No. 19-____

IN THE

Supreme Court of the United States

ENZO LIFE SCIENCES, INC.,

Petitioner,

v.

ROCHE MOLECULAR SYSTEMS, INC., ROCHE DIAGNOSTICS CORPORATION, ROCHE DIAGNOSTICS OPERATIONS, INC., ROCHE NIMBLEGEN, INC., BECTON DICKINSON AND COMPANY, AKA Becton Dickson and Company, BECTON DICKINSON DIAGNOSTICS INC., AKA Becton Dickson Diagnostics, GENEOHM SCIENCES INC., ABBOTT LABORATORIES, ABBOTT MOLECULAR, INC.,

Respondents.

ON PETITION FOR WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT, NOS. 17-2498, -2499, -2545, -2546

PETITION FOR A WRIT OF CERTIORARI

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QUESTIONS PRESENTED

I. In light of a patent's presumption of validity under 35 U.S.C. § 282 and the concomitant clear and convincing standard for proving invalidity, may patent claims that cover a class be invalidated as non-enabled under 35 U.S.C. § 112 based on a finding of high unpredictability in the art despite an absence of any evidence of inoperability within the class?

II. In concluding that the patent claims that cover a class are invalid as non-enabled under 35 U.S.C. § 112 despite an absence of any evidence of inoperability within the class, did the United States Court of Appeals for the Federal Circuit ("Federal Circuit") erroneously shift the burden to the patent owner to prove the claims were enabled, and therefore valid, in violation of the presumption of validity under 35 U.S.C. § 282?

PARTIES TO THE PROCEEDING

All parties to the proceeding are identified in the caption.

RULE 29.6 STATEMENT

Petitioner Enzo Life Sciences, Inc. is a wholly owned subsidiary of Enzo Biochem, Inc., which is a publicly held company that owns 10 percent or more of Enzo Life Sciences, Inc.'s stock.

RELATED PROCEEDINGS

The following federal cases are directly related to this petition before this Court:

- *Enzo Life Sciences, Inc. v. Roche Molecular Systems, Inc., Roche Diagnostics Corporation, Roche Diagnostics Operations, Inc., Roche Nimblegen, Inc., Becton, Dickinson and Company, Becton Dickinson Diagnostics Inc., Geneohm Sciences Inc., Abbott Laboratories, Abbott Molecular, Inc.*, Nos. 2017-2498, 2017-2499, 2017-2545, 2017-2546, United States Court of Appeals for the Federal Circuit. Judgment entered June 20, 2019.
- *Enzo Life Sciences, Inc. v. Abbott Laboratories and Abbott Molecular, Inc.*, Nos. 12-cv-274, 13-cv-225, United States District Court for the District of Delaware. Judgment entered September 1, 2017.
- *Enzo Life Sciences, Inc. v. Roche Molecular Systems, Inc.; Roche Diagnostics Corporation; Roche Diagnostics Operations, Inc.; and Roche*

Nimblegen, Inc., No. 12-cv-106, United States District Court for the District of Delaware. Partial judgment entered on August 2, 2017.

- *Enzo Life Sciences, Inc. v. Becton, Dickinson and Company; Becton Dickinson Diagnostics Inc.; and Geneohm Sciences, Inc.*, No. 12-cv-275, United States District Court for the District of Delaware. Partial judgment entered on July 31, 2017.

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INTRODUCTION

Since at least 1916, this Court has recognized that a patent remains valid even if practicing the disclosed invention requires some degree of experimentation. An inventor may gain the monopoly granted by the patent laws without performing the impossible task of describing the precise embodiment that would be most commercially successful in each case. To invalidate a patent a challenger must do more than show that practicing the patent, as disclosed, requires experimentation; a challenger must show that practicing the patent requires undue experimentation.

This petition arises from the Federal Circuit's relaxation of the standard of proof required to show that a patent is non-enabled under 35 U.S.C. § 112. The patent statutes, this Court's precedent, and Federal Circuit precedent all unequivocally require a patent challenger to demonstrate non-enablement by clear and convincing evidence.

The Federal Circuit's precedent in this case, however, allows a challenger to invalidate a patent that claims a class with particular functionality without clear and convincing evidence of undue experimentation. A challenger need only show that the claimed class is large and that skilled artisans of the time doubted the functionality of the invention. A challenger need not proffer any evidence of inoperability within the class. Without such evidence, and relying instead only on mistaken disbelief in the invention, it is impossible to draw any distinction between permissible and undue experimentation

needed to practice an invention.

In applying such a lax standard, the Federal Circuit's precedential opinion contradicts a century of its own and this Court's precedent and contravenes the standard of proof for proving patent invalidity. For this reason, the Federal Circuit's decision is improper and warrants reversal.

OPINIONS BELOW

The district court's opinions finding U.S. Patent Nos. 6,992,180 (the "'180 patent") and 8,097,405 (the "'405 patent") not enabled are unreported but available at 2017 WL 2829625 and 2017 WL 3585618, respectively, and reprinted at App. 19a–43a and 45a–66a, respectively. The Federal Circuit affirmed the district court judgment, as reported at 928 F.3d 1340 (2019) and reprinted at App. 1a–18a, and denied rehearing in an order that is unreported but reprinted at App. 67a–69a.

JURISDICTION

The Federal Circuit rendered its decision on June 20, 2019, App. 1a, and on October 29, 2019, denied rehearing, App. 67a. On January 16, 2020, Chief Justice Roberts granted application 19A800, extending the time to file this petition to and including February 26, 2020. This Court has jurisdiction pursuant to 28 U.S.C. § 1254(1).

PERTINENT STATUTORY PROVISIONS

35 U.S.C. § 112 (2006) provides in relevant part:

> **Specification**
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same.

35 U.S.C. § 282 provides in relevant part:

> **Presumption of validity; defenses**
>
> **(a) In General.—**
>
> A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.

STATEMENT OF THE CASE

At issue in this case is the standard of proof necessary to establish a patent's invalidity under 35 U.S.C. § 112. Under this Court's precedent, invalidity of a patent claim must be established by clear-and-convincing evidence. In the present case, however, the Federal Circuit has allowed the Respondents to invalidate the claims of two patents based merely on mistaken notions of the art at the time of the invention—without any evidence that members of the class of nucleic acid probes claimed by the patents would fail to exhibit the intended functionality. In so doing, the Federal Circuit's precedential opinion has lowered the standard of proof to merely require evidence that skilled artisans doubted the invention.

I. Background

A. Nucleic Acid Hybridization

Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) are nucleic acids, which are comprised of linked chains of nucleotides. Each nucleotide comprises three parts: sugar, phosphate, and nitrogenous base. The conventional nitrogenous bases in DNA are adenine, guanine, cytosine, and thymine; in RNA, the conventional bases are the same with the substitution of uracil for thymine.

The nitrogenous bases of DNA and RNA bind through non-covalent interactions in specific pairings known as "Watson-Crick base pairs." Adenine pairs with—or is said to be complementary to—thymine or uracil; guanine pairs with, or is complementary to, cytosine. Two linked chains of nucleotides pair—or hybridize—if the arrangement of nucleotides in each

strand results in sufficient Watson-Crick pairing of the bases.

Nucleic acid hybridization enables scientists to detect certain DNA or RNA sequences of interest. Scientists can create a labeled oligonucleotide or polynucleotide—*i.e.*, a linked chain of nucleotides—that contains a sufficiently complementary sequence of bases to pair with, or hybridize to, the nucleic acid of interest. The label, such as a fluorescent molecule that emits a colored light, can be detected when the oligonucleotide or polynucleotide hybridizes to a DNA or RNA of interest, confirming the presence of the sequence of interest. A labeled oligonucleotide or polynucleotide that is both hybridizable and detectable is called a probe.

B. The State Of The Art Before June 1982

Prior to the 1982 priority date of the '180 and '405 patents, nucleic acid hybridization was, in many aspects, well understood. The structure of DNA and RNA, the hybridization of nucleic acids via Watson-Crick base pairing, and creating and using polynucleotide probes through radioactive labeling were well developed within the field. Radioactive labeling, however, involved replacing certain atoms in the nucleotide sequence with radioactive isotopes and, therefore, bore significant safety risks and costs, engendering a need for non-radioactive methods.

The construction and use of non-radioactive probes was a nascent field. In 1981, Dr. David Ward demonstrated that non-radioactive labels could be attached at specific base moieties (known as "Ward positions") to create probes. The prevailing—and

mistaken—perception in the art, however, was that attaching non-radioactive labels anywhere on a nucleic acid other than a Ward position would compromise the hybridizability or detectability of the intended probe.

Despite this misperception, skilled artisans of the time understood a great deal of the science underlying probes labeled non-radioactively at non-Ward positions. For example, skilled artisans understood how to construct a nucleic acid sufficiently complementary to a target sequence and how to detect various labels, such as detecting specific wavelengths of light to locate a fluorescent label. Skilled artisans also understood the chemistry—such as carbodiimide, periodate oxidation, and alkylation chemistries—to attach non-radioactive labels at non-Ward positions.

In other words, by June 1982, skilled artisans could have created a non-radioactively, non-Ward labeled probe and confirmed its functionality—if the prevailing perception against its functionality had not dissuaded them from so doing. The inventors of the '180 and '405 patents had the insight to see past that mistaken perception.

C. The Inventions Of The '180 And '405 Patents

Against the prevailing dogma of the field, scientists at Enzo conceived of making and using probes labeled at phosphate and sugar moieties and non-Ward positions of the base. The team conceived that even polynucleotides labeled non-radioactively at non-Ward positions can be sufficiently complementary to hybridize and function as detectable probes. That insight led to the patents.

The '180 and '405 patent specifications are, in relevant part, identical. App. 4a. They identify the structure of labeled nucleotides, as in "SIG-PM-SM-BASE" or "PM-SM-BASE-Sig," where SIG is a signaling moiety, PM is a phosphate moiety, SM is a sugar moiety, and BASE is a base moiety. The specifications further explain that the inventions "are useful for the tagging or labeling of DNA in a non-disruptive manner" and that a major utility of such inventive polynucleotides is as "DNA or RNA probes" that "contain one or more of the special Sig-containing nucleotides."

The asserted claims of the '180 patent describe phosphate-labeled probes—polynucleotides labeled at the phosphate molecule that hybridize with complementary nucleic acids and are detectable. The invention of the '180 patent is not directed to a specific polynucleotide nor to a specific label nor method nor location of labeling. The inventive insight of the '180 patent was that polynucleotides with labels attached to a phosphate would—contrary to mistaken notions in the art at the time—function as a probe, *i.e.*, hybridize and be detectable.

Claim 1, an independent claim from which asserted claims depend, is exemplary:

> 1. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide or modified nucleotide analog having the formula:
>
> Sig-PM-SM-BASE

> wherein PM is a phosphate moiety, SM is a furanosyl moiety and BASE is a base moiety comprising a pyrimidine, a pyrimidine analog, a purine, a purine analog, a deazapurine or a deazapurine analog wherein said analog can be attached to or coupled to or incorporated into DNA or RNA wherein said analog does not substantially interfere with double helix formation or nucleic acid hybridization, said PM being attached to SM, said BASE being attached to SM and said Sig being covalently attached to PM directly or through a non-nucleotidyl chemical linkage, and wherein said Sig comprises a non-polypeptide, non-nucleotidyl, non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polynucleotide or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, and wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component, a hapten or a combination of any of the foregoing.

The asserted claims of the '405 patent describe two types of hybridization: *in situ* and liquid phase hybridization. Like the invention of the '180 patent, the '405 patent is directed to methods of using polynucleotides that skilled artisans of the time possessed the technical skills to employ, yet never did

so before the critical insight claimed in the patent: that the claimed polynucleotides would work in the claimed hybridization processes.

The *in situ* hybridization claims are directed to using a probe labeled at non-Ward positions for *in situ* hybridization to identify and enumerate chromosomes. Independent claim 64 is exemplary. The liquid phase hybridization claims of the '405 patent describe using a non-radioactively labeled polynucleotide as a probe in a novel process involving hybridization and detection in a liquid medium. All asserted liquid phase hybridization claims depend from independent claim 189.

The specifications of both patents disclose numerous examples of labels, linkages, and chemistries to create the claimed probes and hybridization methods. For example, the specifications disclose labels comprising biotin, iminobiotin, fluorescein, rhodamine, dansyl, haptens, chromogenic compounds, iron oxide (magnetic), ferritin (electron dense), and cobalt (metal component). The specifications also provide examples of chemical linkages, such as poly-L-lysine, 1,6-diaminohexane, linkages comprising CH_2NH, and "olefin linkage arms."

The inventors also provided examples of applying known chemistry to create the claimed probes. Example V discloses creating phosphate-labeled polynucleotides for hybridization and detection by using carbodiimide chemistry to couple polybiotinylated poly-L-lysine or biotinyl-1,6-diaminohexane to phosphate moieties in polynucleotides—both at the ends of the molecule and

internally. The specifications further disclose attaching a label to numerous other non-Ward positions on base moieties—*e.g.*, the N3 position of a pyrimidine; the C2, N3, and N7 positions of a purine; and the N4 position of a cytosine using alkylation chemistry—and that such labels are detectable when the probes are hybridized. And the specifications disclose using vicinal oxidation by periodate to attach biotin to a polynucleotide, which results in the biotin being attached to a sugar analog at the 3' end of a polynucleotide.

Thus, although the specific choices of nucleic acid sequence, label, linker, and nucleotides to be labeled were considered implementation details of the inventions, the '180 and '405 patents disclosed examples of each.

II. Prior Proceedings

A. District Court

This petition arises from four separate suits filed in the United States District Court for the District of Delaware. Enzo filed separate complaints against Roche—*i.e.*, Roche Molecular Systems, Inc., Roche Diagnostics Corp., Roche Diagnostics Operations, Inc., and Roche Nimblegen, Inc.—and BD—*i.e.*, Becton Dickinson and Company, Becton Dickinson Diagnostics Inc., and Geneohm Sciences, Inc.—for infringement of the '180 patent on January 30 and March 6, 2012, respectively. And Enzo filed separate complaints against Abbott—*i.e.*, Abbott Laboratories and Abbott Molecular, Inc.—for infringement of the '180 and '405 patents on March 6, 2012, and February 11, 2013, respectively. The district court had jurisdiction over these actions pursuant to 28 U.S.C.

§§ 1331 and 1338(a).

On June 28, 2017, the district court ruled on two motions for summary judgment of invalidity of the '180 patent in the suits against Roche and BD: the court denied summary judgment regarding written description based on genuine disputes of material fact, but granted summary judgment that the asserted claims of the '180 patent are invalid as non-enabled under 35 U.S.C. § 112. App. 44a–66a.

Enzo agreed that the district court's enablement ruling on the '180 patent would be deemed to apply to the claims asserted against Abbott. On August 15, 2017, the district court denied a motion for summary judgment of invalidity of the '405 patent based on written description, but the district court granted summary judgment for Abbott that the asserted claims of the '405 patent are invalid as non-enabled under 35 U.S.C. § 112. App. 19a–43a.

The district court entered final judgment of invalidity in all suits.

B. Federal Circuit

Enzo timely appealed those judgments to the Federal Circuit, which consolidated those appeals. As phrased by the Federal Circuit, the relevant issue on appeal was "whether [the specification] enables the creation of a labeled probe that is both hybridizable and detectable upon hybridization." App. 10a. The circuit court assumed that "the specification teaches one of skill in the art how to create the broad range of labeled polynucleotides covered by the claims," but the court concluded that "the specification fails to teach one of skill in the art which combinations will produce

a polynucleotide that is hybridizable and detectable upon hybridization." *Id.*

Citing *Wyeth & Cordis Corp. v. Abbott Laboratories*, 720 F.3d 130 (Fed. Cir. 2013) and *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), the Federal Circuit concluded that one of skill in the art would need to engage in undue experimentation to identify probes that possessed the desired functionality—*i.e.*, were both hybridizable and detectable upon hybridization. App. 11a-18a. The keystone of the Federal Circuit decision was its finding of high unpredictability in the art—a finding based upon testimony that one skilled in the art would not have believed, at the time, that the probes taught by the patents would be hybridizable or detectable as probes. App. 15a–16a. That belief, however, was mistaken and, without any evidence of inoperable probes within the claimed class, that belief was immaterial to whether particular probes would hybridize or be detectable. That belief was inconclusive as to the amount of experimentation necessary to practice the claims.

The circuit court affirmed the district court's summary judgment that the '180 and '405 patents were not enabled, and the court denied Enzo's timely petition for a panel rehearing or rehearing *en banc*. App. 67a–69a.

REASONS FOR GRANTING THE PETITION

I. The Federal Circuit's Invalidation Of The Patents Without Evidence Of Inoperable Members Of The Claimed Classes Undermines The Statutory Burden And Standard Of Proof For Challenges To Patent Validity.

A. To Show That A Patent Is Invalid, A Challenger Must Meet A Clear And Convincing Standard Of Proof.

A patent, once issued by the USPTO, "shall be presumed valid," and "[t]he burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity." 35 U.S.C. § 282. "Thus, by its express terms, § 282 establishes a presumption of patent validity, and it provides that a challenger must overcome that presumption to prevail on an invalidity defense." *Microsoft Corp. v. i4i Ltd.*, 564 U.S. 91, 100 (2011).

Although the statute "includes no express articulation of the standard of proof" the party asserting invalidity must meet, both this Court and the Federal Circuit have concluded that § 282 establishes "'a heavy burden of persuasion,' requiring proof of the defense by clear and convincing evidence." *Id.* at 100, 102; *see also, e.g.*, *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1573 (Fed. Cir. 1984) ("Under 35 U.S.C. § 282, a patent is presumed valid, and the one attacking validity has the burden of proving invalidity by clear and convincing evidence."). In *Microsoft Corp. v. i4i Ltd.*, this Court rejected a challenge to the clear and convincing standard of proof required by § 282, noting that

> "[f]or nearly 30 years, the Federal Circuit has interpreted § 282 as we do today. During this period, Congress has often amended § 282, *see, e.g.*, Pub. L. 104–141, § 2, 109 Stat. 352; Pub. L. 98–417, § 203, 98 Stat. 1603; not once, so far as we . . . are aware, has it even considered a proposal to lower the standard of proof. . . . Indeed, Congress has left the Federal Circuit's interpretation of § 282 in place despite ongoing criticism, both from within the Federal Government and without."

564 U.S. at 113.

Since this Court's 2011 decision in *Microsoft Corp.*, the Federal Circuit has continued to apply the clear and convincing standard to invalidity challenges—including those brought under the enablement requirement of 35 U.S.C. § 112. *See, e.g.*, *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1303 (Fed. Cir. 2015) ("[P]atents are presumed to be valid and overcoming that presumption requires clear and convincing evidence.") (citing 35 U.S.C. § 282; *Microsoft Corp.*, 564 U.S. at 113); *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014) ("[P]atents are presumed to be valid and overcoming this presumption requires clear and convincing evidence.") (citing 35 U.S.C. § 282; *Microsoft Corp.*, 564 U.S. at 113). The Federal Circuit purported to apply a clear and convincing standard of proof to this case as well. *See* App. 9a.

B. The Federal Circuit Applies An "Undue Experimentation" Test To Patent Validity Challenges Under The Enablement Requirement Of § 112.

Section 112 of the patent statute describes what must be contained in a patent specification. Among other requirements, the specification must contain "a written description of the invention, and of the manner and process of making and using it . . . [such] as to enable any person skilled in the art to which it pertains, . . . to make and use the same." 35 U.S.C. § 112, ¶ 1 (2006). Thus, an applicant must describe the claimed invention adequately and provide sufficient description to enable the invention's production and use.

Under current Federal Circuit law, a party challenging a patent's validity under the enablement requirement of § 112 "must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.'" *Allergan, Inc.*, 796 F.3d at 1309 (quoting *In re Wands*, 858 F.2d 731, 736–37 (Fed. Cir. 1988)); *Alcon Research Ltd.*, 745 F.3d at 1188.

For at least fifty years, the Federal Circuit (and its predecessor) has applied some variant of this inquiry and, critically, has repeatedly emphasized that necessary experimentation does not invalidate a patent unless such experimentation sums to an undue amount. *See, e.g.*, *Application of Eltgroth*, 419 F.2d 918, 921 (C.C.P.A. 1970) ("[S]ome experimentation, provided it is not an undue amount, is permissible."). "[A] disclosure complies with the how-to-make

requirement of 35 U.S.C. § 112 even though 'some experimentation, provided it is not an undue amount' (and provided that it does not require ingenuity beyond that to be expected of one of ordinary skill in the art), is still required to adapt the invention to particular settings." *Fields v. Conover*, 443 F.2d 1386, 1390–91 (C.C.P.A. 1971) (internal citations omitted). "Assuming some experimentation were needed, a patent is not invalid because of a need for experimentation. A patent is invalid only when those skilled in the art are required to engage in *undue* experimentation to practice the invention." *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1557 (Fed. Cir. 1983). "That some experimentation is necessary does not preclude enablement; the amount of experimentation, however, must not be unduly extensive." *Atlas Powder Co.*, 750 F.2d at 1576.

In short, "[s]ome 'trial and error'" to practice claims does not invalidate a patent. *W.L. Gore & Assocs.*, 721 F.2d at 1557. The standard allows experimentation to encourage inventors to disclose their inventions; otherwise, to require a patent with claims that cover a class or combinations, or other groups with numerous embodiments, to elucidate every possible embodiment without imposing any experimentation on a practitioner would impose a prohibitive burden of disclosure on inventors and undermine the inventor's ability to claim the full scope of their invention. As the Federal Circuit's predecessor noted, "such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent

applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid 'literal' infringement of such claims by merely finding another analogous catalyst complex." *Application of Angstadt*, 537 F.2d 498, 502–03 (C.C.P.A. 1976).

This Court recognized the same considerations over a century ago in rejecting a challenge to a patent's validity on the argument that some testing would be required to practice the full scope of the claims:

> Equally untenable is the claim that the patent is invalid for the reason that the evidence shows that when different ores are treated preliminary tests must be made to determine the amount of oil and the extent of agitation necessary in order to obtain the best results. Such variation of treatment must be within the scope of the claims, and the certainty which the law requires in patents is not greater than is reasonable, having regard to their subject matter. The composition of ores varies infinitely, each one presenting its special problem, and it is obviously impossible to specify in a patent the precise treatment which would be most successful and economical in each case. The process is one for dealing with a large class of substances and the range of treatment within the terms of the claims, while leaving something to the skill of persons applying the invention, is clearly sufficiently definite to guide those skilled in

> the art to its successful application, as the evidence abundantly shows. This satisfies the law.

Minerals Separation v. Hyde, 242 U.S. 261, 270–71 (1916).[1] It is to this Court's reasoning in *Minerals Separation v. Hyde* that Federal Circuit decisions allowing some, but not undue, experimentation may be traced. *See, e.g.*, *In re Wands*, 858 F.2d at 737 n.19 (citing *Minerals Separation*, 242 U.S. at 270–71); *W.L. Gore & Assocs., Inc.*, 721 F.2d at 1557 (citing *Minerals Separation*, 242 U.S. at 270–71).

Thus, under this Court's and the Federal Circuit's longstanding precedent, an issued patent cannot be found invalid without a showing—by clear and convincing evidence—that any experimentation necessary to practice the invention constitutes an undue amount.

C. The Federal Circuit Applies An Eight-Factor Factual Test To Evaluate The Degree Of Experimentation.

As to determining what constitutes an "undue amount," since 1988, the Federal Circuit has applied a multi-factor test "in determining whether a disclosure would require undue experimentation." *In re Wands*, 858 F.2d at 737. "After the challenger has put forward evidence that some experimentation is needed to practice the patented claim, the factors set

[1] This Court's precedent prior to *Hyde* required patents to sufficiently disclose claimed inventions such that skilled artisans were not forced to experiment to practice the claims. *See, e.g.*, *Consol. Elec. Light Co. v. McKeesport Light Co.*, 159 U.S. 465, 475 (1895); *Howard v. Detroit Stove Works*, 150 U.S. 164, 167 (1893); *Bene v. Jeantet*, 129 U.S. 683, 685–86 (1889).

forth in *Wands* then provide the factual considerations that a court may consider when determining whether the amount of that experimentation is either 'undue' or sufficiently routine such that an ordinarily skilled artisan would reasonably be expected to carry it out." *Alcon Research Ltd.*, 745 F.3d at 1188.

The eight factors are "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d at 737. "Enablement is a question of law based on underlying facts." *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013).

D. In The Present Case, The Predictability Of The Art Controlled The Federal Circuit's Analysis Of The *Wands* Factors, Despite A Lack Of Evidence Of Inoperable Embodiments Within The Claimed Class.

In the present case, the Federal Circuit, reviewing the district court's summary judgment decisions *de novo*, App. 8a–9a, applied the *Wands* factors and found undue experimentation necessary to practice the full scope of the asserted claims of both patents. App. 10a–18a. The circuit panel did not, however, consider all of the *Wands* factors; its opinion, which

focused on the '180 patent,[2] discusses only four: the guidance and examples disclosed by the patent; the skill of those in the art; the breadth of the claims; and—the lynchpin of its analysis—the predictability of the art. *Id.*

It is plain from the refrains throughout the panel's opinion that finding the art unpredictable determined the panel's finding on the three additional *Wands* factors discussed. "Given the unpredictability of the art at the time," the circuit court found the guidance in the specification to be insufficient. App. 12a–13a. "[I]n light of the unpredictability in the art," the circuit court also found Example V to be an insufficient working example. App. 13a–15a. "Given such unpredictability in the art," the court further found the breadth of the claims "particularly concerning." App. 16a–17a. The predictability of the art controlled the decision. This matters.

The finding of unpredictability in the art hung on scant evidence. The '180 patent claims phosphate-labeled polynucleotides that function as probes—*i.e.*, are hybridizable and detectable. The evidence of unpredictability in the art cited by the Federal Circuit merely demonstrates a disbelief of the claimed invention as a whole. It does not demonstrate a

[2] The substantive analysis of the Federal Circuit's opinion focuses upon the '180 patent. *See* App. 9a–18a. Upon finding the asserted claims of the '180 patent non-enabled, the circuit court summarily extended its reasoning to the asserted claims of the '405 patent on the rational that "[t]hose claims are broader than the asserted claims of the '180 patent." App. at 18a. Accordingly, the discussions of the Federal Circuit's reasoning throughout this petition are also focused upon the '180 patent but warrant reversal of the Federal Circuit's decision as to both patents.

persistent inability of skilled artisans to distinguish between operable or inoperable embodiments within the claimed class. Indeed, it does not demonstrate anything whatsoever about the frequency—or even existence—of inoperable embodiments. Skilled artisans simply did not believe that phosphate-labeled polynucleotides would function as probes.

The Federal Circuit judgment rests on a few snippets of testimony of two Enzo experts and one inventor. Dr. Backman testified that "it was commonly thought" that labels at non-Ward positions "would interfere with or disrupt the hybridization process." App. 16a. This testimony does not indicate whether labels at non-Ward positions would, in fact, interfere with hybridization. The panel also cited co-inventor Dr. Rabbani's testimony that the inventors' more aggressive modification of the nucleic acid was considered "breaking the dogma." App. 15a–16a. And Dr. Sherman testified that skilled artisans "would have been dissuaded" from testing or using non-Ward–labeled polynucleotides and would have had to test a non-Ward–labeled probe—not "to predict whether it would actually hybridize" insofar as testing the functionality of each particular probe, but to "assure against the prevailing wisdom that [the invention] could work." App. 16a.

None of that testimony indicates how much experimentation would be necessary to change the mistaken perception that the invention would not function as claimed. That disbelief may have been resolved by a single, "aha!" experiment.

Nor does that testimony indicate whether skilled artisans—once dispelled of the mistaken belief that

phosphate-labeled polynucleotides would not hybridize and be detectable—would be able to distinguish between those polynucleotides that would or would not function as probes. Critically, the defendants below presented no evidence of inoperable members within the claimed class. Although the Federal Circuit notes that the claims may encompass "tens of thousands" of possible embodiments, App. 17a, nowhere does the circuit opinion address whether even one of those thousands would fail to function as claimed.

Without evidence of inoperable embodiments within the class of phosphate-labeled probes claimed by the '180 patent, it is as likely that all claimed phosphate-labeled polynucleotides would hybridize and be detectable as it is that only some would exhibit the intended functionality. Without evidence favoring either scenario, the line between routine and undue experimentation cannot be drawn.

Nonetheless, the Federal Circuit incorrectly or erroneously assumed that some embodiments would not function as desired and, therefore, found the asserted claims of both the '180 and '405 patents invalid: "[E]ven if Example V describes one working embodiment with the claimed functionality, undue experimentation would still be required with regard to the many other embodiments of the claims based on the number of possible embodiments and the unpredictability in the art." App. 17a–18a.

E. The Federal Circuit's Invalidation Of Patent Claims Without Evidence Of Inoperable Embodiments In The Claimed Class Warrants Review And Reversal.

The Federal Circuit's precedential decision in this case impermissibly lowers the clear and convincing standard of proof for challengers seeking to invalidate patents under 35 U.S.C. § 112 and impermissibly shifts the burden to the patent owner to prove patent claims are enabled, and therefore valid, in violation of the presumption of validity and assignment of the burden of proof under 35 U.S.C. § 282.

Prior to its decision in this case, the Federal Circuit found claims covering a broad class invalid under § 112 due to unpredictability of the art only upon a showing that some members of the broad class would not exhibit the claimed functionality. For example, in *Wyeth & Cordis Corp. v. Abbott Laboratories*, upon which the circuit panel in this case relied, the Federal Circuit found claims covering a class of compounds with immunosuppressive and antirestinosis effects invalid due to the large number of possible embodiments and unpredictability of the art. 720 F.3d at 1382–83, 1385–86. But, unlike the present case, the patent challenger had offered testimony from the patent owner that "even minor alterations to the . . . molecule could impact its immunosuppressive and antirestinotic properties." *Id.* at 1384–85. In other words, rather than evidence that skilled artisans did not believe in the claimed invention, the challenger showed that not all members of the class would exhibit the claimed functionality: "you really can't tell whether they work"

without "first synthesiz[ing] and then screen[ing] *each* compound." *Id.* at 1385. Because not all members functioned as claimed, that experimentation would necessarily continue for every member of the class.

By contrast, in *Alcon Research Ltd. v. Barr Laboratories, Inc.*, the Federal Circuit ***rejected*** a challenge to broad claims. The district court had held the claims invalid under *In re Wands* upon finding that the claims were too broad and the art too unpredictable. 745 F.3d at 1185. The evidence included testimony that "many 'variables' . . . including pH, buffer, buffer concentration, preservatives, chelating agents, and other excipients *may* affect the chemical stability" and testimony that "when 'you have a lot of variables on top of one another, the experimentation gets out of control quickly.'" *Id.* at 1189 (emphasis in original). The Federal Circuit, however, reversed because no evidence demonstrated whether "changing any of the 'variables' . . . would render Alcon's claimed invention inoperable." *Id.* Without such evidence, conclusions about the predictability of the art were unsubstantiated and "not sufficient" to show "any experimentation, let alone undue experimentation." *Id.* at 1189–90.

More recently, the Federal Circuit decided *Idenix Pharmaceuticals LLC v. Gilead Sciences, Inc.* on similar grounds as in *Wyeth*. 941 F.3d 1149 (Fed. Cir. 2019). The asserted patent claimed methods for treating the Hepatitis C virus ("HVC"). *Id.* at 1154–55. In evaluating the evidence under the *Wands* factors, the Federal Circuit found the number of compounds encompassed by the claims to number "at

least many, many thousands." *Id.* at 1157. And the court found the art highly unpredictable, both because the field was "in its infancy"—similar to the present case—and due to testimony that "not all 2' methyl up ribonucleosides will be effective to treat HCV"—evidence lacking in the present case—and "you don't know whether or not a nucleoside will have activity against HCV until you make and test it." *Id.* at 1159, 1161.

In sum, under these Federal Circuit decisions, a patent challenger must show that not all embodiments within a class exhibit the claimed functionality. Such evidence, combined with evidence of a broad class covered by the claims, could support a conclusion of undue experimentation under the *Wands* factors and, in turn, support a judgment of patent invalidity under § 112.

The precedential decision in the present case, however, lowers the evidentiary burden. Under the precedent set by this case, a patent challenger need only demonstrate that the claims cover a large class and that skilled artisans of the time doubted the functionality of the invention. Without evidence that some members of the claimed class would not exhibit the desired functionality, such doubt fails to meaningfully inform any analysis of experimentation necessary to practice a patent. The evidence does not demonstrate how much experimentation would be necessary to dispel such doubt. Under this precedent, any experimentation necessary to dispel doubt and confirm the functionality of patent claims may be presumed to be undue experimentation.

Such a result contravenes this Court's conclusion

in *Microsoft Corp. v. i4i Ltd.* that, under § 282, patent challengers must meet the "heavy burden of persuasion" of the "clear and convincing" standard of proof. 564 U.S. at 100. Allowing a lower standard of proof to comply—even within the subset of patents over which this precedential opinion will be relevant—undermines the *quid pro quo* of the patent system. The heightened standard of proof is an essential component of the patent "bargain" and the incentives for inventors to disclose their innovations to the public in exchange for patent protection. *See Bonito Boats, Inc. v. Thunder Craft Boats, Inc.,* 489 U.S. 141, 150–51 (1989).

Indeed, by allowing patent challengers to establish undue experimentation based merely on a mistaken dogma present in the art—without any evidence of substantial experimentation necessary to overcome that mistaken belief—the Federal Circuit's precedential decision in this case effectively and improperly shifts the burden onto the patentee to demonstrate that such disbelief could be dispelled through routine experimentation. The patentee would be tasked with proving the operability of every member of a claimed class, despite an absence of evidence that a skilled artisan would encounter any inoperable members of the claimed class, let alone such a significant number of inoperable members that the artisan would have had to engage in an unduly extensive trial-and-error process to practice the claims. Nearly 150 years of this Court's precedent make clear that a patent-holder like Enzo is not tasked with disproving doubts about the validity of its duly issued patent: "As early as 1874 [this Court] explained that the burden of proving [invalidity] 'rests

upon [the defendant], and every reasonable doubt should be resolved against him.'" *Microsoft Corp.*, 564 U.S. at 105 (quoting *Coffin v. Ogden*, 85 U.S. 120, 124 (1873)); *see also Minerals Separation v. Hyde*, 242 U.S. at 271 ("[I]t is obviously impossible to specify in a patent the precise treatment which would be most successful and economical in each case."). Shifting the burden, as the Federal Circuit has done in this precedential case, violates the plain language of § 282 that "[t]he burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity." 35 U.S.C. § 282.

CONCLUSION

For the foregoing reasons, the petition for a writ of certiorari should be granted.

Respectfully submitted.

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APPENDIX

APPENDIX A — OPINION OF THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT, FILED JUNE 20, 2019

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

ENZO LIFE SCIENCES, INC.,

Plaintiff-Appellant

v.

ROCHE MOLECULAR SYSTEMS, INC., ROCHE DIAGNOSTICS CORPORATION, ROCHE DIAGNOSTICS OPERATIONS, INC., ROCHE NIMBLEGEN, INC., BECTON, DICKINSON AND COMPANY, AKA BECTON DICKSON AND COMPANY, BECTON DICKINSON DIAGNOSTICS INC., AKA BECTON DICKSON DIAGNOSTICS, GENEOHM SCIENCES INC., ABBOTT LABORATORIES, ABBOTT MOLECULAR, INC.,

Defendants-Appellees

2017-2498, 2017-2499, 2017-2545, 2017-2546

Appeals from the United States District Court for the District of Delaware in Nos. 1:12-cv-00106-LPS, 1:12-cv-00274-LPS, 1:12-cv-00275-LPS, 1:13-cv-00225-LPS, Chief Judge Leonard P. Stark.

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*This opinion was originally filed under seal and has been unsealed in full.

Appendix A

June 20, 2019, Sealed Opinion Issued;
July 5, 2019*, Public Opinion Issued

Before PROST, Chief Judge, REYNA and WALLACH, Circuit Judges.

PROST, *Chief Judge*.

Enzo Life Sciences, Inc. ("Enzo") appeals the decision of the U.S. District Court for the District of Delaware granting summary judgment against Enzo and holding that the asserted claims are invalid for lack of enablement. We affirm as to non-enablement and do not reach the other issues presented on appeal.

I

Deoxyribonucleic acid ("DNA") and ribonucleic acid ("RNA") are nucleic acids. They are made of a series of building blocks, called nucleotides, linked together in a chain. A single nucleotide is made up of a sugar, a phosphate, and a nitrogenous base. DNA nucleotides have one of four nitrogenous bases: adenine (A); guanine (G); cytosine (C); and thymine (T). RNA has the same bases, except it uses uracil (U) instead of thymine (T).

A polynucleotide refers to multiple nucleotides linked together in a chain.[1] The nucleotides located at each end of a polynucleotide chain are referred to as terminal

1. An oligonucleotide is simply a shorter polynucleotide (e.g., just a few nucleotides in length).

nucleotides. All other nucleotides in a polynucleotide chain are referred to as internal nucleotides.

Two strands of polynucleotides can pair with each other, i.e., hybridize, through hydrogen bonding between the bases on each polynucleotide strand. The bases T and U pair with A, while G pairs with C. This is referred to as complementary base pairing or "Watson-Crick base pairing," and this pairing is how the now-familiar double helix shape is formed. Two polynucleotide strands will hybridize if the arrangement of nucleotides in each strand is such that enough bases can pair with each other. For example, whether two strands will hybridize depends in part on the number of complementary base pairs that exist between the two polynucleotides.

Hybridization techniques are used to detect the presence of certain nucleic acid sequences of interest, i.e., target sequences, such as genetic alterations. In such procedures, scientists use a hybridization "probe"—i.e., a labeled polynucleotide that is hybridizable and remains detectable after hybridization occurs—that is sufficiently complementary to the target sequence. The probe will hybridize with the target sequence if the target sequence is present, and the label on the probe then allows scientists to detect the hybridized probe.

Nucleic acid hybridization was well understood by June 1982, which is the claimed priority date of the patents at issue in this appeal. The prevailing method of labeling probes at that time was via radioactive labeling. Radioactive labeling generally involved replacing certain

atoms in the nucleotide sequence with corresponding radioactive isotopes.

Non-radioactive labeling was just developing at the time of the claimed inventions. In 1981, Dr. David Ward and others at Yale University successfully developed a nonradioactive probe by attaching a label to a polynucleotide via a chemical linker at a base position of a nucleotide. *See* J.A. 4129-33 (publication by Dr. Ward and others titled "Enzymatic synthesis of biotin-labeled polynucleotides: Novel nucleic acid affinity probes"). Dr. Ward demonstrated that attaching labels at certain positions of the nucleotide ("the Ward positions") would not disrupt the polynucleotide's ability to hybridize and be detected upon hybridization.

In December 1981, Enzo licensed the exclusive rights to the patent portfolio covering Dr. Ward's discovery. *See* J.A. 4258-75. Shortly thereafter, in June 1982, Enzo filed a patent application covering non-radioactive labeling at additional positions on a nucleotide. The two patents in this appeal issued from applications filed in 1995 that claim priority from this 1982 application.

Both patents in this appeal generally relate to the use of non-radioactively labeled polynucleotides in nucleic acid hybridization and detection applications. The patents share the same specification in relevant part. *See* J.A. 90 n.6.

A

U.S. Patent No. 6,992,180 ("the '180 patent") relates to non-radioactive labeling of polynucleotides where the

label is attached at the *phosphate* position of a nucleotide. The claims are not directed to any specific polynucleotide, nor do they focus on the chemistry or linker used to attach a label, the number of labels to attach to a polynucleotide, or where within the polynucleotide to attach those labels. Instead, the claims encompass *all* polynucleotides with labels attached to a phosphate, as long as the polynucleotide remains hybridizable and detectable upon hybridization. Claim 1 of the '180 patent is representative:

> 1. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising ***at least one modified nucleotide or modified nucleotide analog*** having the formula
>
> Sig-PM-SM-BASE
>
> wherein PM is a phosphate moiety, SM is a furanosyl moiety and BASE is a base moiety comprising a pyrimidine, a pyrimidine analog, a purine, a purine analog, a deazapurine or a deazapurine analog wherein said analog can be attached to or coupled to or incorporated into DNA or RNA ***wherein said analog does not substantially interfere with double helix formation or nucleic acid hybridization***, said PM being attached to SM, said BASE being attached to SM, and ***said Sig being covalently attached to PM*** directly or through a non-nucleotidyl chemical linkage, and wherein said Sig comprises a non-polypeptide, non-nucleotidyl, ***non-radioactive label***

> ***moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polynucleotide or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof***, and wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component, a hapten or a combination of any of the foregoing.

'180 patent claim 1 (emphases added).

"Sig" represents a signaling moiety (i.e., a label); PM represents a phosphate moiety; SM represents a sugar moiety; and BASE represents a base moiety.

B

The asserted claims of U.S. Patent No. 8,097,405 ("the '405 patent") fall into two categories: (1) *in situ* hybridization claims; and (2) liquid phase hybridization claims.

The *in situ* hybridization claims (claims 63, 64, 65, 95, 103, 128, and 144) describe a process that uses a probe non-radioactively labeled at any non-Ward position to identify chromosomes. *In situ* hybridization is where probes are hybridized to a target that is fixed, usually on a glass slide. Claim 64 is exemplary.

The liquid phase hybridization claims (claims 196 and 198) describe a process that uses a non-radioactively labeled probe to hybridize and detect a target sequence in a liquid medium, rather than on a glass slide. These claims cover using probes labeled non-radioactively at *any position* on the nucleotide, *including* the three Ward positions. The asserted liquid phase hybridization claims depend from claim 189.

C

This consolidated appeal involves four district court cases.[2] The '180 patent is at issue in all four cases, while the '405 patent is at issue only in the cases against Abbott.

In January 2012, Enzo filed suit against Roche Molecular Systems, Inc., Roche Diagnostics Corp., Roche Diagnostics Operations, Inc., and Roche Nimblegen, Inc. (collectively, "Roche") alleging infringement of the '180 patent. J.A. 1212-16 (Compl.) (Case No. 1:12-cv-106). In March 2012, Enzo filed separate suits against Becton, Dickinson and Co., Becton Dickinson Diagnostics Inc., and GeneOhm Sciences, Inc. (collectively, "BD"); and Abbott Laboratories and Abbott Molecular, Inc. (collectively, "Abbott") alleging infringement of the '180 patent. J.A. 2833-36 (Compl.) (Case No. 1:12-cv-275 against BD); J.A. 1964-67 (Compl.) (Case No. 1:12-cv-274 against Abbott). In February 2013, Enzo filed a second suit against Abbott alleging infringement of the '405 patent. J.A. 3973-77 (Compl.) (Case No. 1:13-cv-225).

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2. Appeal Nos. 17-2354 and 17-2355 were dismissed by agreement of the parties in those appeals. ECF No. 98.

In June 2017, in the cases against Roche and BD, the district court denied summary judgment with respect to written description, but granted summary judgment in favor of the defendants, holding that all asserted claims of the '180 patent were invalid as not enabled. *See* J.A. 59-77, 99-117. The district court entered partial final judgment of invalidity pursuant to Federal Rule of Civil Procedure 54(b) with respect to the claims of the '180 patent in the cases against BD and Roche. J.A. 14-18 (BD), 5-9 (Roche).

In the two Abbott cases, Enzo agreed that the district court's earlier enablement ruling as to the '180 patent would be deemed to apply to the claims of that patent asserted against Abbott. J.A. 23, 14950-51. As to the '405 patent, in August 2017, the district court denied Abbott's motion as to written description but granted summary judgment in favor of Abbott, holding the claims invalid for lack of enablement. J.A. 78-98. The district court entered final judgment of invalidity of all asserted claims of the '180 and '405 patents on September 1, 2017. J.A. 10-13, 23-26.

Enzo timely appealed each judgment. This court consolidated the appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

II

In reviewing a grant of summary judgment, we apply the law of the regional circuit. *Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 676 (Fed. Cir. 2015). The Third Circuit reviews a district court's grant of summary

judgment de novo. *Melrose, Inc. v. City of Pittsburgh*, 613 F.3d 380, 387 (3d Cir. 2010). "Summary judgment is appropriate only where, drawing all reasonable inferences in favor of the nonmoving party, there is no genuine issue as to any material fact and . . . the moving party is entitled to judgment as a matter of law." *Id.* (quoting *Ruehl v. Viacom, Inc.*, 500 F.3d 375, 380 n.6 (3d Cir. 2007)). "[U]nless there is sufficient evidence favoring the nonmoving party for a jury to return a verdict for that party," there is no need for a trial, and summary judgment is appropriate. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 249, 106 S. Ct. 2505, 91 L. Ed. 2d 202 (1986).

III

The enablement requirement asks whether "the specification teach[es] those in the art to make and use the invention without undue experimentation." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). To satisfy this requirement, "[t]he specification must contain sufficient disclosure to enable an ordinarily skilled artisan to make and use the entire scope of the claimed invention at the time of filing." *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1381 (Fed. Cir. 2012). "Enablement is a question of law based on underlying factual findings." *Id.* at 1380.

"To prove that a claim is invalid for lack of enablement, a challenger must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.'" *Alcon Research Ltd. v. Barr Labs.*,

Inc., 745 F.3d 1180, 1188 (Fed. Cir. 2014) (quoting *In re Wands*, 858 F.2d at 736-37).[3] In analyzing undue experimentation, we consider factors such as: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *In re Wands*, 858 F.2d at 737.

In our view, the issue in this appeal is not simply whether the specification enables labeling; the question is whether it enables creation of a labeled probe that is both hybridizable and detectable upon hybridization. Many of the alleged factual disputes raised by Enzo and many of the arguments raised by Appellees relate to the details of *creating* the labeled polynucleotide. For example, Roche and BD contend that the specification fails to sufficiently disclose internal phosphate labeling. But even if we assume that the specification teaches one of skill in the art how to create the broad range of labeled polynucleotides covered by the claims, as explained below, the specification still fails to teach one of skill in the art which combinations will produce a polynucleotide that is hybridizable and detectable upon hybridization, as required by the claim language.

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3. In this case, the parties agree that the relevant person of ordinary skill in the art is a scientist with a doctorate in chemistry, biochemistry, biophysics, molecular biology, or a similar field. Appellant's Br. 30 (noting the parties' agreement).

With this focus on the functionality required by the claims, we agree with Appellees that our decision in *Wyeth and Cordis Corp. v. Abbott Laboratories*, 720 F.3d 1380 (Fed. Cir. 2013), controls this case. In *Wyeth*, we affirmed a grant of summary judgment and held the asserted claims invalid for lack of enablement because it would have required undue experimentation to determine which compounds in the claimed class would have the required functionality. *Id.* at 1385-86. The claims in *Wyeth* were construed to require a compound having certain functionality (e.g., immunosuppressive effects). *Id.* at 1383. The claims covered a class of compounds that met those functional requirements. *Id.* at 1385. The patentee's witnesses testified that minor alterations to the molecule disclosed in the specification could impact the required functionality. *Id.* The patent challengers in that case thus argued that a person of ordinary skill in the art would need to screen each compound to determine what candidates would have the claimed functionality. *Id.* We agreed. *Id.* We noted the breadth of the claims, the limited guidance provided in the specification, the large number of possible candidates falling within the claimed genus (tens of thousands), and the fact that it would be necessary to first synthesize and then screen each of those candidates to determine whether it had the required functionality. *Id.* We further noted that one of the patentee's scientists had confirmed the unpredictability in the art by testifying that one would need to test each compound to understand whether it would have the desired functionality. *Id.* We thus concluded that there was no genuine dispute that practicing the full scope of the claims would require undue experimentation. *Id.*

Appendix A

The facts in this appeal largely mirror those in *Wyeth*. As in *Wyeth*, the asserted claims here require not just a particular structure, but a particular functionality (i.e., the labeled polynucleotides must be hybridizable and detectable upon hybridization). As explained below, the specification fails to teach one of skill in the art whether the many embodiments of the broad claims would exhibit that required functionality.

The scope of the claims is quite broad. Claim 1 of the '180 patent encompasses all phosphate-labeled polynucleotides that are hybridizable and detectable. The claim places almost no limitations on the structure of the claimed polynucleotide, other than the fact that the label is attached to the phosphate portion of the nucleotide. It does not restrict the chemistry used to attach the label, the chemical linker used, the number of labels within a probe, or the location of the labels on the probe (i.e., whether they are terminal or internal). As to the type of non-radioactive label used, the claim provides broad categories, such as any "electron dense component" or "magnetic component."

The specification's guidance as to how such variables would or would not impact the functionality of the claimed probes is sparse. For example, Enzo directs our attention to a sentence in the specification that states that "[a] particularly important and useful aspect of the special nucleotides of this invention is the use of such nucleotides in the preparation of DNA or RNA probes." '180 patent col. 54 ll. 18-20; *see also id.* col. 54 ll. 18-33 (describing generally how a probe works). Enzo's expert, Dr. Backman, explained that a skilled artisan would have understood this reference to using the polynucleotide as

a "probe" as meaning a polynucleotide that is capable of hybridizing and being detected upon hybridization. J.A. 5840-41 ¶ 57 (Backman Decl.). But at the time of the invention, the art was highly unpredictable. As Enzo's expert explained:

> At the time of the inventions of the '180 patent, it was commonly thought that the addition of a non-radioactive label to a nucleic acid sequence at positions other than a few known as 'non-disruptive positions' . . . would interfere with or disrupt the hybridization process, rendering the nucleotide ineffective for diagnostic purposes.

J.A. 4728 ¶ 74 (Backman Opening Report).

Given the unpredictability of the art at the time and the serious doubts held by those of skill in the art regarding whether labels could be attached to non-Ward positions without disrupting hybridization, merely stating that a labeled polynucleotide will work as a probe is not sufficient to enable one of skill in the art to know that it would indeed function as a probe—i.e., be hybridizable and detectable upon hybridization.

Enzo also presents Example V as an example of an internal phosphate-labeled polynucleotide that is hybridizable and detectable. Appellant's Br. 32-33. Example V states in full:

> Biotin and polybiotinylated poly-L-lysine were coupled to oligoribonucleotides using a

> carbodiimide coupling procedure described by Halbran and Parker, *J. Immunol.*, 96 373 (1966). As an example, DNA (1 ug/ml), 1 ml) in tris buffer pH 8.2, sheared with 0.1 N sodium hydroxide was denatured by boiling for 10 minutes and quick cooling in an ice bath. Biotinyl-1,6-diaminohexane amide (2 mg, 6 umol) or polybiotinylated poly-L-lysine (2 mg) and l-ethyl-3-diisopropylaminocarboimide HCl (10 mg, 64 umol) were added, and the pH readjusted to 8.2. After 24 hours at room temperature in the dark, the mixture was dialyzed against 10 mM tris buffered saline. DNA was precipitated ethanol.

'180 patent col. 33 ll. 33-44.

Appellees contend that Example V is not a working example. During prosecution, Enzo admitted that Example V is a "'paper', rather than [a] 'working example[].'" J.A. 4703 (stating in an amendment made during prosecution that "Applicants have determined that the examples set forth . . . [except certain examples other than Example V] are 'paper', rather than 'working examples'"); J.A. 6657 (same). Additionally, Enzo's expert testified that he was not aware of Enzo having ever tested a phosphate-labeled probe for hybridizability and detectability. J.A. 8547-48 p. 84 l. 5-p. 85 l. 16 (Backman deposition); J.A. 8551-52 p. 124 l. 10-p. 125 l. 11 (Backman deposition); *see also* J.A. 6441 p. 133 ll. 6-15 (Backman deposition) ("Q: . . . is there any bench experiment disclosed in the '180 patent in which the '180 inventors attempted to determine whether the

product of Example V, that is, the Sig moiety attached to an oligo- or polynucleotide could be detected after it had hybridized to a compl[e]mentary nucleic acid of interest? A. . . . no, they did not do an actual bench experiment to that effect."); *id.* p. 131 ll. 7-19. Regardless, even viewing Example V as a working example, Example V is insufficient to enable the breadth of the claims here, especially in light of the unpredictability in the art.[4]

The deficiencies in the description as to enablement cannot be cured in this case by looking to the knowledge of those skilled in the art at the time of the invention. Although "a specification need not disclose what is well known in the art," that rule is "not a substitute for a basic enabling disclosure." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). As we have said before, a patentee "cannot simply rely on the knowledge of a person of ordinary skill to serve as a substitute for the missing information in the specification." *ALZA Corp. v. Andrx Pharms., LLC*, 603 F.3d 935, 941 (Fed. Cir. 2010). And, more importantly, all parties acknowledge that serious doubts existed in the art as to whether the use of non-radioactive probes at non-Ward positions would be useful as probes. For example, an inventor of the '180 patent who is also Enzo's CEO explained that, at the time, it was thought "aggressive chemical modification of nucleic

4. Nothing stated herein would necessarily disallow proper constructive examples, which are intended to fulfill both written description and enablement requirements. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1577 (Fed. Cir. 1984) ("Use of prophetic examples, however, does not automatically make a patent non-enabling.").

acid would lead to destruction of his [sic] content." J.A. 6470 p. 1265 l. 5-p. 1266 l. 15 (Dr. Rabbani deposition); *see also* J.A. 6465 p. 31 l. 12-p. 33 l. 13 (Dr. Rabbani explaining how more aggressive modification of the nucleic acid was considered "breaking the dogma"). Enzo's expert, Dr. Backman, also pointed out the view of the art at the time, stating that "[a]t the time of the inventions of the '180 patent, it was commonly thought that the addition of a nonradioactive label to a nucleic acid sequence at positions other than [the Ward positions at the base] would interfere with or disrupt the hybridization process." J.A. 4728 ¶ 74 (Backman's Opening Report); J.A. 4184 ll. 10-24 (Dr. Rabbani deposition). Indeed, Enzo's expert explained that for one of skill in the art to be comfortable that a particular polynucleotide would work as a probe, "they would need to actually make the compound and test it in a hybridization experiment, which they would have been dissuaded from doing because of Ward." J.A. 8454 p. 150 ll. 8-15 (Sherman deposition) (discussing a polynucleotide labeled at the terminal phosphate and using carbodiimide chemistry and biotin); *see also* J.A. 8456 ll. 3-11 (Sherman deposition) ("Q: . . . But if they had been motivated to make this probe, non-Ward labeled probe, your view is that they would have to make it and test it in order to predict whether it would actually hybridize as of June 1982, right? A: Well, they would have to make it and assure against the prevailing wisdom that it could work."); J.A. 8454-55 p. 150 l. 17-p. 151 l. 18 (Sherman deposition).

Given such unpredictability in the art, and considering the testimony of Enzo's expert that each labeled polynucleotide would need to be tested to

determine whether it is hybridizable and detectable upon hybridization, the breadth of the claims here is particularly concerning in the enablement inquiry. *See In re Fisher*, 427 F.2d 833, 839, 57 C.C.P.A. 1099 (CCPA 1970) ("In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved."). Appellees contend that millions of embodiments of the claims exist based on the many variables involved in creating one of the claimed labeled polynucleotides. Enzo disputes this number, arguing it is improperly inflated because it counts every possible polynucleotide sequence that could exist as a separate embodiment. Even assuming Enzo is correct that the length and sequence of the polynucleotide do not give rise to separate embodiments, the other variables (such as the type of label, the type of linker used to attach the label, and the location of the labels within the polynucleotide) still result in an extremely large number of possible embodiments. Indeed, Enzo's expert explained that the number of possible polynucleotides that would fit within the limitations of claim 1 would be at least "tens of thousands." J.A. 6438 p. 120 l. 20-p. 121 l. 11 (Backman deposition).

In sum, even if Example V describes one working embodiment with the claimed functionality, undue experimentation would still be required with regard to the many other embodiments of the claims based on the number of possible embodiments and the unpredictability in the art. *See Genentech*, 108 F.3d at 1366 ("Patent protection is granted in return for an enabling disclosure

of an invention, not for vague intimations of general ideas that may or may not be workable.").

We conclude by briefly addressing the asserted claims of the '405 patent. Those claims are broader than the asserted claims of the '180 patent; rather than covering only *phosphate*-labeled polynucleotides, they also cover labeling at other locations on a nucleotide. Like the claims of the '180 patent, the asserted claims of the '405 patent require the claimed polynucleotides to be hybridizable and detectable upon hybridization. Because the specification does not enable the narrower scope of polynucleotides claimed in the '180 patent, it also cannot enable the broader scope of polynucleotides claimed in the '405 patent. As such, even though the asserted claims of the '405 patent pertain to certain processes, the claims are still not enabled for the reasons described with respect to the '180 patent.

In sum, viewing the evidence in the light most favorable to Enzo, we agree with the district court's grant of summary judgment.

IV

For the foregoing reasons, we affirm the district court's grant of summary judgment that the asserted claims of the '180 patent and the '405 patent are invalid for lack of enablement.

AFFIRMED

APPENDIX B — MEMORANDUM OPINION OF THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE, FILED AUGUST 15, 2017

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

C.A. No. 12-274-LPS

ENZO LIFE SCIENCES, INC.,

Plaintiff,

v.

ABBOTT LABORATORIES
AND ABBOTT MOLECULAR, INC.,

Defendants.

August 15, 2017, Decided;
August 15, 2017, Filed

MEMORANDUM OPINION

STARK, U.S. District Judge:

Pending before the Court are: (i) Defendants Abbott Laboratories and Abbott Molecular Inc.'s (collectively, "Abbott" or "Defendants") Motion for Summary Judgment of Invalidity of U.S. Patent No. 8,097,405 (the "'405 patent") for Failure to Comply with the Written Description

Requirement (D.I. 413 at 6-16), and (ii) Abbott's Motion for Summary Judgment of Invalidity of the '405 Patent for Nonenablement (D.I. 458). For the reasons set forth below, the Court will deny Abbott's motion with respect to written description and will grant Abbott's motion with respect to nonenablement.

I. BACKGROUND

Plaintiff Enzo Life Sciences, Inc. ("Enzo" or "Plaintiff") filed this patent infringement action against Abbott, alleging infringement of the '405 patent as well as U.S. Patent No. 6,992,180 ("the '180 patent").

The '405 patent, which is the subject of the pending motions, generally pertains to non-radioactive labeling and "relate[s] to nucleic acid[1] detection technology that relies upon the ability of nucleic acid (DNA or RNA) strands to hybridize — or bind together." (D.I. 430 at 7) (internal quotation marks omitted) While "the prevailing perception in the art [at the time of the invention] was that specific base moieties (the so-called 'Ward' positions) were the only possible positions for labeling," the '405 patent discloses that nucleotides "with non-radioactive labels attached to certain positions of a nucleotide — the phosphate moiety, sugar moiety, or non-Ward positions on the base moiety — could . . . be used as detectable nucleic acid probes." (D.I. 423 at 5-6 (emphasis omitted); *see also* D.I. 427 at A2130)

1. "Nucleic acids (DNA or RNA) are made up of 'nucleotide[s],' each of which 'typically consists of three parts: a base, a sugar, and a phosphate.'" (D.I. 430 at 7) (quoting D.I. 431-2 Ex. 16 at 9)

Appendix B

The '405 patent was issued on January 17, 2012 and claims priority to June 23, 1982. (*See* D.I. 423 at 6) The asserted claims of the '405 patent "fall into two categories: the *in situ* hybridization claims and the liquid phase claims." (D.I. 430 at 8) The *in situ* hybridization claims — claims 63, 64, 65, 94, 103, 128, and 144 — "recite processes for counting or identifying chromosomes through 'specific hybridization' to a 'locus or loci' of a chromosome, using probes labeled at specified positions." *(Id.)* The liquid phase claims — claims 196 and 198 — "specify permissible Sigs [detectable labels] and detection methods, respectively."[2] (*Id.* at 9)

Abbott moved for summary judgment of invalidity of the '405 patent for lack of written description on May 12,

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2. Claims 94, 103, 128, and 144 depend from independent claims 63, 64, and 65, among other claims. Claims 196 and 198 depend from independent claims 188 and 189, both of which recite the following limitations that are pertinent here:

> A process for detecting the presence of a nucleic acid of interest in a sample, comprising: providing or generating (i) a detectable non-radioactively labeled oligonucleotide or polynucleotide, . . . and (ii) a sample that may contain said nucleic acid of interest; forming in liquid phase, hybrids comprising said detectable non-radioactively labeled oligonucleotide or polynucleotide specifically hybridized with said nucleic acid of interest; and detecting hybrids non-radioactively to detect the presence of said nucleic acid of interest.

('405 patent col. 54 ll. 31-67, col. 55 ll. 1-10)

2017 (D.I. 410 at 6-16; D.I. 413 at 6-16),[3] and the parties completed briefing on July 7, 2017 (D.I. 413, 423, 448). On June 28, 2017, while summary judgment briefing was underway, the Court issued a Memorandum Opinion in a related case, *Enzo Life Sciences, Inc. v. Gen-Probe Inc.*, C.A. No. 12-104-LPS, granting a defense motion for summary judgment that the asserted claims of the '180 patent are invalid for nonenablement. (C.A. No. 12-104-LPS D.I. 284) ("Gen-Probe Opinion" or "GP Op.") On the same day, the Court issued an oral order in the instant case, requiring the parties to submit a joint status report discussing their respective position(s) on how the Court should proceed with respect to the summary judgment motions pending here. (D.I. 441)

In their July 10 status report, the parties agreed that the Gen-Probe Opinion invalidated all of the '180 patent claims asserted against Abbott and that all pending motions pertaining to the '180 patent were now moot. (*See* D.I. 450 at 4-5) The status report also included Abbott's request for leave to file a motion for summary judgment of invalidity of the '405 patent for nonenablement. (*See id.* at 6) In Abbott's view, good cause was established by the Gen-Probe Opinion, because "the '405 patent is related to and has essentially the same specification as the '180 patent." (*Id.* at 5)

The Court granted Abbott's request for leave. (D.I. 451) Thereafter, between July 18 and August 1, 2017, the

3. D.I. 413 is an amendment to Abbott's opening brief, D.I. 410, and was filed on May 12, 2017. When citing to Abbott's opening brief, this Memorandum Opinion refers to D.I. 413, not D.I. 410.

parties submitted additional letter briefing with respect to enablement. (D.I. 459, 461, 462) The Court heard oral argument on August 8, 2017. (*See* Transcript ("Tr."))

II. LEGAL STANDARDS

A. Summary Judgment

Under Rule 56(a) of the Federal Rules of Civil Procedure, "[t]he court shall grant summary judgment if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." The moving party bears the burden of demonstrating the absence of a genuine issue of material fact. *See Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 585-86, 106 S. Ct. 1348, 89 L. Ed. 2d 538 (1986). An assertion that a fact cannot be — or, alternatively, is — genuinely disputed must be supported either by "citing to particular parts of materials in the record, including depositions, documents, electronically stored information, affidavits or declarations, stipulations (including those made for purposes of the motion only), admissions, interrogatory answers, or other materials," or by "showing that the materials cited do not establish the absence or presence of a genuine dispute, or that an adverse party cannot produce admissible evidence to support the fact." Fed. R. Civ. P. 56(c)(1)(A) & (B). If the moving party has carried its burden, the nonmovant must then "come forward with specific facts showing that there is a genuine issue for trial." *Matsushita*, 475 U.S. at 587 (internal quotation marks omitted). The Court will "draw all reasonable inferences in favor of the nonmoving party,

and it may not make credibility determinations or weigh the evidence." *Reeves v. Sanderson Plumbing Prods., Inc.*, 530 U.S. 133, 150, 120 S. Ct. 2097, 147 L. Ed. 2d 105 (2000).

To defeat a motion for summary judgment, the nonmoving party must "do more than simply show that there is some metaphysical doubt as to the material facts." *Matsushita*, 475 U.S. at 586; *see also Podobnik v. U.S. Postal Serv.*, 409 F.3d 584, 594 (3d Cir. 2005) (stating party opposing summary judgment "must present more than just bare assertions, conclusory allegations or suspicions to show the existence of a genuine issue") (internal quotation marks omitted). The "mere existence of some alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment;" a factual dispute is genuine only where "the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247-48, 106 S. Ct. 2505, 91 L. Ed. 2d 202 (1986). "If the evidence is merely colorable, or is not significantly probative, summary judgment may be granted." *Id.* at 249-50 (internal citations omitted); *see also Celotex Corp. v. Catrett*, 477 U.S. 317, 322, 106 S. Ct. 2548, 91 L. Ed. 2d 265 (1986) (stating entry of summary judgment is mandated "against a party who fails to make a showing sufficient to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof at trial"). Thus, the "mere existence of a scintilla of evidence" in support of the nonmoving party's position is insufficient to defeat a motion for summary judgment; there must be "evidence on which the jury could reasonably find" for the nonmoving party. *Anderson*, 477 U.S. at 252.

B. Patent Validity Under 35 U.S.C. § 112

Paragraph 1 of 35 U.S.C. § 112[4] states in pertinent part:

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

The statute sets out separate requirements for written description and enablement. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010) (holding that written description and enablement requirements are separate). Nonetheless, these requirements "often rise and fall together." *Id.* at 1352.

1. Written Description

Whether a specification satisfies the written description requirement is a question of fact. *See GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 729 (Fed. Cir. 2014); *see also Alcon, Inc. v. Teva Pharms. USA, Inc.*, 664 F. Supp. 2d 443, 468 (D. Del. 2009) ("Satisfaction of the

4. The patent statute was amended in September 2011 by the America Invents Act ("AIA"). *See* Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284, 300-01 (2011). The pre-AIA version of § 112 applies in this case. The post-AIA version of this portion of the statute (§ 112(a)) is identical to the pre-AIA verison.

written description requirement is a fact-based inquiry, depending on 'the nature of the claimed invention and the knowledge of one skilled in the art at the time an invention is made and a patent application is filed.'") (quoting *Carnegie Mellon Univ. v. Hoffinann-La Roche Inc.*, 541 F.3d 1115, 1122 (Fed. Cir. 2008)). Despite being a question of fact, the issue of invalidity for lack of written description can be amenable to summary judgment. *See, e.g., Carnegie Mellon*, 541 F.3d at 1126-28 (affirming summary judgment of invalidity for lack of written description); *see also Helicos Biosciences Corp. v. Illumina, Inc.*, 888 F. Supp. 2d 519, 530-31 (D. Del. 2012) ("While compliance with the written description requirement is a question of fact, the issue is 'amenable to summary judgment in cases where no reasonable fact finder could return a verdict for the non-moving party.'") (quoting *Power Oasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1307 (Fed. Cir. 2008)).

To comply with the written description requirement, a patent's specification "must clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed." *Ariad*, 598 F.3d at 1351 (internal brackets and quotation marks omitted). "[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "[T]he hallmark of written description is disclosure. Thus, 'possession as shown in the disclosure' is a more complete formulation" of the written description requirement. *Id.* "[T]he test requires an objective inquiry into the four comers of the specification from the perspective of a person of

ordinary skill in the art." *Id.* "[T]he written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement." *Id.* at 1352. However, "a description that merely renders the invention obvious does not satisfy the requirement." *Id.*

2. Enablement

"Enablement is a question of law based on underlying factual findings." *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *Id.* (internal quotation marks omitted). "Enablement serves the dual function in the patent system of ensuring adequate disclosure of the claimed invention and of preventing claims broader than the disclosed invention." *Id.* at 1380-81. "Thus, a patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage." *Id.* at 1381. "The scope of the claims must be less than or equal to the scope of the enablement to ensure that 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).

"Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual

considerations." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). These factors include "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.* Although "a specification need not disclose what is well known in the art," "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). A patent "cannot simply rely on the knowledge of a person of ordinary skill to serve as a substitute for the missing information in the specification." *ALZA Corp. v. Andrx Pharms., LLC*, 603 F.3d 935, 941 (Fed. Cir. 2010).

III. DISCUSSION

A. Written Description

1. Written Description for Hybridization and Detection of Probes Labeled at Non-Ward Positions

Abbott seeks summary judgment that the '405 patent contains insufficient written description for non-Ward-labeled probes used for hybridization and detection. (*See* D.I. 413 at 9) In Abbott's view, the '405 patent specification "at best describes that probes . . . labeled at non-Ward positions could be made, would hybridize to complementary nucleic acids of interest, and would be

detected," but describes no such testing. (*Id.* at 11) Abbott further contends that "it would have been necessary to make and test [a non-Ward-labeled probe]" because, as of the priority date, "non-Ward labeling was believed to be disruptive and unsuitable" and the Ward patent[5] taught away from attaching a non-radioactive label to any position other than a Ward position. (*Id.* at 9, 11 (internal quotation marks omitted; alteration in original); *see also* D.I. 411-4 Ex. 21 at 63)

Enzo responds that the specification "provide[s] numerous specific examples of labeling probes at . . . non-Ward positions." (D.I. 423 at 14) Specifically, Enzo contends that Example V discloses phosphate labeling (*see* '405 patent col. 5 11. 40-53); Example XXXIII describes base labeling at non-Ward positions (*see* '405 patent col. 4 11. 16-24, col. 13 11. 23-53); and the specification describes labeling at the sugar moiety (*see* '405 patent col. 3 11. 45-53). (*See* D.I. 423 at 14-15) Enzo further contends that the specification discloses that "hybridization and detection are the plain purposes to which each of the above examples are directed." (*Id.* at 15; *see also* '405 patent col. 29 11. 34-38) According to Enzo, a person of ordinary skill in the art ("POSA") would have "understood each of the examples discussed above to be a complete embodiment of the claimed probes" (D.I. 423 at 15 n.10) (emphasis omitted) and would have also been aware of "a variety of additional chemistries" for labeling at non-Ward positions

5. The Ward patent discloses labeling at the Ward positions of the base moiety. The '405 patent incorporates by reference the specification of the Ward patent. (*See* D.I. 413 at 7; '405 patent col. 3 ll. 15-17)

(*id.* at 16). Thus, in Enzo's view, "[a]t a minimum, the presence of numerous specific examples of the inventions, and both sides' expert opinions regarding those examples, creates disputes of material fact," precluding summary judgment. (*Id.* at 17)

The Court agrees with Enzo that genuine disputes of material fact preclude summary judgment on whether the '405 patent contains sufficient written description for non-Ward-labeled probes used for hybridization and detection. (*See, e.g.*, D.I. 411-4 Ex. 21 at 63; D.I. 427 at A2331-55; '405 patent col. 29 11. 34-38) A reasonable factfinder could find, as Abbott contends, that no portion of the specification discloses non-Ward-labeled probes that could successfully hybridize or be detected. (*See* D.I. 413 at 9, 11) By contrast, a reasonable factfinder could also find, as Enzo asserts, that various parts of the specification disclose non-Ward-labeled polynucleotides that are useful for hybridization and detection. (*See* D.I. 423 at 14-16)

Accordingly, the Court will deny this portion of Abbott's motion for summary judgment.

2. Written Description for the *In Situ* Hybridization Claims

Abbott seeks summary judgment that the '405 patent lacks adequate written description for the claimed processes recited in the *in situ* hybridization claims — specifically, the processes for "determining whether the number of copies of a particular chromosome in a cell is normal or abnormal," "identifying a chromosome of

interest in a cell containing other chromosomes," and "identifying a plurality or all of the chromosomes of a cell of interest." (D.I. 413 at 15; *see also* '405 patent col. 34 ll. 62-64, col. 36 ll. 1-2, col. 37 ll. 7-8) Abbott contends that "[t]he only portions of the '405 patent [that] Enzo identifies as containing any disclosure of th[ose] processes are the title and abstract," both of which were added 20 years after the priority date. (D.I. 413 at 15-16) (emphasis omitted) Abbott further contends that Example 9 of the Ward patent cannot provide adequate written description for the *in situ* hybridization claims because that Example was prophetic and could not be practiced until 1996. (*See id.* at 16; D.I. 411-4 Ex. 27 at 31-34)

Enzo counters that Example 9 provides sufficient written description for the *in situ* hybridization claims because Abbott's own expert admitted that "[c]ertain embodiments [of Example 9] certainly could be practiced without question" in 1981. (D.I. 425 at A809; *see also* D.I. 423 at 19 n.10) Enzo further contends that "*in situ* hybridization with human and nonhuman chromosomes was well known by 1982" and, therefore, was available to a POSA as of the priority date. (D.I. 423 at 9)

The Court concludes that the record reveals a genuine dispute of material fact with respect to whether Example 9 could be practiced before the priority date. While Abbott contends that the relevant portions of Example 9 could not be practiced until approximately 14 years after the priority date (*see* D.I. 411-4 Ex. 27 at 31-34), Enzo cites record evidence that "[c]ertain embodiments . . . certainly could be practiced without question" before the priority

date (D.I. 425 at A809). A reasonable jury, viewing such evidence, could find for either Abbott or Enzo on this dispute.

Accordingly, the Court will deny this portion of Abbott's motion for summary judgment.

3. Written Description for the Liquid Phase Claims

Abbott requests that the Court grant summary judgment that the '405 patent lacks adequate written description for the liquid phase claims. In support, Abbott argues that the specification of the '405 patent "does not describe any oligo-or polynucleotide . . . used for specific hybridization in liquid phase to detect a nucleic acid of interest in a sample," as required by the liquid phase claims. (D.I. 413 at 13)

Enzo responds that the specification "explicitly describe[s]" the probes useful for "detection or hybridization in the liquid phase between the DNA sought to be detected and the DNA detecting probe." (D.I. 423 at 15 (internal quotation marks omitted); *see also* '405 patent col. 19 11. 63-65; col. 20 11. 1-10)) Enzo further asserts that "[h]ybridization in the liquid phase was known in the art" and, therefore, available to a POSA as of the priority date. (D.I. 423 at 9)

The record demonstrates genuine disputes of fact with respect to whether the '405 patent contains adequate written description for the liquid phase claims.

A reasonable jury could find for either side, based on the record evidence. (*See, e.g.*, D.I. 411-4 Ex. 28 at 163; '405 patent col. 19 ll. 63-65, col. 20 ll. 1-10)

Accordingly, the Court will deny this portion of Abbott's motion for summary judgment.

B. Enablement

Abbott seeks summary judgment that the asserted claims of the '405 patent are invalid for nonenablement on the basis of the Court's reasoning in the Gen-Probe Opinion. (*See* GP Op.) (granting summary judgment that asserted claims of '180 patent are invalid for nonenablement) In Abbott's view, the Court's reasoning in the Gen-Probe Opinion supports invalidating the '405 patent on enablement grounds because "[a] specification[6] that does not enable the narrower scope of polynucleotides claimed in the '180 patent cannot enable the broader scope of polynucleotides recited in the '405 patent." (D.I. 459 at 1; *see also* Tr. at 6-7, 17) Abbott further contends that the claims of the '405 patent, like those of the '180 patent, "do not limit the length or sequence of the polynucleotides and, thus, cover [the] use of at least the same millions (or more) phosphate-labeled polynucleotides that were not enabled in the '180 patent." (D.I. 459 at 1) (internal quotation marks omitted)

With respect to other polynucleotides labeled at non-Ward positions, Abbott asserts that Enzo "cannot identify

6. It is undisputed that the specifications of the '405 patent and '180 patent are identical in relevant part. (*See* Tr. at 6)

any Example [in the '405 patent's specification] that describes [the] chemistry for the vast majority of the other non-Ward labeling positions that the '405 patent seeks to capture," including the chemistry for all non-Ward base labeling positions. (*Id.* at 2) Abbott further argues that the methods disclosed in the asserted claims are not enabled because Enzo's expert, Dr. Sherman, admitted that "there [is] no data in the '405 patent showing that a probe labeled at a non-Ward position . . . would successfully hybridize." (D.I. 459-1 Ex. 6 at 193-94) According to Abbott, the lack of any such experiment being reported in the specification establishes that a POSA would have had to engage in "undue experimentation" in order to confirm that non-Ward-labeled probes work, given the "vast number of possible variants to the claimed invention." (D.I. 459 at 2) (internal quotation marks omitted)

Enzo responds that "the '405 [p]atent specification describes in great detail a wide variety of non-radioactively[-]labeled polynucleotides that can be used in the claimed methods, including probes labeled . . . at . . . non-Ward positions." (D.I. 461 at 3) (citing '405 patent col. 3 ll. 20-67, col. 4 ll. 1-24, col. 5 ll. 40-53, col. 12 ll. 48-67, col. 13 ll. 1-54, col. 22 ll. 56-67, cols. 23-24, col. 25 ll. 1-66 as disclosing probes labeled at sugar, phosphate, and certain base moieties) Enzo further contends that "skilled artisans were aware of additional chemistries for attaching labels at the other non-Ward positions" that are not explicitly disclosed in the specification. (*Id.*) In Enzo's view, the variations in "polynucleotide sequence, length, labels, linkers, and position of labeling" would not "render any application of the claimed methods inoperable" and,

therefore, a POSA could practice the invention "without engaging in undue (if any) experimentation." (*Id.* at 2-3) (emphasis omitted)

According to Enzo, the specific limitations recited in the asserted claims are adequately described in the specification or were already known in the art. With respect to the *in situ* hybridization claims in particular, Enzo notes that Abbott's expert admitted that "the practice of the claimed methods would have been enabled with over 50 different probe designs and that deploying those alleged probes in the claimed *in situ* hybridization processes would have yielded predictable results." (D.I. 461 at 5) (internal quotation marks and emphasis omitted) Enzo further contends that the specification's disclosure of probes labeled at non-Ward positions would also have enabled a POSA to practice the *in situ* hybridization claims. (*See id.* at 4; *see also id.* at 3)

At oral argument, Enzo's counsel further argued that the embodiments recited in the liquid phase claims were "irrelevant" because "[t]he novelty of liquid phase hybridization claims lies . . . in the inventive combination of performing liquid phase hybridization with a non-radioactive probe, whatever the structure of the probe, followed by detection." (Tr. at 24-25) As such, in Enzo's view, "the exact nature, structure, location of labeling, sequence, etc. of the non-radioactive[ly]-labeled probe is tangential to the invention" and, thus, cannot "render the invention [recited in the liquid phase claims] invalid for lack of enablement." (*See id.* at 26-27; *see also id.* at 31-32 (citing '405 patent col. 19 ll. 62-67, col. 20 ll. 2-10, 26-43 as

providing support for counsel's argument that "the novelty [of the invention] . . . lies in the use of [a] particular type of hybridization in the liquid phase . . . using non-radioactive labels, followed by detection of those labels"))

In its reply, Abbott argues that Enzo's opposition "repeat[s] arguments that the Court has already rejected" in the Gen-Probe Opinion. (D.I. 462 at 1) (emphasis omitted) Specifically, Abbott notes that even though the Court has already concluded that "no 'part[] of the specification indicates whether an internal phosphate-labeled polynucleotide maintain[s] hybridizability and detectability'" (*id.*) (quoting GP Op. at 15; second alteration in original), Enzo insists that the specification of the '405 patent "'completely' discloses polynucleotides 'labeled at the phosphate moiety'" (*id.*) (quoting D.I. 461 at 1). In Abbott's view, given the lack of disclosure in the specification, a POSA would be required to engage in undue experimentation to identify and determine whether the claimed phosphate-, sugar-, and base-labeled polynucleotides "might be useful in the claimed processes." (*Id.*) Abbott further contends that a POSA would have considered non-Ward-labeled probes to be inoperative, in view of the state of the art at the pertinent time. (*See id.* at 2)[7]

While Enzo contends that the specification discloses the limitations of the asserted claims, Abbott replies that

7. The Court agrees with Abbott that while inoperability can be a basis for nonenablement, it is not a prerequisite to a finding of nonenablement. (*See* D.I. 462 at 2) (citing *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013))

"[t]he '405 patent does not describe the claimed *in situ* hybridization processes at all" and also fails to "describe[] . . . the conditions (e.g. probe concentration, temperature, salt concentration, etc.) under which the [liquid-phase] process[es] can occur." (*Id.*) (citing testimony of Enzo's expert that liquid-phase hybridization "depends on such conditions") Abbott further asserts that the distinction between the '180 and '405 patent claims "makes no difference" to the Court's analysis: although "the '180 patent claims products [and] the '405 patent claims processes," the claimed processes of the '405 patent "depend on the hybridizability and detectability of the claimed probes." (*Id.*) "Without enabled probes," Abbott argues, "the processes [claimed in the '405 patent] cannot be enabled." (*Id.; see also id.* at 1 (arguing that certain probes are not enabled to maintain hybridizability and detectability); Tr. at 9 (counsel for Abbott asserting that "[t]he '405 patent claims are process claims, but this only makes them less enabled, not more"))

"To prove that a claim is invalid for lack of enablement, a challenger must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.'" *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014) (quoting *Wands*, 858 F.2d at 736-37). Having applied this standard to the record evidence, and taking that evidence in the light most favorable to Enzo as the non-moving party, the Court concludes that there is no genuine dispute of fact that the asserted claims of the '405 patent are nonenabled. A reasonable jury could not find for Enzo. Instead, the only

conclusion a reasonable jury could reach is that clear and convincing evidence proves the '405 patent is invalid for noneablement.

"[T]he specification must teach those of skill in the art how to make and how to use the invention ***as broadly as it is claimed***." *In re Goodman*, 11 F.3d 1046, 1050 (Fed. Cir. 1993) (internal quotation marks omitted; emphasis added). Here, even though the specifications of the '180 and '405 patents are identical in all relevant respects, the asserted claims of the '405 patent are even broader than the asserted claims of the '180 patent that the Court invalidated as nonenabled in the Gen-Probe Opinion. (*See* GP Op.; D.I. 449-1 Ex. 4 at 148-49) Given the breadth of the asserted claims and given the Court's conclusions in the Gen-Probe Opinion, the Court agrees with Abbott that "[a] specification that does not enable the narrower scope of polynucleotides claimed in the '180 patent cannot enable the broader scope of polynucleotides recited in the '405 patent." (D.I. 459 at 1)

Enzo argues that the specification of the '405 patent adequately describes "the broader scope of [non-Ward-labeled] polynucleotides recited in the '405 patent." (*Id.; see also* D.I. 461 at 3 (citing parts of specification that describe claimed polynucleotides)) But the Court already rejected this contention in the Gen-Probe Opinion, finding that no "part[] of the specification indicates whether an internal phosphate-labeled polynucleotide maintain[s] hybridizability and detectability." (GP Op. at 15 (internal quotation marks omitted; second alteration in original); *see also Amgen, Inc. v. Genetics Inst., Inc.*, 98 F.3d 1328,

1331 (Fed. Cir. 1996) ("[S]ince the '195 specification did not enable EPO having a specific activity of at least 160,000 IU/AU, enablement of that product could not be relitigated for the identical '837 specification.")) Similarly, with respect to the '405 patent in particular, no part of the specification discloses base labeling at ***all*** non-Ward positions, much less whether all non-Ward base-labeled probes would maintain hybridizability and detectability. (*See* D.I. 459 at 2; *see also Genentech*, 108 F.3d at 1366 ("Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.")). Given the claims' scope and the specification's limited disclosure, Abbott correctly asserts that a POSA "would have no choice but to make and test a vast number of possible variants to the claimed invention." (D.I. 459 at 2) (internal quotation marks omitted) Undue experimentation would be required, rendering the claims non-enabled.

That the asserted claims are process claims does nothing to reduce the amount of experimentation required. This is because each process in the asserted claims "depend[s] on the hybridizability and detectability of the claimed probes." (D.I. 462 at 2) But since the specification does not enable the claimed probes — no "part[] of the specification indicates whether an internal phosphate-labeled polynucleotide maintain[s] hybridizability and detectability," and no part of the specification discloses base labeling at ***all*** non-Ward positions (GP Op. at 15 (internal quotation marks omitted; second alteration in original); *see also* Tr. at 9 (counsel for Abbott stating that "[i]f the polynucleotide is not enabled at all, . . . the

processes using that polynucleotide cannot be enabled")) — the processes recited in the asserted claims of the '405 patent are also non-enabled.

The Court agrees with Abbott's comparison of the present situation to that confronted by the Federal Circuit in *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380 (Fed. Cir. 2013). In *Wyeth*, the Federal Circuit affirmed a grant of summary judgment based on nonenablement. *See id.* at 1386. Here, "(1) the claims are far broader than in *Wyeth*,[8] (2) the disclosures here are far less than in *Wyeth*,[9] (3) the relevant field is even more unpredictable than in *Wyeth*,[10] and (4) the trial-and-error process would have taken even longer than in *Wyeth*."[11] (GP Op. at 15)

8. As Abbott argues, "the millions (or more) of [non-Ward]-labeled polynucleotides with varying sequences and lengths covered by each asserted claim of the ['405] patent far exceed the tens of thousands of sirolimus analogs in *Wyeth* and the millions or more of phosphate-labeled polynucleotides covered by the '180 patent." (D.I. 459 at 3) (internal quotation marks omitted; alterations in original)

9. Abbott argues that, "[w]hile the specification in *Wyeth* disclosed at least one working example of the claimed invention (sirolimus) . . . , the ['405] patent discloses none." (D.I. 459 at 3) (internal quotation marks omitted; second alteration in original) Abbott further points out that, "unlike for the '180 patent, Enzo does not even argue that there is a prophetic example showing the labeling chemistry for each non-Ward position." (*Id.*)

10. Abbott notes that "Enzo's own expert explicitly admitted that, in 1982, there was 'no' 'ab[ility] to predict which chemical transformations and which label types and positions would be likely to work.'" (D.I. 459 at 3) (quoting D.I. 459-1 Ex. 6 at 148)

11. Abbott contends, "[t]he [trial-and-error] process would have been even longer for the '405 patent than for the '180 patent because the claimed scope of polynucleotides is greater." (D.I. 459 at 3)

(internal quotation marks omitted) It follows that here, as in *Wyeth*, there is no genuine dispute that the claims are invalid due to nonenablement.

This same conclusion is supported by consideration of the *Wands* factors. *See* 858 F.2d at 737. Based on the record, a reasonable factfinder could only find: "(1) the quantity of experimentation necessary to arrive at embodiments equal to the full scope of the claims is undue; (2) insufficient direction or guidance is presented in the patent to allow a POSA to avoid undue experimentation; (3) insufficient working examples are present;[12] (4) the invention arises in a field of art that was highly unpredictable at the time of the invention; (5) the prior art showed that the pertinent field was unpredictable; (6) even though the relative skill of those in the art was high, POSAs at the time did not have sufficient knowledge to fill in all that is missing from the patent; (7) the art was, as already noted, highly unpredictable; and (8) the claims are extremely broad." (GP Op. at 16) (internal quotation marks omitted)

Enzo opposes this conclusion, arguing that the liquid phase claims are enabled because "the exact nature, structure, location of labeling, sequence, etc. of the non-radioactive[ly] PA-labeled probe is tangential" to the invention recited in the liquid phase claims. (Tr. at 27) As stated above, however, the processes claimed in the liquid phase claims cannot be enabled if the polynucleotides

12. Abbott notes that the specification contains no working examples for any non-Ward position. (*See* D.I. 459 at 3)

are not enabled. (*See id.* at 9) Moreover, even if one such process with one particular embodiment were enabled, that would still fail to enable the full scope of the liquid phase claims. This is because a POSA at the pertinent time had "no" "ab[ility] to predict which chemical transformations and which label types and positions would be likely to work," according even to Enzo's expert, Dr. Sherman. (D.I. 459-1 Ex. 6 at 148) Thus, the presence of one enabling embodiment would be insufficient to enable the entire scope of the claim, as of the priority date. *See In re Goodman*, 11 F.3d at 1050 ("[T]he specification must teach those of skill in the art how to make and how to use the invention as broadly as it is claimed.").

Accordingly, the Court will grant Abbott's motion for summary judgment that the '405 patent is invalid for nonenablement.[13]

13. The Court is not persuaded by Enzo's citation to *Delaware Display Group LLC v. Vizio, Inc.*, 2017 U.S. Dist. LEXIS 28656, 2017 WL 784988, at *5 (D. Del. Mar. 1, 2017), in which Judge Andrews rejected a nonenablement challenge, reasoning that tangential, non-novel aspects of claims do not require enablement. Here, the record would not permit a reasonable factfinder to find that all of what is nonenabled in the liquid phase claims of the '405 patent is non-novel or tangential to the claimed invention. (*See* D.I. 427 at A2130 ("There was skepticism in the art about non-radioactively labeling a nucleic acid probe at a position other than the Ward positions before June 23, 1982."); *id.* at A2134 (stating that invention claimed in '405 patent "facilitates the use of non-radioactive labels in the hybridization [and] detection process"))

IV. CONCLUSION

For the foregoing reasons, the Court will deny Abbott's motion with respect to the written description requirement and will grant Abbott's motion with respect to nonenablement. An appropriate Order follows.

APPENDIX C — MEMORANDUM OPINION OF THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE, FILED JUNE 28, 2017

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

June 28, 2017, Decided;
June 28, 2017, Filed

C.A. No. 12-104-LPS

ENZO LIFE SCIENCES, INC.,

Plaintiff,

v.

GEN-PROBE INCORPORATED,

Defendant.

C.A. No. 12-106-LPS

ENZO LIFE SCIENCES, INC.,

Plaintiff,

v.

ROCHE MOLECULAR SYSTEMS, INC.; ROCHE DIAGNOSTICS CORPORATION; ROCHE DIAGNOSTICS OPERATIONS, INC.; AND ROCHE NIMBLEGEN, INC.,

Defendants.

Appendix C

C.A. No. 12-275-LPS

ENZO LIFE SCIENCES, INC.,

Plaintiff,

v.

BECTON, DICKINSON AND COMPANY;
BECTON DICKINSON DIAGNOSTICS INC.;
AND GENOHM SCIENCES, INC.,

Defendants.

C.A. No. 12-276-LPS

ENZO LIFE SCIENCES, INC.,

Plaintiff,

v.

HOLOGIC, INC.,

Defendant.

MEMORANDUM OPINION

June 28, 2017
Wilmington, Delaware

/s/ Leonard P. Stark

Appendix C

STARK, U.S. District Judge:

Pending before the Court are: (i) Defendants Gen-Probe Inc. ("Gen-Probe"); Roche Molecular Systems, Inc, Roche Diagnostics Corporation, Roche Diagnostics Operations, Inc., and Roche Nimblegen, Inc. (collectively, "Roche"); Becton, Dickinson and Company, Becton Dickinson Diagnostics Inc., and Geneohm Sciences, Inc. (collectively, "BD"); and Hologic, Inc.'s ("Hologic," and collectively, with Gen-Probe, Roche, and BD, "Defendants") Motion for Summary Judgment of Invalidity of U.S. Patent No. 6,992,180 (the '180 patent") for Failure to Comply with the Written Description Requirement (C.A. No. 12-104-LPS D.I. 227),[1] and (ii) Gen-Probe's and Hologic's Motion for Summary Judgment of Invalidity of the '180 Patent for Nonenablement (D.I. 221).

For the reasons set forth below, the Court will deny Defendants' motion with respect to the written description requirement and will grant Gen-Probe's and Hologic's motion with respect to nonenablement.

I. BACKGROUND

Plaintiff Enzo Life Sciences, Inc. ("Plaintiff" or "Enzo") filed patent infringement actions against Defendants, alleging infringement of the '180 patent as well as U.S. Patent No. 7,064,197 ("the '197 patent"). "The '180 patent generally relates to non-radioactive nucleic acid detection technology," while "[t]he '197 patent generally relates to nucleic acid hybridization technology involving non-porous solid supports." (C.A. No. 12-106-LPS D.I. 260 at 3)

1. Unless otherwise noted, all citations to the docket are to C.A. No. 12-104-LPS.

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The '180 patent, which is the subject of the pending motions, was issued on January 31, 2006 and claims priority to June 23, 1982. (D.I. 247 at 3) Defendants' motions focus on representative claim 1 of the '180 patent, which states, in relevant part:

> An oligo - or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo - or polynucleotide comprising at least one modified nucleotide or modified nucleotide analog having the formula
>
> Sig-PM-SM-BASE
>
> wherein . . . said Sig comprises a non-polypeptide, non-nucleotidyl, non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo-or polynucleotide or when said oligo - or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, and wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component, a hapten or a combination of any of the foregoing.

'180 patent col. 5911. 62-67, col. 6011. 1-21.[2]

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2. All asserted claims include, or depend from claims that include, the pertinent limitations in representative claim 1. (*See* D.I. 228 at 7 n.6)

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On December 15, 2016, Defendants moved for summary judgment of invalidity of the '180 patent for lack of written description (D.I. 227) and enablement (D.I. 221). Enzo filed its briefs in opposition to Defendants' motions on February 16, 2017 (D.I. 251 (written description), D.I. 247 (enablement)), and Defendants filed their reply briefs on March 20, 2017 (D.I. 269 (written description), D.I. 266 (enablement)). The Court heard oral argument on both motions on April 4, 2017. (*See* Transcript ("Tr."))[3]

II. LEGAL STANDARDS

A. Summary Judgment

Under Rule 56(a) of the Federal Rules of Civil Procedure, "[t]he court shall grant summary judgment if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." The moving party bears the burden of demonstrating the absence of a genuine issue of material fact. *See Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 585-86, 106 S. Ct. 1348, 89 L. Ed. 2d 538 (1986). An assertion that a fact cannot be — or, alternatively, is — genuinely disputed must be supported either by "citing to particular parts of materials in the record, including depositions, documents, electronically stored information, affidavits or declarations, stipulations (including those made for purposes of the motion only), admissions, interrogatory answers, or other materials,"

3. The Court heard argument at the same time on the parties' other motions, which will be resolved by separate opinion(s).

or by "showing that the materials cited do not establish the absence or presence of a genuine dispute, or that an adverse party cannot produce admissible evidence to support the fact." Fed. R. Civ. P. 56(c)(1)(A) & (B). If the moving party has carried its burden, the nonmovant must then "come forward with specific facts showing that there is a genuine issue for trial." *Matsushita*, 475 U.S. at 587 (internal quotation marks omitted). The Court will "draw all reasonable inferences in favor of the nonmoving party, and it may not make credibility determinations or weigh the evidence." *Reeves v. Sanderson Plumbing Prods., Inc.*, 530 U.S. 133, 150, 120 S. Ct. 2097, 147 L. Ed. 2d 105 (2000).

To defeat a motion for summary judgment, the nonmoving party must "do more than simply show that there is some metaphysical doubt as to the material facts." *Matsushita*, 475 U.S. at 586; *see also Podobnik v. U.S. Postal Serv.*, 409 F.3d 584, 594 (3d Cir. 2005) (stating party opposing summary judgment "must present more than just bare assertions, conclusory allegations or suspicions to show the existence of a genuine issue") (internal quotation marks omitted). The "mere existence of some alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment;" a factual dispute is genuine only where "the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247-48, 106 S. Ct. 2505, 91 L. Ed. 2d 202 (1986). "If the evidence is merely colorable, or is not significantly probative, summary judgment may be granted." *Id.* at 249-50 (internal citations omitted); *see also Celotex Corp. v. Catrett*, 477 U.S. 317, 322, 106 S. Ct.

2548, 91 L. Ed. 2d 265 (1986) (stating entry of summary judgment is mandated "against a party who fails to make a showing sufficient to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof at trial"). Thus, the "mere existence of a scintilla of evidence" in support of the nonmoving party's position is insufficient to defeat a motion for summary judgment; there must be "evidence on which the jury could reasonably find" for the nonmoving party. *Anderson*, 477 U.S. at 252.

B. Patent Validity Under 35 U.S.C. § 112

Paragraph 1 of 35 U.S.C. § 112[4] states in pertinent part:

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

The statute sets out separate requirements for written description and enablement. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010) (holding

4. The patent statute was amended in September 2011 by the America Invents Act ("AIA"). *See* Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284, 300-01 (2011). The pre-AIA version of § 112 applies in this case. The post-AIA version of this portion of the statute (§ 112(a)) is identical to the pre-AIA verison.

that written description and enablement requirements are separate). Nonetheless, these requirements "often rise and fall together." *Id.* at 1352.

1. Written Description

Whether a specification satisfies the written description requirement is a question of fact. *See GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 729 (Fed. Cir. 2014); *see also Alcon, Inc. v. Teva Pharms. USA, Inc.*, 664 F. Supp. 2d 443, 468 (D. Del. 2009) ("Satisfaction of the written description requirement is a fact-based inquiry, depending on 'the nature of the claimed invention and the knowledge of one skilled in the art at the time an invention is made and a patent application is filed.") (quoting *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1122 (Fed. Cir. 2008)). Despite being a question of fact, the issue of invalidity for lack of written description can be amenable to summary judgment. *See, e.g., Carnegie Mellon*, 541 F.3d at 1126-28 (affirming summary judgment of invalidity for lack of written description); *see also Helicos Biosciences Corp. v. Illumina, Inc.*, 888 F. Supp. 2d 519, 530-31 (D. Del. 2012) ("While compliance with the written description requirement is a question of fact, the issue is 'amenable to summary judgment in cases where no reasonable fact finder could return a verdict for the non-moving party.") (quoting *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1307 (Fed. Cir. 2008)).

To comply with the written description requirement, a patent's specification "must clearly allow persons of ordinary skill in the art to recognize that the inventor

invented what is claimed." *Ariad*, 598 F.3d at 1351 (internal brackets and quotation marks omitted). "[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "[T]he hallmark of written description is disclosure. Thus, 'possession as shown in the disclosure' is a more complete formulation" of the written description requirement. *Id.* "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Id.* "[T]he written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement." *Id.* at 1352. However, "a description that merely renders the invention obvious does not satisfy the requirement." *Id.*

2. Enablement

"Enablement is a question of law based on underlying factual findings." *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *Id.* (internal quotation marks omitted). "Enablement serves the dual function in the patent system of ensuring adequate disclosure of the claimed invention and of preventing claims broader than the disclosed invention." *Id.* at 1380-81. "Thus, a patentee chooses broad claim

language at the peril of losing any claim that cannot be enabled across its full scope of coverage." *Id.* at 1381. "The scope of the claims must be less than or equal to the scope of the enablement to ensure that 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).

"Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). These factors include "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.* Although "a specification need not disclose what is well known in the art," "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." *Genentech*, 108 F.3d at 1366. A patent "cannot simply rely on the knowledge of a person of ordinary skill to serve as a substitute for the missing information in the specification." *ALZA Corp. v. Andrx Pharms., LLC*, 603 F.3d 935, 941 (Fed. Cir. 2010).

Appendix C

III. DISCUSSION

A. Written Description

1. Written Description for the Functional Limitations of Claim 1

Defendants seek summary judgment that the '180 patent lacks adequate written description for the functional limitations of claim 1: "(1) the labeled polynucleotide is hybridized to a nucleic acid sequence of interest, and (2) . . . the label is detectable when the labeled polynucleotide is so hybridized." (D.I. 228 at 6) In Defendants' view, the specification does not adequately describe these limitations because Example V — which, according to Defendants, is "the only example anywhere in the intrinsic record that purports to describe the manufacture or synthesis of a phosphate labeled polynucleotide" — "undisputed[ly] . . . provides [no] description relating to hybridization or detectability upon hybridization." (*Id.* at 7) Defendants further contend that Enzo's technical expert admitted that the rest of the specification contains "no example, experiment, or data . . . to suggest that the product of Example V could hybridize or that its label is detectable when hybridized." (*Id.* at 11; *see also* D.I. 229-1 Ex. 5 at 131-32)

Enzo responds that "[a] person of ordinary skill ['POSA')] would have understood" the words "probe" and "hybridization probe" in the '180 patent specification "to (1) be capable of hybridizing and (2) be detectable upon hybridization." (D.I. 251 at 4) In Enzo's view, a

POSA would have also understood that "hybridization and detection is the plain purpose to which Example V is directed." (*Id.* at 9) In addition to Example V, Enzo argues that the specification's "explicit disclosures of phosphate attachment[s], labels, linkages, and exemplary chemistry for making the labeled nucleic acids . . . would have served as common structural features that allowed [POSAs] to recognize that the inventors possessed phosphate-labeled polynucleotides capable of hybridization and subsequent detection." (*Id.* at 10) At oral argument, Enzo additionally pointed to column 54 line 18 — a portion of the specification in addition to Example V — as supplying the method for probes that is "useful for hybridization and detection." (Tr. at 95; *see also* '180 patent col. 5411. 18-23 ("A particularly important and useful aspect of the special nucleotides of this invention is the use of such nucleotides in the preparation of DNA or RNA probes. Some probes would contain a nucleotide sequence substantially matching the DNA or RNA sequence of genetic material to be located and/or identified."))

The record demonstrates genuine disputes of material fact with respect to whether the '180 patent contains adequate written description to support the functional limitations of claim 1. A reasonable jury could find, as Defendants assert, that neither Example V nor the rest of the specification "provides any description relating to hybridization or detectability upon hybridization." (D.I. 228 at 7) Alternatively, a reasonable jury could instead find, as Enzo contends, that Example V and/or the rest of the specification would allow a POSA "to recognize that the inventors possessed phosphate-labeled polynucleotides

capable of hybridization and subsequent detection." (D.I. 251 at 10) Hence, the record contains sufficient evidence from which a reasonable jury could find for either Defendants or Enzo on written description with respect to claim 1's functional limitations. (*See, e.g.*, D.I. 228 at 11; D.I. 229-1 Ex. 5 at 131-32; D.I. 251 at 9-10; '180 patent col. 54 11. 18-23)

Accordingly, the Court must deny this portion of Defendants' motion for summary judgment.

2. Written Description for Making Internal Phosphate-Labeled Polynucleotides

Defendants argue that the Court should grant summary judgment that the specification of the '180 patent lacks adequate written description for "making . . . internal phosphate-labeled oligonucleotides" (D.I. 228 at 9) (emphasis omitted); that is, nucleic acids "having a label positioned internally rather than at the end of the nucleic acid" (*id.* at 1). In support of their motion, Defendants note "[i]t is undisputed that, if the synthesis scheme of Example V worked at all, it would only succeed in attaching a biotin to [a] terminal phosphate," not an internal phosphate. (*Id.* at 8) (emphasis omitted) Defendants further contend that, "[w]ith respect to Example V, Enzo told the Patent Office that Example V resulted in a terminal label — and not an internal label." (*Id.* at 13) In Defendants' view, the rest of the specification similarly lacks an "example, experiment, or model of any specific species of [an] internal phosphate-labeled polynucleotide." (*Id.*)

Enzo counters that "Example V of the '180 [p]atent specification discloses a method that attaches biotin at phosphate moieties, whether terminal or internal, by way of the amine groups on biotinylated poly-L-lysine and biotinyl-1,6-diaminohexane." (D.I. 251 at 15; *see also* D.I. 252 Ex. 9 at A307 (expert testimony)) Enzo further contends that a POSA "would have been aware of art showing how to incorporate moieties such as aryl, alkyl, and methyl phosphonates at internal positions that would have been understood as suitable chemistry for likewise incorporating a signaling moiety (and linkage) at internal positions." (D.I. 251 at 16; *see also* D.I. 252-1 Ex. 38 at A807-08, 813-14) Thus, in Enzo's view, "at a minimum, a dispute of material fact exists as to whether Example V discloses internal labeling" and whether a POSA would have been aware of "suitable chemistry for . . . incorporating a signaling moiety . . . at internal positions." (D.I. 251 at 16)

The Court agrees with Enzo that genuine disputes of material fact preclude summary judgment on this issue. The parties disagree as to whether Example V discloses a method that attaches biotin to internal phosphate moieties. (*Compare* D.I. 228 at 8, 13 *with* D.I. 251 at 15) The parties further disagree on whether a POSA would have been aware of suitable chemistry for internal labeling. (*Compare* D.I. 228 at 17 *with* D.I. 251 at 16) Both sides cite record evidence for their contentions, including expert opinions, such that a reasonable jury could find for either side: finding insufficient written description for internal phosphate labeling or, alternatively, adequate written description for internal phosphate labeling. Therefore,

the record demonstrates genuine disputes of material fact with respect to whether Example V discloses internal phosphate labeling and whether the chemistry for internal phosphate labeling was known in the art.

Accordingly, the Court must deny this portion of Defendants' motion for summary judgment.

B. Enablement

Defendants Gen-Probe and Hologic (collectively, hereinafter, "Hologic")[5] request that the Court grant summary judgment that the '180 patent is invalid for nonenablement because the specification lacks any "meaningful disclosure . . . on how to make and use the vast number of phosphate-labeled polynucleotides covered by the asserted claims." (D.I. 222 at 7) In support of its argument, Hologic points to the following statement in the '180 patent about a phosphate-modified nucleotide:

> The special nucleotides of this invention include a phosphoric acid P moiety (also designated hereinbelow as "PM"), a sugar or monosaccharide S moiety (also designated hereinbelow as "SM"), a base B moiety (also designated hereinbelow as "BASE"), a purine or a pyrimidine and a signal[]ing chemical moiety Sig covalently attached thereto, e[it]her to the P, S or B moiety.

(D.I. 222 at 7) (quoting '180 patent at col. 48 11. 60-66)

5. Gen-Probe became a part of Hologic in August 2012. (D.I. 222 at 1 n.1)

Hologic argues that "[t]he above disclosure does not indicate . . . any specific nucleotide, any specific label, any specific linker, any specific position of a phosphate-modified nucleotide within the polynucleotide, or any specific sequence of length of the polynucleotide." (D.I. 222 at 7) In Hologic's view, the rest of the specification similarly "provides no guidance on how to select, among numerous possibilities, the sequence and length of the polynucleotide, the location and number of internal phosphate labels, or the location and number of nucleotide analogs." (*Id.* at 12)

Hologic further argues that the unpredictability in the state of the art contributes to rendering the '180 patent invalid for nonenablement. (*See id.* at 8-9, 13-15) Hologic cites testimony of Enzo's expert, Dr. Backman, who opined that, as of the priority date, "it was commonly thought that . . . chemically labeling the phosphate group would interfere with hybridization." (*Id.* at 8) (internal quotation marks omitted) Hologic additionally cites the testimony of one of the '180 patent inventors, Dr. Stavrianopoulos, who acknowledged that internal labeling "required methods and principles of organic chemistry [that were] unknown" as of the priority date (*id.* at 14) and remain "difficult . . . even today" (*id.* at 10) (internal quotation marks omitted). In Hologic's view, making an internal-phosphate-polynucleotide would have also required "extensive experimentation" because, while "each asserted claim covers all polynucleotides up to 100,000 DNA nucleotides long" (*id.* at 6), yet "the maximum length for chemical synthesis of a polynucleotide in 1982 was 15 nucleotides" (*id.* at 9) (citing Dr. Stavrianopoulos's testimony).

Furthermore, according to Hologic, "[t]he synthesis of a polynucleotide longer than 100,000 nucleotides was not achieved until 2008." (*Id.*)

Enzo responds that "[t]he '180 [p]atent specification discloses signaling moieties, . . . provides several examples of chemical linkages, . . . discloses exemplary lengths of the claimed polynucleotides (*e.g.*, 5 to 500 nucleotides), . . . [a]nd . . . discloses that the label is detectable." (D.I. 247 at 7) In particular, Enzo contends that Example V "describes a method for attaching biotin at terminal and internal phosphate moieties of DNA polynucleotides." (*Id.* at 7-8) ("Example V . . . appl[ies] chemistry known in the art to create an embodiment of the invention") Enzo further contends that a POSA attempting to practice the invention "would not have considered every conceivable variation" or sequence of the claimed polynucleotide (*id.* at 12) (emphasis omitted), because "the specific sequence of the claimed polynucleotide is . . . no[t] germane to the claimed inventions" (*id.* at 1) (emphasis omitted). Finally, in Enzo's view, practicing the inventions would have required, "at most, routine [experimentation]," as the chemistry for internal labeling "w[as] known in the art" and a polynucleotide longer than 15 nucleotides "could be joined together through ligation." (*Id.* at 14-15; *see also id.* at 6 ("The inventions of the '180 [p]atent . . . pertain to nucleic acid hybridization and detection, which was a decades-old field by the time of the original application for the '180 [p]atent."))

In its reply, Hologic argues that "Enzo's contention that . . . claim scope is 'irrelevant' . . . turns the enablement

requirement on its head," as "[t]he law makes clear that a specification must enable the full scope of the claimed invention." (D.I. 266 at 4) (emphasis omitted) Hologic notes that "the claims are not limited to the preferred embodiments" — but, even if they were, "[n]othing in the [specification] teaches one how to select the length and sequence of a polynucleotide within the preferred 5 to 500 nucleotides or how to decide where to place the 1 to 100 phosphate-labeled nucleotides within the polynucleotide of 5-to-500 nucleotides long." (*Id.* at 6-7) In Hologic's view, the specification also "fails to describe" other aspects of the invention — for example, a "phosphate-labeled polynucleotide[] that maintain[s] hybridizability and detectability." (*Id.* at 5) Hologic further argues that Example V "does not describe any actual phosphate labeling" (*id.* at 1), does not disclose "the sequence or the length of the precipitated DNA" (*id.* at 2), and does not "indicat[e] whether the reaction is complete or successful" (*id.*).

While Enzo asserts that "the missing information could be found within the knowledge of a skilled artisan," Hologic replies that "the specification . . . must supply the novel aspects of an invention in order to constitute adequate enablement." (*Id.* at 5) (internal quotation marks omitted) Moreover, even taking into account what a POSA knew at the pertinent time, that still "fails to show any actual example of internal phosphate labeling by any method prior to June 1982." (*Id.* at 3) (discussing Dr. Backman's testimony; emphasis omitted) Finally, Hologic disputes Enzo's assertion that the inventions of the '180 patent pertain to a "decades-old field." (D.I. 247 at 6) In

Hologic's view, "the field of the claimed invention . . . is the phosphate labeling of a polynucleotide," which was "new" and "highly unpredictable" as of the priority date. (D.I. 266 at 6) (citing testimony of Dr. Backman, Enzo's expert, that "[t]here was ignorance in the art about non-radioactively labeling a nucleic acid probe . . . before [the priority date]") (internal emphasis and quotation marks omitted; first alteration in original)

"To prove that a claim is invalid for lack of enablement, a challenger must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.'" *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014) (quoting *Wands*, 858 F.2d at 736-37). The Court finds that there is no genuine dispute of fact that the '180 patent specification lacks enablement. A reasonable jury simply could not find for Enzo. Instead, the only conclusion a reasonable jury could reach is that clear and convincing evidence proves the '180 patent is invalid for noneablement.

"[T]he specification must teach those of skill in the art how to make and how to use the invention ***as broadly as it is claimed***." *In re Goodman*, 11 F.3d 1046, 1050 (Fed. Cir. 1993) (internal quotation marks omitted; emphasis added). Here, the claims are extremely broad. Even limiting claim scope to the preferred embodiments (for argument's sake), Hologic correctly points out that the specification does not teach "one how to select the length and sequence of a polynucleotide within the preferred 5 to 500 nucleotides or how to decide where to place the 1 to 100 phosphate-labeled nucleotides within the polynucleotide of

5-to-500 nucleotides long." (D.I. 266 at 7) Moreover, even if the Court accepts Enzo's contentions that Example V discloses internal labeling and that "[t]he inventions of the '180 patent . . . pertain to . . . hybridization and detection" (D.I. 247 at 6), neither Example V nor other parts of the specification indicates whether an internal phosphate-labeled polynucleotide "maintain[s] hybridizability and detectability" (D.I. 266 at 5; *see also generally Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997) ("Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.")) As such, again as Hologic explains, a POSA "would have no choice but to make and test a vast number of possible variants to the claimed invention." (D.I. 266 at 7) That is, undue experimentation would be required, rendering the claims non-enabled.

The Court agrees with Hologic's comparison of the present situation to that confronted by the Federal Circuit in *Wyeth v. Abbott Laboratories*, 720 F.3d 1380 (Fed. Cir. 2013). In *Wyeth*, the Federal Circuit affirmed a grant of summary judgment based on nonenablement. *See id.* at 1386. Here, "(1) the claims are far broader than in *Wyeth*,[6] (2) the disclosures here are far less than in *Wyeth*,[7] (3) the

6. As Hologic argues, the "millions (or more) of phosphate-labeled polynucleotides with varying sequences and lengths covered by each asserted claim of the '180 patent far exceed the tens of thousands of sirolimus analogs in *Wyeth*." (D.I. 222 at 11)

7. As Hologic argues, "[w]hile the specification in *Wyeth* disclosed at least one working example of the claimed invention (sirolimus), the '180 patent discloses none." (D.I. 222 at 12)

relevant field is even more unpredictable than in *Wyeth*, and (4) the trial-and-error process would have taken even longer than in *Wyeth*." (D.I. 266 at 4) It follows that, here, as in *Wyeth*, there is no genuine dispute that the claims are invalid due to nonenablement.

This same conclusion is supported by consideration of the *Wands* factors. *See* 858 F.2d at 737. Based on the record, a reasonable factfinder could only find: (1) the quantity of experimentation necessary to arrive at embodiments equal to the full scope of the claims is undue; (2) insufficient direction or guidance is presented in the patent to allow a POSA to avoid undue experimentation; (3) insufficient working examples are present;[8] (4) the invention arises in a field of art that was highly unpredictable at the time of the invention; (5) the prior art showed that the pertinent field was unpredictable; (6) even though the relative skill of those in the art was high, POSAs at the time did not have sufficient knowledge to "fill in" all that is missing from the patent; (7) the art was, as already noted, highly unpredictable; and (8) the claims are extremely broad. (*See* D.I. 223-1 Ex. 1 ¶¶ 503-33)

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8. Enzo admitted during prosecution of the '180 patent that Example V is a "'paper,' rather than 'working example[] . . . .'" (D.I. 223-3 Ex. 17 at ENZO-0096256) In this litigation, Enzo attempts to create a dispute of fact by pointing to testimony that one inventor has some recollection of Example V being performed "around '82, I don't remember that now." (D.I. 250 at A294) Even assuming a reasonable finder of fact could conclude, on this record, that some version of Example V was carried out by the inventors, the overall record remains one on which a reasonable finder of fact could only find that the claims are not enabled.

Enzo opposes this conclusion, arguing that "chemistries . . . known in the art at the relevant time . . . could have been used to create a polynucleotide" that meets claim 1's limitations. (D.I. 247 at 14) Enzo's argument, however, "ignore[s] the essence of the enablement requirement." *Genentech*, 108 F.3d at 1366. "It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." *Id.* "[W]hen there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required." *Id.* Thus, Enzo's references as to what "wa[s] known in the art" (D.I. 247 at 14) are unavailing; "a failure 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," *Genentech*, 108 F.3d at 1366.[9]

Accordingly, the Court will grant Hologic's motion for summary judgment that the '180 patent is invalid for nonenablement.[10]

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9. Additionally, even if the Court were to consider Enzo's assertions as to the state of the art at the priority date, the record indisputably establishes that "there was ***ignorance*** in the art about non-radioactively labeling a nucleic acid probe (including non-radioactively labeling any oligo - or polynucleotide in a probe) at a phosphate moiety before June 23, 1982." (D.I. 267-1 Ex. 30 at 20) (emphasis added) Enzo's assertions, therefore, do not conclusively establish that the relevant chemistries were "well known in the art" at the time the '180 patent was filed. *Genentech*, 108 F.3d at 1366.

10. The Court recognizes that, during prosecution, Enzo overcame a nonenablement rejection. (*See* D.I. 247 at 3-4) (citing

IV. CONCLUSION

For the foregoing reasons, the Court will deny Defendants' motion with respect to the written description requirement and will grant Hologic's motion with respect to nonenablement. An appropriate Order follows.

D.I. 250-1 at A583-623, 636-49, 651-58, 660-66, 668-75, 677-83, 685-91, 693-775, 777-84, 786-802, 804-23) However, as Hologic aptly observes, "the Examiner only considered Enzo's argument and was not presented with the overwhelming evidence of nonenablement set forth in Defendants' summary judgment briefing." (D.I 266 at 4 n.4)

APPENDIX D — DENIAL OF REHEARING OF THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT, FILED OCTOBER 29, 2019

NOTE: This order is nonprecedential.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

ENZO LIFE SCIENCES, INC.,

Plaintiff-Appellant

v.

ROCHE MOLECULAR SYSTEMS, INC., ROCHE DIAGNOSTICS CORPORATION, ROCHE DIAGNOSTICS OPERATIONS, INC., ROCHE NIMBLEGEN, INC., BECTON, DICKINSON AND COMPANY, AKA BECTON DICKSON AND COMPANY, BECTON DICKINSON DIAGNOSTICS INC., AKA BECTON DICKSON DIAGNOSTICS, GENEOHM SCIENCES INC., ABBOTT LABORATORIES, ABBOTT MOLECULAR, INC.,

Defendants-Appellees

2017-2498, 2017-2499, 2017-2545, 2017-2546

Appeals from the United States District Court for the District of Delaware in Nos. 1:12-cv-00106-LPS, 1:12-cv-00274-LPS, 1:12-cv-00275-LPS, 1:13-cv-00225-LPS, Chief Judge Leonard P. Stark.

Appendix D

ON PETITION FOR PANEL REHEARING AND REHEARING EN BANC

Before PROST, *Chief Judge*, NEWMAN, LOURIE, DYK, O'MALLEY, REYNA, WALLACH, TARANTO, CHEN, HUGHES, and STOLL, *Circuit Judges*[*].

PER CURIAM.

O R D E R

Appellant Enzo Life Sciences, Inc. filed a combined petition for panel rehearing and rehearing en banc. A response to the petition was invited by the court and filed by Appellees Abbott Laboratories, Abbott Molecular, Inc., Becton Dickinson Diagnostics Inc., Becton, Dickinson and Company, GeneOhm Sciences Inc., Roche Diagnostics Corporation, Roche Diagnostics Operations, Inc., Roche Molecular Systems, Inc. and Roche NimbleGen, Inc. The petition was referred to the panel that heard the appeal, and thereafter the petition for rehearing en banc was referred to the circuit judges who are in regular active service.

Upon consideration thereof,

IT IS ORDERED THAT:

The petition for panel rehearing is denied.

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[*] Circuit Judge Moore did not participate.

Appendix D

The petition for rehearing *en banc* is denied.

The mandate of the court will issue on November 5, 2019.

FOR THE COURT

October 29, 2019
Date

/s/ Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court