acknowledging that he was not aware of "anyone anywhere using methodology like [he] used to arrive at the guess" about hybridization after the streptavidin beads are added).

[5] Dr. Cooper did not even testify about how long this short period is. Illumina's post-trial brief cited deposition testimony suggesting 30 minutes but conceded that it did not proffer such evidence at trial. Appx15301-15302.

On top of these deficiencies, Dr. Cooper's theory was also internally inconsistent. To support the first part of his theory, Dr. Cooper invoked the reaction's "complexity" to argue that at least 100 different target sequences would remain unbound during the hybridization step. Appx2673-2675. Yet to support the second part of his theory, Dr. Cooper argued that the same reaction would happen in minutes. Appx1965. He offered no testimony or evidence to reconcile these contradictory positions.

Despite having no burden to rebut Illumina's entirely speculative theory, Ariosa showed that Dr. Cooper's hypothetical side reaction does not occur. Dr. Quackenbush, Ariosa's expert, listened to Dr. Cooper's theory and concluded that it had no support whatsoever. Appx2393. Dr. Quackenbush relied in part on the kinetics of the three hybridization reactions that Dr. Cooper hypothesized would need to occur in the minutes between addition of the beads and the removal of the probes. Appx2396-2397. He testified that this reaction—which, under Dr. Cooper's theory, did ***not*** happen during the two-hour mixing period designed to allow the free-floating target sequences to hybridize—would be much less likely to happen after the target sequences were weighed down with the beads. Appx2394.

The district court accepted Dr. Cooper's testimony as substantial evidence because it was "based on theoretical foundations," Appx22, but speculation does

not become a theory just because a professor says it. To constitute substantial evidence, a theory must be tied to scientific facts. The limited facts that Dr. Cooper relied on support, at most, his probabilistic assertions that at least 100 different single-stranded target sequences remain after the two-hour hybridization period, and that those sequences would quickly bind to the beads after the beads are added. Appx22-23. But even accepting those facts, they do not support the last step of his theory—that the solid-support-bound single-stranded target sequences would bind ***to all three probes*** before the probes are washed away. The district court's conclusion that "there is still ample time for the 100 single-stranded target sequences (attached to the beads) to hybridize to their respective three probes," Appx23, is utterly conclusory and unsupported; even Dr. Cooper did not explain why the time was "ample," nor did he explain why he thought that it was sufficient to hybridize to all three probes, given the failure to do so during the two-hour period specifically designed for hybridization. Because Illumina presented no theory based on facts or scientific principles, it cannot constitute substantial evidence. *See Bowers v. Baystate Techs., Inc.*, 320 F.3d 1317, 1334 (Fed. Cir. 2003) (reversing jury verdict of infringement where "the record contained undisputed evidence showing that the limitations of [a claim limitation were] not met"); *cf. ACCO Brands, Inc. v. ABA Locks Mfr. Co.*, 501 F.3d 1307, 1313-1314 (Fed. Cir. 2007) (reversing jury verdict of inducement because the only evidence

supporting direct infringement was expert speculation that the device would be used in infringing mode rather non-infringing mode).

III. THE '794 PATENT'S ASSERTED CLAIMS ARE INVALID AS ANTICIPATED

A. The '794 Patent is Anticipated By Straus.

The district court improperly denied JMOL on Straus's anticipation of the '794 patent's asserted claims. Illumina did not deny that Straus's Figure 5 expressly disclosed nearly every element of claim 1 of the '794 patent in the same order. Instead, Illumina focused on only two claim elements: (1) the use of more than 100 probes in a sample containing at least 100 targets, and (2) a universal priming site on the probes. But Straus discloses both of those elements too, in a manner that allowed a skilled artisan to at once envisage the claimed arrangement or combination.

Straus's Figure 5 states that the method is designed to test a sample for "numerous" pathogens using probe-halves. Appx5400. As Straus makes clear, the goal was to test for "a large number of organisms" in a single test. Appx5407(¶8); *see also* Appx5409(¶21); Appx5418(¶130). In particular, Straus expressly disclosed the use of "more than two hundred and fifty … different amplifiable probes." Appx5410(¶39); *see also* Appx5411(¶43); Appx5419(¶¶138-139); Appx2470. A skilled artisan reading Straus would thus readily understand that Figure 5's method to test for "numerous" pathogens includes using at least 100

different target sequences and over 100 different single-stranded probes, as the '794 patent claims.

As for the claimed universal priming site, Straus repeatedly emphasizes the benefit of limiting variation among priming sites on the probes: "The genomic profiling assay avoids the usual amplification artifacts that arise during multiplex amplification by using a very small number of amplification sequences to direct the amplification of a large number of distinct ID probes." Appx5422(¶176); Appx5410(¶31) ("no more than four pairs of amplification sequences"); Appx5411(¶43). In particular, Straus expressly discloses the use of amplification sequences "common to most or ***all*** of the probes." Appx5422(¶176); Appx2471. Straus also makes clear that for probe-halves—as disclosed in Figure 5 and Figure 3—"each probe has a unique ID and tag sequence, but a ***common*** pair of primer binding sites," depending on whether it is a left or right probe-half. Appx5422(¶183). Straus thus clearly discloses that, in designing the large number of probes (>250) for performing Figure 5's method, there would be substantial if not complete identity in the probes' priming sites. This anticipated claim 1 of the '794 patent.

Illumina provided no basis for a reasonable jury to disregard Straus's clear teachings. Its expert first asserted that "all of the elements of the claim have to be in one disclosure or figure." Appx2599. That is wrong; "a reference can anticipate

a claim even if it does not expressly spell out all the limitations arranged or combined as in the claim, if a person of skill in the art, reading the reference, would at once envisage the claimed arrangement or combination." *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1381 (Fed. Cir. 2015) (internal quotation marks omitted); *see also Blue Calypso*, 815 F.3d at 1344; *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1379 (Fed. Cir. 2001) ("[A]nticipation only requires that those suggestions be enabling to one of skill in the art.").

Next, Illumina argued that Straus discloses multiple priming sites "as opposed to an identical universal priming site across all of the targets." Appx2600. But the '794 patent contains no such requirement; as Illumina's expert later admitted, it requires only that a "universal priming site" appear on at least 100 different probes, not that it appear on every single probe. Appx223(68:54-56); Appx2651. As discussed above, Straus discloses the use of amplification moieties "common to most or ***all*** of the probes." Appx5422(¶176); Appx2471.

Finally, Illumina argued that Figure 5's array included only 48 wells. Appx2602. But Straus does not indicate that the simplified picture of the array in Figure 5 was intended to override its repeated teaching of more than 250 probes. *See Nystrom v. TREX Co.*, 424 F.3d 1136, 1149 (Fed. Cir. 2005) ("[P]atent drawings do not define the precise proportions of the elements[.]").

Illumina has attempted to remove from the public domain a method that Straus clearly taught. No reasonable jury could have found that Straus failed to anticipate claim 1 of the '794 patent. And Illumina did not even dispute that the asserted dependent claims are anticipated if claim 1 is anticipated. Appx2474-2476.

B. Assignor Estoppel Should Not Prevent Ariosa From Challenging The Validity Of The '794 Patent.

Illumina cannot shield the asserted claims from invalidation through the doctrine of assignor estoppel. Assignor estoppel, in its present form, rests on a shaky foundation. Multiple decisions have questioned the doctrine's viability after *Lear, Inc. v. Adkins*, 395 U.S. 653 (1969). *See Diamond Scientific Co. v. Ambico Co.*, 848 F.2d 1220, 1223 (Fed. Cir. 1988) (collecting cases). Yet this Court has not only applied the doctrine, but "expanded assignor estoppel dramatically from its roots." Lemley, *Rethinking Assignor Estoppel*, 54 Hous. L. Rev. 513, 519 (2016). This expansion has been heavily criticized, and in 2018 the Supreme Court invited the Solicitor General's views on the doctrine in a case that later settled. Order, *EVE-USA, Inc. v. Mentor Graphics Corp.*, No. 17-804, 138 S. Ct. 1608 (Apr. 23, 2018) (mem.). If necessary, Ariosa preserves the right to challenge this questionable precedent at the appropriate time.

No change in precedent is needed, however, for this Court to reverse or vacate the district court's improper application of assignor estoppel because the

district court abused its discretion in at least two ways. ***First***, although the court summarized the parties' dispute regarding whether Drs. Oliphant and Stuelpnagel are properly listed as inventors on the '794 patent, the court never actually ruled on the inventorship issue. Appx53. That error alone requires vacatur—if Drs. Oliphant and Stuelpnagel were not inventors, they had no ownership rights in the '794 patent to assign and assignor estoppel cannot apply. The court was therefore required to rule on the issue before applying assignor estoppel.

Drs. Oliphant and Stuelpnagel were not properly listed as inventors on the '794 patent. Their contribution was recited in claim 5 of U.S. Patent Application No. 10/177,727, which was dropped before the application matured into the '794 patent. Appx1853-1855; Appx2080. Their invention was limited to allele-specific extension and ligation with perfect complementarity at the four bases comprising the interrogation and detection positions at the 3' end of the probe. Appx5375-5376; *see* Appx2080. Only if all four bases at the 3' interrogation position are perfectly complementary to that allele can the target sequence be amplified—i.e., allele-specific extension. Appx1851-1852; Appx1854; Appx2083. If the allele is not present, the interrogation position cannot perfectly complement the sequence, amplification will not occur, and no allele will be detected.

The claims of the '794 patent are directed to an entirely different purpose and method. The '794 patent claims merely ***substantial*** complementarity, and

amplification can occur whether or not an allele is present, which prevents the assay from detecting only a particular allele or genotyping the sample. Appx2089 ("[T]here's no allele specificity. There's no genotyping."); Appx2090 (noting that substantial complementarity "would specifically prohibit genotyping").

Ariosa squarely presented its argument to the district court, Appx15360-15376, and the court acknowledged the dispute about whether the asserted claims of the '794 patent are directed to the Oliphant and Stuelpnagel invention, Appx53. Because the court never resolved the dispute, the case should at least be remanded for that analysis.

Second, the court improperly discounted that, even if Drs. Oliphant and Stuelpnagel invented certain aspects of the '794 patent, Ariosa is not challenging the validity of ***their*** invention. As an equitable doctrine, assignor estoppel is not "susceptible of automatic application" and requires careful examination of "the balance of equities between the parties." *Diamond Scientific*, 848 F.2d at 1225-1226. Here, not only did Drs. Oliphant and Stuelpnagel assign their rights before the '794 patent issued, but it is undisputed that Harmony V1 and V2 do not "use[] Dr. Oliphant and Stuelpnagel's invention of allele-specific extension and ligation," Appx2631. Illumina has not asserted infringement of their invention, and Ariosa has not challenged its validity. This combination of factors sets this case apart from the usual circumstance in which an inventor who assigned his rights in an

application is estopped from challenging the validity of his own invention when the patent issues.

Although existing precedent holds that assignor estoppel can apply to an assignment made before a patent issues, the Supreme Court has cautioned:

> It is apparent that the scope of the right conveyed in such an assignment is much less certainly defined than that of a granted patent, and the question of ***the extent of the estoppel against the assignor of such an inchoate right is more difficult to determine*** than in the case of a patent assigned after its granting. When the assignment is made before patent, the claims are subject to change by curtailment or enlargement by the Patent Office with the acquiescence or at the instance of the assignee and the extent of the claims to be allowed may ultimately include more than the assignor intended to claim. This difference might justify the view that the range of relevant and competent evidence in fixing the limits of the subsequent estoppel should be more liberal than in the case of an assignment of a granted patent.

Westinghouse Elec. & Mfg. Co. v. Formica Insulation Co., 266 U.S. 342, 352-353 (1924). The fact that Ariosa is not challenging the invention that Drs. Oliphant and Stuelpnagel made is precisely the type of consideration that should tip the balance against assignor estoppel here.

The animating idea behind the doctrine of assignor estoppel is that "the implicit representation by the assignor that the patent rights that he is assigning (presumably for value) are not worthless … sets the assignor apart from the rest of the world and can deprive him of the ability to challenge later the validity of the patent." *Diamond Scientific*, 848 F.2d at 1224. It is one thing to find such an

"implicit representation" where, as in *Westinghouse* and *Diamond Scientific*, the assignor was the *sole* inventor and the claims that ultimately issued from the assigned application were necessarily directed to that inventor's work.[6] It is quite another thing to find such an implicit representation when an inventor who has made a limited contribution assigns an application in the routine course of his employment and later wishes to challenge invalid claims that go beyond that invention. The inventor may have an inchoate ownership right in any patent that eventually issues, but the inventor's assignment does not (and cannot) vouch for or profit from the assumed validity of future claims directed to the work of others.[7]

Ariosa is not asking this Court to adopt a bright-line rule. But on the equities of this case, estopping Ariosa from challenging claims that Drs. Oliphant and Stuelpnagel did not invent was an abuse of discretion. Assignor estoppel should not be extended any further than it already has been.

---

[6] The equities might also be different when someone other than an inventor owns the entire application and sells it.

[7] The statute requires only that a joint inventor's oath accompanying an application attest that "such individual believes himself or herself to be … an original joint inventor of *a* claimed invention *in the application*." 35 U.S.C. § 115(b)(2). As for the oath that Illumina required its employees to execute in their assignment, it stated: "Assignors believe themselves to be the original inventors of the invention disclosed and claimed in said application for Letters Patent." Appx3441. Drs. Oliphant and Stuelpnagel made no general representation regarding the validity of future claims.

IV. THE '430 PATENT'S ASSERTED CLAIMS ARE INVALID FOR LACK OF ENABLEMENT

The '430 patent—asserted only against Harmony V1—claims far more than it actually teaches, thus running afoul of the Patent Act's enablement requirement. Claim 1's step (f) broadly covers ***all ways*** of "determining the presence or absence of a fetal aneuploidy" using "enumerated sequence reads" from the chromosome of interest and a reference chromosome. Appx293(63:9-67). But the specification does not disclose ***any*** way to make that determination using the ***non-random*** sequences required by step (e), let alone enable the ***full scope*** of what is claimed.

The determination required by step (f) is difficult. Among the many problems, "small chromosomes only get some reads" while "big ones get lots of reads," Appx1344, and "noise and variation" mean that "some samples … have much higher counts than any other samples," Appx2351. Using a non-random method exacerbates these problems because it produces less information than whole-genome sequencing, necessitating the use of sophisticated algorithms to compensate. Appx2479-2480. Unrebutted testimony showed that another company, Sequenom, tried and "failed miserably" to overcome these challenges, Appx2477, and that Ariosa succeeded in the "arduous" process of developing an algorithm for calculating the risk of fetal aneuploidy only after substantial work and innovation, Appx2344-2347.

The ’430 patent did not provide guidance to overcome these difficulties, and certainly not guidance commensurate with the full scope of its claims. The ’430 patent undisputedly “does not explicitly disclose” any algorithm that would allow a skilled artisan to perform step 1(f). Appx15; Appx2407; Appx1344. To try to fill this gap, Illumina relied on the ’430 patent’s incorporation by reference of several pieces of prior art discussing methods for determining fetal aneuploidy. Those disclosures fall far short of enabling the full scope of what the ’430 patent claims.

The ’430 patent correctly describes the disclosures incorporated by reference as “[m]ethods for determining fetal aneuploidy using ***random*** sequencing techniques.” Appx268(12:49-55). Adapting those disclosures for use in a ***non-random*** method, as claimed by the ’430 patent, would have required undue experimentation. *See ALZA Corp. v. Andrx Pharms., LLC*, 603 F.3d 935, 941 (Fed. Cir. 2010) (holding that a patent disclosing only osmotic dosage forms that incorporated by reference a textbook discussing non-osmotic dosage forms was not enabled). Dr. Rava, a named inventor of the ’430 patent, admitted that random sequencing techniques could not be used in a non-random method without modification. Appx1344-1345. And although Dr. Rava opined, without explanation, that the random methods might be “optimized” for use in a non-random method, the ’430 patent does not provide any guidance on how to make that modification. *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed.

Cir. 1997) ("[F]ailure to meet the enablement requirement … cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art.").

More fundamentally, even if the disclosure incorporated by reference could successfully be adapted, that limited disclosure would still be insufficient to show that the "***full scope*** of the claimed invention [was] enabled." *Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 999 (Fed. Cir. 2008). "A patentee who chooses broad claim language must make sure the broad claims are fully enabled" to ensure "the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims." *Id.* (internal quotation marks omitted); *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1381 (Fed. Cir. 2012) ("[A] patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage[.]"). Here, the '430 patent uses broad, functional language in step (f) to encompass ***any*** way of "determining" fetal aneuploidy based on a comparison of enumerated sequence reads. No reasonable jury could find that the '430 patent's barebones disclosure supports such a broad claim. *See National Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.,* 166 F.3d 1190, 1195-96 (Fed. Cir. 1999) (patent claiming application of a system in video games and movies was invalid where it only enabled use in video games); *see also In re Wright*, 999 F.2d 1557, 1564 (Fed.

Cir. 1993) (claims to a vaccine for multiple avian RNA viruses not enabled by teaching a vaccine for a single strain of avian RNA virus).

V. THE DISTRICT COURT DID NOT ABUSE ITS DISCRETION IN DENYING A PERMANENT INJUNCTION

A. Illumina's Permanent Injunction Appeal Fails At The Threshold Because Illumina Has Waived Any Argument Regarding A Causal Nexus

Illumina's demand that this Court "reverse[] and "remand[] with an order to grant [Illumina] a permanent injunction," Br. 14, 51, fails for a straightforward reason: Illumina has not offered this Court any basis for finding "that a sufficiently strong causal nexus relates the alleged harm to the alleged infringement." *Apple Inc. v. Samsung Elecs. Co.*, 695 F.3d 1370, 1374 (Fed. Cir. 2012) ("*Apple II*"). Having failed to address the matter in its opening brief, Illumina cannot address it in reply. *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1319 (Fed. Cir. 2006) ("[A]rguments not raised in the opening brief are waived.").

Causal nexus is a component of Illumina's burden of proving "that it has suffered an irreparable injury." *eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 391 (2006); *see also Apple Inc. v. Samsung Elecs. Co.*, 678 F.3d 1314, 1324 (Fed. Cir. 2012) ("*Apple I*") ("To show irreparable harm, it is ***necessary*** to show that the infringement caused harm in the first place."); Appx57 (district court noting causal nexus as a "requirement" of proving irreparable injury). Yet Illumina's brief does not even ***mention*** causal nexus, much less point to any proof.

Illumina's waiver makes it unnecessary to consider its grab bag of objections to the district court's finding that it failed to show irreparable harm. Even if Illumina's objections had merit—and they do not, *see infra* pp. 62-72—the district court's finding of no irreparable harm could be independently affirmed based on Illumina's failure to show a causal nexus. The fact that the district court did not itself reach causal nexus is immaterial; this Court may reject Illumina's demand for reversal "on any ground the law and the record will support." *Glaxo Grp. Ltd. v. TorPharm, Inc.*, 153 F.3d 1366, 1371 (Fed. Cir. 1998).[8]

Illumina's attempt to whistle past the causal-nexus graveyard is understandable given the state of the record. Illumina does not use the '794 patent or contend that any of its licensees, customers, or other industry participants do. *See* Br. 16 (the '794 patent "has not been licensed"); Br. 19 (Illumina discontinued "Golden Gate," the only product that allegedly practiced the '794 patent, in 2015).[9] Illumina's own brief states plainly that "the royalty Illumina receives from its customers for its patent rights as part of its NIPT licensing program ***is unrelated to Ariosa's infringement*** because Illumina has not licensed the '794 Patent." Br. 29. Nor does Illumina contend that any such entity has expressed any interest in using

[8] Illumina addressed causal nexus in a single footnote below, Appx10014 n.7, but does not offer this Court even that.

[9] Golden Gate was a DNA assay, not a non-invasive prenatal technology (NIPT). Appx1589-1590.

the '794 patent. Accordingly, Illumina can scarcely argue that "the patented features impact consumers' decisions to purchase the accused devices." *Apple IV*, 809 F.3d at 642; *see also id.* at 643 (focusing on "consumers' perceptions of the infringing features," and finding a causal nexus where the infringed patents "were important to product sales" and where "customers sought these features in the [products] they purchased").

The lack of a causal nexus is reinforced by Illumina's own infringement theory, which undisputedly depends on an unintentional, unobserved, and wholly theoretical accident of timing concocted by its expert. *See supra* pp. 40-47. Illumina did not even attempt to show that Ariosa's Harmony V2 customers ascribe any significance to the speculative possibility that more than 100 cfDNA sequences might remain unbound after the two-hour hybridization period ***and*** might subsequently hybridize to all three probes after the streptavidin beads are added but before unbound samples are washed away. Appx1963-1969. Illumina did not prove that Ariosa's customers ***even know about*** this theoretical notion. As Illumina's expert Dr. Cooper admitted, Harmony V2's "goal" is to "allow hybridization to occur ***before*** the solid support," Appx2003; no evidence suggests that any subsequent (unobserved and unintended) hybridization has any meaningful or measurable effect on Harmony's functioning, efficacy, or commercial success, or was known to any customer. Accordingly, no evidence

supports—let alone compels—a finding that Dr. Cooper's fanciful scenario causes Illumina to "lose[] sales ***because*** [Harmony V2] contain[s] [Illumina's] patented features." *Apple IV*, 809 F.3d at 644. "The causal nexus requirement is not satisfied simply because removing an allegedly infringing component would leave a particular feature, application, or device less valued or inoperable." *Apple II*, 695 F.3d at 1376. Rather, Illumina would still have to show that Harmony V2's supposed post-streptavidin hybridization "impact[s] consumers' decisions to purchase" the test. *Apple IV*, 809 F.3d at 642. Again, Illumina made no such argument below, and has waived any such argument here.

In connection with a different argument, Illumina suggests that Harmony V2 has a low cost, Br. 33, but that could not show a causal nexus either. Illumina has not demonstrated that the specific steps claimed in the '794 patent reduce cost compared to unclaimed methods or that they are responsible for harming Illumina. "It is not enough for the patentee to establish some insubstantial connection between the alleged harm and the infringement," *Apple II*, 695 F.3d at 1375; the record must establish a "connection between the patented features and the demand" for the product at issue, *Apple IV*, 809 F.3d at 642. The allegedly infringing "feature" here is a minimal amount of hybridization that supposedly occurs ***after*** the two-hour hybridization period is over—a "feature" that is entirely unintentional, does not affect Harmony V2's function or quality, and was unknown

to the market until Dr. Cooper speculated about it in this litigation. No court could find a causal nexus on such a record.

Because Illumina has waived any argument that there is a causal nexus, and could not prove one in any event, the Court may and should affirm the denial of an injunction without more.[10]

B. Even If Considered, Illumina's Irreparable-Harm And Inadequacy-Of-Monetary-Damages Arguments Show No Abuse Of Discretion

Even apart from Illumina's dispositive failure to address causal nexus, the record overwhelmingly confirms that the district court did not abuse its discretion in finding that Illumina failed to prove both irreparable harm and the inadequacy of monetary damages.

As an initial matter, Illumina waited two years after Harmony's launch to sue and did not seek an injunction until ***six years*** afterwards. For a company supposedly suffering irreparable harm, Illumina did not act with any urgency. *See Apple I*, 678 F.3d at 1325-1326 (affirming assessment of irreparable harm based, in part, on delay in seeking preliminary injunction); *Polymer Techs., Inc. v. Bridwell*,

[10] Illumina does not alternatively seek vacatur and remand for further proceedings regarding causal nexus, so that remedy is inappropriate. And further proceedings would be wasteful and unnecessary. The district court would abuse its discretion were it to find that Illumina proved causal nexus on this record. *Cf. Apple Inc. v. Samsung Elecs. Co.*, 735 F.3d 1352, 1366 (Fed. Cir. 2013) ("[A]necdotal statements about single design elements do not establish that [patented features] are drivers of consumer demand[.]").

103 F.3d 970, 976 (Fed. Cir. 1996) ("unreasonable delay in bringing suit" "may be relevant to an analysis of irreparable harm").

In any event, the district court did not abuse its discretion in finding that Illumina failed to prove it would be irreparably harmed by maintaining the longstanding status quo. There are numerous independent bases for that conclusion, including the district court's finding that Illumina and Ariosa are not direct competitors and that Illumina was willing to license Ariosa; Illumina's failure to identify any specific losses apart from alleged loss of royalties; and Illumina's failure to explain why any asserted losses cannot be compensated by damages.

1. The district court did not abuse its discretion in finding that—as Illumina admits—Illumina does not compete with Ariosa.

As the district court found and Illumina's own witnesses admitted, Ariosa does not compete with Illumina, but at most with Illumina's third-party licensees. Appx57-59. Illumina's Chairman Jay Flatley declared that, "immediately" after Illumina acquired Verinata, Illumina "announced" that it was going to "exit the retail market … and get rid of the sales force." Appx1615. Illumina "began working directly on doing that" so as ***not*** to be "***in competition*** with Sequenom [and] Ariosa." *Id.*; *see also* Appx1416 (Head of Corporate Development Naclerio: after Verinata's acquisition, Illumina "would get out of the business of selling tests

directly"); Appx1420 (Naclerio) (explaining how Illumina executed that strategy); Appx1464 (Illumina told Ariosa it would "avoid competing with them"); Appx2200 (Illumina expert Malackowski) ("[D]uring 2013, Verinata exited the retail market and ***no longer acted in direct competition with Ariosa***.").

As held in *ActiveVideo Networks, Inc. v. Verizon Communications, Inc.*, 694 F.3d 1312 (Fed. Cir. 2012), lack of direct competition is a substantial basis for finding no irreparable harm. In *ActiveVideo*, this Court reversed an injunction because the defendant (Verizon) did not directly compete with the patentee (ActiveVideo), but only with ActiveVideo's third-party licensees. *Id.* at 1338. The harm to ActiveVideo was therefore indirect, and ActiveVideo's loss was "[s]traight-forward monetary harm" and "certainly not irreparable." *Id.*; *see also Edwards Lifescis. AG v. CoreValve, Inc.*, 699 F.3d 1305, 1315 (Fed. Cir. 2012) (affirming "the grant of a royalty-bearing license instead of imposing an injunction in situations where the patentee would experience no competitive injury"). Accordingly, as the district court held, monetary damages sufficed to remedy whatever lost license fees Illumina might suffer due to Ariosa's Harmony V2 sales. Appx59-60; *see ActiveVideo*, 694 F.3d at 1337 ("[T]he issues of irreparable harm and adequacy of remedies at law are inextricably intertwined.").

Illumina tries to evade *ActiveVideo* by arguing that Illumina sells "platform products," allegedly in competition with "Roche." Br. 28-29. As discussed below,

this focus on Roche is inapposite. *See infra* pp. 66-69. Nor does Illumina even identify the specific "platform products" it has in mind, demonstrate that it is losing sales of those products, prove that those losses are caused by the Harmony V2 test and connected to the '794 patent, or establish that any losses cannot be adequately compensated by damages. *See infra* pp. 69-72.

Illumina's sale of other "products" also does nothing to distinguish *ActiveVideo*. ActiveVideo itself sold other products: it licensed its "Cloud TV platform" software to Cablevision, and as a function of that licensing, "s[old] VoD [video-on-demand] hardware and software to providers of video services." 694 F.3d at 1338.[11] That did not change this Court's conclusion that ActiveVideo's harm was quantifiable and remediable via monetary damages. The district court did not abuse its discretion in drawing the same conclusion here.

Illumina also argues that, unlike ActiveVideo, Illumina has not licensed the '794 patent. Br. 28-29. That only digs Illumina's causal-nexus hole deeper, as it shows that the market does not use or particularly care about the '794 patent's claimed invention. Whatever harm Illumina claims to suffer is not traceable to Ariosa's supposed use of an invention that Illumina's licensees don't use.

[11] *See also* Brief for Cross-Appellant, *ActiveVideo*, 2012 WL 481415, at *51 (Fed. Cir. Jan. 26. 2012) (noting the "hardware, support, maintenance, and professional services" ActiveVideo provided its licensees).

Illumina argues that it did not license the '794 patent to maintain market exclusivity, Br. 15, 37-40, but the district court was well within its discretion in finding the contrary: "Illumina did not have an intention to retain market exclusivity" because "Illumina intended to license the '794 patent to Ariosa." Appx61. Illumina's counsel expressly represented at trial that it intended to license the '794 patent to Ariosa, telling the jury that Illumina brought suit only because Ariosa would not "***take a license*** to the intellectual property of Illumina, and ***pay for*** the intellectual property ***it uses***." *Id.* (citing Appx1128). This statement could only have referred to the '794 patent, as that was the only patent Illumina accused Ariosa of "using" at the time of trial. Illumina no doubt believed it advantageous to tell the jury it was a reasonable actor seeking only to license its patent to Ariosa, not to exclude Ariosa from the market. *See, e.g.*, Appx1417 ("if anyone wants to … take a license, we're happy to do that"). But, having claimed willingness at trial to "license everyone," Appx1481, Illumina cannot cry abuse of discretion when the district court held it to its word.

2. Illumina's arguments regarding Roche do not show an abuse of discretion.

To try to evade the district court's finding that Illumina does not compete against the actual accused test (Harmony V2) or the company that makes it (Ariosa), Illumina argues that it sells unspecified "platform products" (which do not practice the '794 patent) that it claims compete with other unspecified ***Roche***

products (which also do not practice the '794 patent). Br. 22-23. Illumina's attempt to collapse Ariosa and Roche is meritless and certainly does not show an abuse of discretion. As the district court noted when balancing hardships, Roche was dismissed pursuant to stipulation, and "the focus of the trial was on Ariosa"; accordingly, "the jury verdict refers only to Ariosa and does not mention Roche," such that "Ariosa is the relevant party." Appx61-62. When the court assessed the competition relevant to irreparable-injury analysis, it similarly looked to Ariosa alone. *See* Appx58 ("Unlike Illumina, *Ariosa* does not utilize a licensing model; instead *Ariosa* sells the Harmony V2 test directly."); Appx59 ("[T]he Court finds that only third party licensees directly compete with *Ariosa*.").

Illumina asks this Court to find as a factual matter that Roche has "essentially eliminated Ariosa," Br. 8, but its position is unsupported by the very evidence it cites, and it certainly does not show an abuse of discretion. The first cited document specifies that Harmony "was developed, and its performance characteristics determined *by Ariosa Diagnostics, Inc*.," and it refers to an unaccused product, "AcfS," as "the *Ariosa* cell-free DNA system." Appx10277. The second cited document, which provides a series of FAQs, is even clearer: it answers the question "How do I incorporate the Harmony Prenatal Test into my practice," by instructing the user to "[a]dminister a simple blood draw directly or through a participating laboratory and *send it to Ariosa Diagnostics* using the

specimen collection and transportation kit." Appx10279-10280. Nothing in these documents supports—much less compels—a finding that Roche "eliminated" Ariosa.

The remainder of Illumina's factual argument is just as faulty. Illumina's claim that Roche "convert[ed] Ariosa employees to Roche employees," Br. 8, rests on testimony of a single individual, who acknowledged that Ariosa still exists:

> Q. And you're an employee of Roche now?
>
> A. I am.
>
> Q. You introduced yourself as Ariosa. Does Ariosa still exist, to your knowledge?
>
> A. *Ariosa still does exist.*
>
> Q. But you're a Roche employee?
>
> A. I'm an employee of Roche, and Ariosa is wholly owned by Roche.

Appx2528.

Illumina ignores other evidence of Ariosa's continued corporate existence. The Clinical Laboratory Improvement Act of 1988 ("CLIA") requires laboratories to receive government certification before they "may solicit or accept materials derived from the human body for laboratory examination." 42 U.S.C. § 263a(b). Ariosa, not Roche, owns and operates the CLIA-certified laboratory where Harmony V2 is performed, and Ariosa is the only entity with the necessary government authorizations to perform the Harmony V2 test. Appx10277 ("Ariosa

Diagnostics, Inc." is "a CLIA-certified and CAP-accredited clinical laboratory in San Jose, CA"); *see also* Appx15351(¶2); Appx10587-10591(¶2). Roche is not CLIA-certified, cannot perform the Harmony V2 test, and therefore cannot infringe (and has not been found to infringe) Illumina's '794 patent. Appx15351(¶2); Appx10589(¶2).

3. Illumina's asserted competition against Roche involving non-infringing products does not show irreparable harm.

Even had it been appropriate to consider Roche's sale of non-infringing products, Illumina failed to show any cognizable irreparable harm due to such competition, establish a causal nexus between those non-infringing sales and the '794 patent's claimed invention, or overcome the district court's finding that any "harm resulting from competing against Roche" is "compensable by monetary damages." Appx60.

Illumina argues that Roche and Illumina supposedly offer products that compete for the same clinical-lab customers. Br. 24-26. But Illumina offers no support suggesting that such competition is in any way ***related to the '794 patent***. Indeed, it offers no support from the trial record at all. General references on appeal to "platform products" without identifying what the products are, the nature of the market, the other competitors in the market, and how the "products" supposedly relate to the '794 patent (which not even Illumina or its licensees use) cannot establish irreparable harm.

Illumina tries to fill that yawning gap with a declaration of Illumina executive Jeffrey Eidel. Br. 22-26, 31-33. But the district court was not required to credit Mr. Eidel's speculative post-trial assertions for at least three reasons. First, the declaration was shot through with unsupported claims about which Mr. Eidel lacks any personal knowledge. He speculated about supposed "sunk costs" and business plans of third parties for which he provided no foundation, Appx10023-10024(¶10); posited an unsupported "estimate" of the number of Harmony tests he thought Ariosa performed in 2017, Appx10023(¶9); and offered his wholly uninformed "belief" about Roche's supposed business plans and motivations, Appx10026(¶13). The district court was justified in disregarding such claims. *See Delaware Valley Floral Grp., Inc. v. Shaw Rose Nets, LLC*, 597 F.3d 1374, 1382 (Fed. Cir. 2010) (affirming district court's refusal to consider declaration "because it was not based on personal knowledge"); *cf. Phigenix, Inc. v. Immunogen, Inc.*, 845 F.3d 1168, 1174 (Fed. Cir. 2017) (rejecting declarations that, among other things, described the declarants' "belie[f]s" because they did not contain "supporting facts," were merely "conclusory," and "failed] to lay the requisite foundation to be 'admissible in evidence'" (quoting Fed. R. Civ. P. 56(c)(4))).

Second, the declaration was riddled with hearsay. Mr. Eidel made numerous assertions about what other companies told him Roche supposedly told them.

Appx10024-10026(¶¶11-12); *see Rotec Indus., Inc. v. Mitsubishi Corp.*, 215 F.3d 1246, 1256-1257 (Fed. Cir. 2000) (affirming rejection of declaration because it was "based upon hearsay and lacks the personal knowledge required to be admissible").

Third, Mr. Eidel's unsupported claims of competition were directly controverted by Nick Sterling, a Roche senior manager, in his own declaration. Appx10587-10591. Mr. Sterling explained—based on personal knowledge, unlike Mr. Eidel's declaration—that Roche does not compete directly with Illumina: the Harmony test has never been [redacted], Appx10589(¶4), and Mr. Eidel's assertions about supposed competition concerning [redacted], and [redacted] are erroneous, *see, e.g.*, Appx10590(¶7) ("[redacted] does not have a lab for processing NIPT tests. Further, [Roche] has not supplied free equipment (or any equipment) to [redacted] to set up a lab"); Appx10590(¶8) ("Ariosa is not in discussions with [redacted] or [redacted] to perform Harmony NIPT testing for them, and we do not view them as potential customers…."); Appx10590-10591(¶9) ("Ariosa has never sold the Harmony test to [redacted] or [redacted]. Neither company has a contract with Ariosa to purchase Harmony NIPT, and neither company has been set up as a customer account, which is necessary for Ariosa to accept samples and provide results.").

The district court was not compelled to credit Mr. Eidel's speculative hearsay over Mr. Sterling's first-hand knowledge, and Illumina has not shown that the court abused its discretion by declining to do so.

Finally, Illumina claims that it competes with a product called AcfS. Br. 34-35; Appx10589(¶3). But Illumina did not bring any claims relating to AcfS in the district court, and AcfS was not found infringing. To the contrary, Illumina admitted that "AcfS products are irrelevant to this case." Appx15161.

Accordingly, Illumina has shown no abuse of discretion in the district court's finding that it failed to prove irreparable harm and inadequacy of monetary damages.

C. The District Court Did Not Abuse Its Discretion In Finding That The Balance Of Hardships And Public Interest Do Not Support A Permanent Injunction

Because Illumina does not even try to establish a causal nexus, and the district court did not abuse its discretion in finding that Illumina failed to prove either irreparable injury or the inadequacy of monetary damages, this Court need not address the balance of hardships or public interest. But the district court did not abuse its discretion in considering those factors either.

Again, *ActiveVideo* is on point: even if Illumina might incur "hardship if it was not compensated[,] … there is no evidence that an injunction is necessary to avoid hardship" to Illumina. 694 F.3d at 1341. Any harm to Illumina can be

remedied monetarily, and its own delay in filing suit and seeking an injunction belie its contrary arguments. *See supra* pp. 62-72. Ariosa's business, by contrast, could "be decimated if a permanent injunction is issued," Appx62, in part due to the uncertainty caused by the amorphous nature of Illumina's infringement theory.

Illumina complains that the court erred by stating that an injunction would make Ariosa incur the cost of "switching ***from*** Illumina sequencers." Br. 43-44 (quoting Appx62). But this is a harmless typo. The evidence the court cited for this point—Ariosa's CEO explaining the extraordinary expense Ariosa incurred when it switched from Illumina's sequencing platform to the Affymetrix gene array platform, *see* Appx62 (citing Appx2314)—shows that the court knew that Ariosa switched away from Illumina's sequencing platform, and was likely acknowledging the expense Ariosa would have to incur if an injunction forced it to switch back again. In other words, it appears the court wrote "from" when it meant "to." A harmless error is not an abuse of discretion. *See Reebok Int'l Ltd. v. J. Baker, Inc.*, 32 F.3d 1552, 1559 (Fed. Cir. 1994).

Windsurfing International, Inc. v. AMF, Inc., 782 F.2d 995 (Fed. Cir. 1986), does not help Illumina. This Court has explained that "*Windsurfing* [cannot] be applied mechanically," and that the decision "does not overcome the equities of a case." *Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 897 F.2d 511, 515 (Fed. Cir. 1990). As one court recognized:

> Taken to its logical limits, that [*Windsurfing*] proposition would effectively preempt consideration of the 'balance of hardships' factor in any case in which infringement (or misappropriation) has been found. Recognizing that point, the Federal Circuit has qualified that broad language from *Windsurfing* …. The language from *Windsurfing* has come to stand for the more modest and unsurprising proposition that a party "should not be permitted to prevail on a theory that 'successful exploitation of infringing technology shields [that] party from injunctive relief …."

Bianco v. Globus Med., Inc., No. 2:12-CV-00147-WCB, 2014 WL 1049067, at *10 (E.D. Tex. Mar. 17, 2014) (quoting *Broadcom Corp. v. Qualcomm, Inc.*, 543 F.3d 683, 704 (Fed. Cir. 2008)); *accord Hynix Semiconductor Inc. v. Rambus Inc.*, 609 F. Supp. 2d 951, 970 (N.D. Cal. 2009) ("[W]here infringement is not willful, perhaps because of serious questions as to the patent's validity … , the potential destruction of an infringer's business should carry some weight in the balancing of harms under the four-factor test reaffirmed in *eBay*. To ignore the harm to the infringer because it 'cannot be heard to complain' runs contrary to *eBay*'s mandate to 'consider[ ] the balance of hardships between the plaintiff and defendant[.]'" (quoting *eBay*, 547 U.S. at 391)).

The court's evaluation of the public interest was also within its discretion. "If the general public interest in upholding patent rights alone was sufficient to mandate injunctive relief when none of the other three factors support injunctive relief, then we would be back to the general rule that a patentee should always receive an injunction against infringement." *ActiveVideo*, 964 F.3d at 1341.

Indeed, "an injunction may not serve the public interest" where, as here, "legal damages may well be sufficient to compensate for the infringement." *eBay*, 547 U.S. at 396-397 (Kennedy, J., concurring).

The court also rightly relied on the fact that Illumina did not practice the '794 patent. As the court explained, "the public interest will not be served by the issuance of a permanent injunction," because "it is inconsistent for plaintiffs to be arguing on the one hand that the … patent represents an important new invention and then argue on the other hand that it should make no difference if no one is allowed to actually use it." Appx63 (internal quotation marks omitted).

Illumina attempts to blame Ariosa for its decision to discontinue Golden Gate in 2015, Br. 45-46, but it offers no evidence for that baseless assertion. Illumina points to no evidence that its decision to discontinue Golden Gate in 2015 (three years after Ariosa launched Harmony) had any connection whatsoever to Ariosa and Harmony.[12] *See Creative Compounds, LLC v. Starmark Labs.*, 651 F.3d 1303, 1312 (Fed. Cir. 2011) ("[E]videntiary shortcomings are not overcome by … attorney argument[.]").

Because Illumina has not attempted to show a causal nexus and because the district court was within its discretion in finding that none of the *eBay* factors

[12] Illumina cites the deposition testimony of Ronald McGrath, Appx11370, but that testimony merely states that Illumina discontinued Golden Gate in 2015.

favors Illumina, the Court should affirm the district court's order denying a permanent injunction.

VI. THE DISTRICT COURT DID NOT ABUSE ITS DISCRETION IN ADDRESSING ILLUMINA'S REQUESTS FOR SUPPLEMENTAL DAMAGES AND INTEREST

Illumina next challenges the way the district court handled its requests for supplemental damages and interest, but those challenges are either premature or meritless. Illumina filed a single post-trial motion seeking: (1) additional damages based on Harmony V2 sales from January 1, 2017 (shortly before the close of fact discovery) to the jury verdict; (2) an accounting of Harmony V2 sales between the verdict and any injunction; and (3) prejudgment interest at the prime interest rate, compounded quarterly, "in an amount to be later determined."[13] Appx11565. The district court denied the first two requests, indicating that it would consider them after appeal. Appx64 (citing *Apple, Inc. v. Samsung Elecs. Co.*, 67 F. Supp. 3d 1100, 1118 (N.D. Cal. 2014), and describing it as "denying plaintiff's request that the Court calculate and award supplemental damages pending the resolution of appeals"). It also indicated that it would award prejudgment interest after appeal, but not at the prime rate, because Illumina had "not presented evidence suggesting it needed to borrow money because it was deprived of the damages award."

[13] Illumina also sought statutory post-judgment interest on the damages award, and the district court confirmed that it will award post-judgment interest after appeal. Appx229.

Appx228. Instead, the court agreed with Ariosa that the 52-week Treasury Bill rate would adequately compensate Illumina. *Id.*

Illumina now claims "confusion" regarding the court's order on the first two issues. Br. 46, 49. But there is no confusion—Illumina is free to renew its requests on any remand. This Court need not decide in the first instance whether Illumina is entitled to the supplemental damages it seeks, which it would implicitly have to do if it were to "instruct the district court to award supplemental damages" as Illumina demands. Br. 49.

The pre-verdict supplemental damages question is not as straightforward as Illumina suggests. Illumina contends that the jury verdict did not compensate it for a nearly 13-month period, but the record does not suggest that the jury verdict was that narrow. The verdict form said nothing about this date cutoff; it simply asked the jury "[w]hat damages has Illumina proven that it is more likely than not entitled to as a result of Ariosa's infringement … ?" Appx11557 (awarding $15,730,062 in response for the '794 patent); *see also* Appx11558 (awarding $10,998,185 in response for the '430 patent). Trial testimony showed that Ariosa sold Harmony V2 throughout 2017, but nothing in the jury instructions indicated that the jury should award damages only through the end of 2016. Appx2847; Appx2865-2872. Courts routinely deny motions to amend damages judgments where plaintiffs fail to make the damages period clear at trial and in the verdict

form. *See Apple, Inc. v. Samsung Elecs. Co.*, 926 F. Supp. 2d 1100, 1104 (N.D. Cal. 2013) ("While it is true that the jury did not hear evidence of sales [for a portion of the pre-verdict period,] it is also possible that the jury considered this fact in arriving at its ultimate award."); *TransPerfect Global, Inc. v. MotionPoint Corp.*, No. 10-cv-2590-CW, 2014 WL 6068384, at *3-5 (N.D. Cal. Nov. 13, 2014) (surveying cases). The district court, which heard the evidence and argument along with the jury, should decide in the first instance whether the existing judgment already compensates Illumina for sales between January 2017 and the verdict. *See Telcordia Techs., Inc. v. Cisco Sys., Inc.*, 612 F.3d 1365, 1378 (Fed. Cir. 2010) ("District courts have broad discretion to interpret an ambiguous verdict form, because district courts witness and participate directly in the jury trial process. The district court was in a position to assess whether the verdict figure represented past infringement as well as ongoing infringement.").

Illumina finally challenges the district court's decision to set prejudgment interest at the 52-week Treasury Bill rate, but district courts have "wide latitude in the selection of interest rates." *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 939 F.2d 1540, 1545 (Fed. Cir. 1991). Prejudgment interest awards at the Treasury Bill rate are well within the court's discretion. *See Laitram*, 115 F.3d at 955; *Datascope Corp. v. SMEC, Inc.*, 879 F.2d 820, 829 (Fed. Cir. 1989). Illumina articulates no reason why a higher rate is appropriate here; it cites only case law holding that a

district court ***may*** award interest at a higher rate. That in no way shows an abuse of discretion.

CONCLUSION

The liability judgment on the '794 and '430 patents should be reversed or, alternatively, vacated and remanded. The district court's orders denying a permanent injunction and declining to award pre-verdict supplemental damages and an accounting should be affirmed. If the judgment is not otherwise vacated, the district court's order awarding prejudgment interest at the 52-week Treasury Bill rate should be affirmed.

Respectfully submitted,

/s/ Mark C. Fleming

MARK C. FLEMING
TIMOTHY A. COOK
KATHERINE P. KIECKHAFER
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

THOMAS G. SAUNDERS
CHRISTOPHER ASTA
WILMER CUTLER PICKERING
HALE AND DORR LLP
1875 Pennsylvania Avenue NW
Washington, DC 20006
(202) 663-6000

ROBERT J. GUNTHER, JR.
CHRISTOPHER R. NOYES
OMAR A. KHAN
WILMER CUTLER PICKERING
HALE AND DORR LLP
7 World Trade Center
250 Greenwich Street
New York, NY 10007
(212) 230-8800

Attorneys for Defendants – Cross-Appellants Ariosa Diagnostics, Inc, and Roche Molecular Systems, Inc.

DAVID I. GINDLER
LISA S. GLASSER
ALAN J. HEINRICH
IRELL & MANELLA LLP
1800 Avenue of the Stars, Suite 900
Los Angeles, CA 90067
(310) 277-1010

Counsel for Defendant – Cross-Appellant Ariosa Diagnostics, Inc.

February 28, 2019

CERTIFICATE OF SERVICE

I hereby certify that, on this 28th day of February, 2019, I filed the foregoing Non-Confidential Brief for Defendants – Cross-Appellants Ariosa Diagnostics, Inc, and Roche Molecular Systems, Inc. with the Clerk of the United States Court of Appeals for the Federal Circuit via the CM/ECF system, which will send notice of such filing to all registered CM/ECF users.

/s/ Mark C. Fleming

MARK C. FLEMING
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

CERTIFICATE OF COMPLIANCE

Pursuant to Fed. R. App. P. 32(g), the undersigned hereby certifies that this brief complies with the type-volume limitation of Federal Circuit Rule 32(a).

1. Exclusive of the exempted portions of the brief, as provided in Fed. R. App. P. 32(f) and Fed. Cir. R. 32(b), the brief contains 16,497 words.

2. The brief has been prepared in proportionally spaced typeface using Microsoft Word 2010 in 14 point Times New Roman font. As permitted by Fed. R. App. P. 32(g), the undersigned has relied upon the word count feature of this word processing system in preparing this certificate.

/s/ Mark C. Fleming
MARK C. FLEMING
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

February 28, 2019