Nos. 2017-2498, -2499, -2545, -2546

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, AND ABBOTT MOLECULAR, INC.,

Defendants-Appellees.

On Appeal from the United States District Court
for the District of Delaware (Stark, C.J.), Case Nos. 12-106, 12-275, 12-274, and 13-225

APPELLEES' COMBINED RESPONSE TO PETITION FOR PANEL REHEARING AND REHEARING EN BANC

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CERTIFICATE OF INTEREST FOR ABBOTT LABORATORIES AND ABBOTT MOLECULAR, INC.

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

Abbott Laboratories and Abbott Molecular, Inc.

2. The name of any real party in interest represented by us, and not identified in response to Question 3, is: None.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the parties represented by us are:

Abbott Molecular, Inc. is a wholly-owned subsidiary of Abbott Laboratories. No other company owns 10% or more of the stock of Abbott Laboratories or Abbott Molecular, Inc.

4. The names of all law firms and the partners or associates who appeared for the party now represented by us in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

Kirkland & Ellis LLP: Jeanna Wacker, Stefan M. Miller, Peter Silverman.

Winston & Strawn LLP: Melinda K. Lackey, Maureen L. Rurka, Elizabeth J. Thompson.

Phillips, Goldman, McLaughlin & Hall, P.A.: John C. Phillips, Jr., David A. Bilson, Megan C. Haney.

Potter Anderson & Corroon, LLP: Richard L. Horwitz, David E. Moore, Bindu Ann George Palapura.

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

Enzo Life Sciences, Inc. v. Hologic, Inc., No. 1:15-cv-00271-LPS-CJB.

CERTIFICATE OF INTEREST FOR ROCHE AND BECTON DICKINSON APPELLEES

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

Roche Molecular Systems, Inc., Roche Diagnostics Corporation, Roche Diagnostics Operations, Inc., Roche Nimblegen, Inc., Becton, Dickinson and Company, Becton Dickinson Diagnostics Inc., and Geneohm Sciences Inc.

2. The name of any real party in interest represented by us, and not identified in response to Question 3, is: None.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the parties represented by us are:

Roche Nimblegen, Inc., which has changed its name to Roche Sequencing Solutions, Inc., is a wholly-owned subsidiary of Roche Molecular Systems, Inc. Roche Molecular Systems, Inc., Roche Diagnostics Corporation, and Roche Diagnostics Operations, Inc. are wholly owned subsidiaries of Roche Holdings, Inc. and indirect subsidiaries of Roche Holding Ltd. Novartis AG, a publicly-held company, owns more than 10% of the voting shares of Roche Holding Ltd.

Becton Dickinson Diagnostics, Inc. merged into Becton, Dickinson and Company. Geneohm Sciences Inc. merged into its parent, Becton Dickinson Infusion Therapy Systems Inc. ("BDITS"). BDITS is a wholly owned subsidiary of Becton, Dickinson and Company. T. Rowe Price owns more than 10% of the voting shares of Becton, Dickinson and Company.

4. The names of all law firms and the partners or associates who appeared for the party now represented by us in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

Wilmer Cutler Pickering Hale and Dorr LLP: Sadaf R. Abdullah (former), Jonathan E. Barbee (former), Jeffrey Coleman (former), Cortney C. Hoecherl (former), William W. Kim, Jason H. Liss, Jane M. Love (former),

Nancy L. Schroeder (former), Gregory P. Teran (former), Tiffany Tejeda-Rodriguez, Jamie T. Wisz (former)

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

Enzo Life Sciences, Inc. v. Hologic, Inc., No. 1:15-cv-00271-LPS-CJB.

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INTRODUCTION

Enzo's petition presents run-of-the-mill issues about applying settled legal principles to facts analogous to cases this Court has seen before, none of which warrants *en banc* review. In a classic case of overreaching, Enzo obtained patents covering commercially valuable technology that it did not invent—patents with specifications that fail to describe that technology, and technology to which Enzo made no contribution.

Enzo claims priority to a 1982 patent application disclosing the bare idea for labeling polynucleotides to create a genetic probe. Twenty years later, Enzo added claims in continuation applications that broadly covered a vast genus of probes through functional claim language without disclosing *how* to label in a way that creates probes *that actually perform the claimed functions*. The district court correctly held Enzo cannot bootstrap a high-level description of desired functionality into later-filed claims that preempt years of research by others. A unanimous panel of this Court affirmed that finding of non-enablement.

The panel found the "scope of the claims quite broad" and the specification's guidance "sparse." Op.11. In particular, the panel

reasoned that the specification does not teach which of the "extremely large number of possible embodiments" will be hybridizable and detectable and which will not. Op.15. The undisputed evidence instead showed that a skilled artisan, armed with the specification, would have had no idea how to make a probe that was both hybridizable and detectable except through trial-and-error testing of *tens of thousands of possible candidates*, one at a time.

The panel correctly concluded that is the opposite of enablement. Indeed, as the panel found, this case is controlled by *Wyeth & Cordis Corp. v. Abbott Laboratories*, which held that when "there is no genuine dispute that practicing the full scope of the claims would require [testing] *each* of at least tens of thousands of compounds," the required experimentation is necessarily "excessive." 720 F.3d 1380, 1385-86 (Fed. Cir. 2013). The panel correctly held "[t]he facts in this appeal largely mirror those in *Wyeth*" and that decision "controls this case." Op.10.

Enzo nonetheless accuses the panel of relying on some facts and ignoring others, repeating the refrain that summary judgment was not appropriate. That case-specific disagreement certainly does not warrant *en banc* review and, in any event, is wrong on its own terms. Enzo's

attempt to recast its factbound disagreement with the panel's decision as presenting an intra-circuit conflict or an issue of exceptional importance is meritless.

The panel's decision does not conflict with any case Enzo cites in its petition. Far from conflicting with *Wyeth*, the panel hewed closely to that decision, discussing it at length and relying on it in reaching its well-reasoned decision. Nor do the cases Enzo cites adopt some categorical rule that a defendant must identify at least one inoperative embodiment to establish non-enablement—a "rule" which, if adopted, would effectively force defendants to engage in undue experimentation to prove a claim invalid. Enzo's attempt to manufacture a conflict in this Court's precedents is wholly unavailing.

The panel's decision likewise does not raise any issues of exceptional importance. Enzo simply wants to rehash the same arguments the district court and panel properly rejected. Its petition should be denied.

STATEMENT OF THE CASE

A. Background

DNA is made of a series of nucleotides linked together in a chain known as a polynucleotide. Appx8633. Each individual nucleotide

includes a base, a sugar, and a phosphate. *Id.* DNA nucleotides have one of four chemical bases: adenine (A), guanine (G), cytosine (C), and thymine (T). The sugar and phosphate groups of the nucleotides form a backbone supporting the bases, allowing them to interact with one another. Appx8634.

Two strands of polynucleotides can attach together—or "hybridize"—through hydrogen bonding between bases on each polynucleotide; A pairs with T and C pairs with G. Appx9301. Scientists have used these principles to develop "hybridization probes"—a labeled polynucleotide that is hybridizable and remains detectable after hybridization occurs. Appx15266. The probe is designed to hybridize with a sufficiently complementary sequence of interest, called a "target," after which the label gives off a signal that may be detectable by laboratory equipment. By using this technique, diagnostic laboratories can detect the presence of various disorders.

Hybridization probes were typically labeled radioactively as of June 1982, the claimed priority date of the asserted patents. Appx15266-15267. Such radioactively-labeled probes replace a non-radioactive atom in the polynucleotide with a radioactive isotope. *Id.*

Non-radioactive labeling was just developing at the time of the claimed inventions. To label a probe non-radioactively, the polynucleotide's chemical structure must be modified by attaching a label to one or more of its nucleotides. Appx5839. As Enzo's founder and CEO Dr. Rabbani testified, in 1982, there was "barely[] the idea of chemical modification of nucleic acid in any form or fashion." Appx6465(31:23-32:2). He also admitted that scientists at the time viewed nucleic acids "as a holy molecule" that "cannot [be] chemically modified [] and expect[ed] to retain its attribute, its character." Appx8527-8528(37:22-38:2). Dr. Rabbani further explained that any attempt to attach a non-radioactive label to a DNA sequence was expected to disrupt the sequence's ability to hybridize by "completely destroy[ing] the hydrogen binding or just weaken[ing] it," a fatal flaw in probes designed to emit a detectable signal *upon hybridization* with the target sequence. Appx6470(1266:5-8); *see* Appx8459-8460(157:19-158:2).

In 1981, Dr. David Ward and others at Yale University successfully developed the first non-radioactive probe. Appx4129-4133. They discovered that attaching one non-radioactive label—biotin—at one of three positions on the nucleotide's *base* would not disrupt the

polynucleotide's ability to hybridize and be detected upon hybridization. The three base positions Dr. Ward identified became known as the "Ward positions." Appx8207(11:11-14). Identifying those three positions and isolating biotin as a suitable label took Dr. Ward and his team approximately three years of intense research. Appx4219; Appx4222; Appx4226-4228; Appx9475-9499.

Enzo licensed the exclusive rights to the patent portfolio covering Dr. Ward's discovery in December 1981. Appx8221; Appx8207; Appx8239-8256. Six months later, in June 1982, Enzo filed a patent application that copied nearly all of Dr. Ward's patent verbatim, named Enzo's people (not Ward's) as inventors, and claimed all other "non-Ward" labeling positions. The claims in Enzo's original 1982 application were not directed to hybridization probes, but instead claimed labeled polynucleotides that were detectable *before any hybridization occurs*. *E.g.*, Appx17636 (Claim 143).

Enzo filed the applications for what became the '180 and '405 patents in June 1995. Appx423; Appx466. Both patents have essentially the same disclosure. Appx475(2:10-12); Appx430-444. Enzo did not add the claims asserted here until years later—adding the asserted '405

patent claims in 2000 and the '180 patent claims in 2004. Appx10794-10796; Appx19997.

The shared specification of the '180 and '405 patents does not provide a single working example of a polynucleotide that remains hybridizable and detectable after being labeled at a non-Ward position. Nor did it offer any other teachings to dispel the undisputed dogma in 1982 that "the non-radioactive label could not be attached" at non-Ward positions "because it would 'disrupt' the capability of the labeled nucleotide to function … as a hybridization probe." Appx9825; Appx8207(10:16-11:1) (discussing this "dogma"). Yet the scope of the claims Enzo added decades after its original application is sweeping.

The '180 patent's asserted claims encompass all phosphate-labeled polynucleotides that remain hybridizable and detectable after being labeled at a non-Ward position. Those claims do not place any restrictions on (1) the type of phosphate to which the label is attached, (2) the chemistry used to attach the label, (3) the chemical linkage used, (4) the number of labels within a probe, or (4) the phosphate positions on the polynucleotide where the labels are placed (terminal or internal). *E.g.*, Appx459 (Claim 1); Appx491-492(34:62-35:67); Appx501(54:31-56);

Appx15790. Nor do the claims place any meaningful limit on the types of non-radioactive label employed. Appx459(60:16-21); Appx491-492(34:62-35:67); Appx501(54:39-45). Enzo's expert ultimately acknowledged that the claims cover at least "[h]undreds of thousands" of potential labels. Appx6438(118:25-119:1); Appx4110).

The '405 patent's asserted claims cover processes using an even broader genus of polynucleotides. Appx465-503. The *in situ* hybridization claims (claims 63, 64, 65, 95, 103, 128, and 144) permit labeling not only at the phosphate but also at *any non-Ward position*; that includes any of the thirteen non-Ward positions on the base and any of the five positions on the sugar. Appx80; Appx491-493, Appx495-496. The liquid phase hybridization claims (claims 196 and 198) cover using probes labeled non-radioactively at *any position* on the nucleotide, including the three Ward positions. Appx9537-9538.

B. Procedural History

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

In June 2017, in the cases against Roche and Becton Dickinson, the district court granted summary judgment to the defendants, holding that all asserted claims of the '180 patent were invalid as not enabled. Appx55. Enzo agreed that the district court's enablement ruling for the '180 patent would apply in the two Abbott cases as well. Appx23; Appx14950-14951. With respect to the '405 patent, the district court again granted summary judgment of non-enablement. Appx78-98; Appx15567-15595. The district court pointed out that "the specifications of the '180 and '405 patents are identical in all relevant respects," and "the asserted claims of the '405 patent are *even broader* than the asserted claims of the '180 patent." Appx94 (emphasis added).

A unanimous panel of this Court affirmed. Op.16. Like the district court, the panel found the specification "fails to teach one of skill in the art which combinations will produce a polynucleotide that is hybridizable and detectable upon hybridization." Op.9-10. In reaching that conclusion, the panel held that *Wyeth* "controls this case," explaining that "[t]he facts in this appeal largely mirror those in *Wyeth*." Op.10. Applying *Wyeth*'s reasoning, the panel ultimately held "undue experimentation" would be required to practice the full scope of the '180

patent claims "based on the number of possible embodiments and the unpredictability in the art." Op.15. And, because the '405 patent's asserted claims are even broader, the Court also affirmed that those claims are not enabled. *Id.* at 16.

REASONS THE PETITION SHOULD BE DENIED

En banc review is disfavored and will ordinarily not be granted unless it is "necessary to secure or maintain uniformity of the court's decisions" or "the proceeding involves a question of exceptional importance." Fed. R. App. P. 35(a). Neither requirement is satisfied here. Enzo's petition challenges the panel's application of settled precedent and quibbles with the panel's review of the record in this case. Rather than rehash the same case-specific arguments the district court and a unanimous panel have already correctly rejected, the Court should deny Enzo's petition for *en banc* review.

I. En Banc Review Is Not Warranted Because The Panel's Decision Is Consistent With This Court's Precedent.

As an initial matter, the panel decision does not conflict with any of the cases Enzo cites in its petition. A patentee who chooses broad, functional claim language must ensure that skilled artisans can practice its "full scope without undue experimentation." *Wyeth*, 720 F.3d at 1384.

To enable an entire, broadly claimed genus, the specification thus must at least teach how to "determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." *In re Vaeck*, 947 F.2d 488, 495-96 (Fed. Cir. 1991).

The panel decision faithfully applied those principles here. The asserted claims of both patents cover a broad genus of *working probes*, but nothing in the specification purports to teach a skilled artisan how to create a labeled polynucleotide that he knows, *ex ante*, will be both hybridizable and detectable. To the contrary, as Enzo's own expert conceded, it "would have been necessary" to make and test each probe within the scope of the claims to confirm that it actually works. Appx8454-8456(150:7-152:11). This Court has consistently held such sweeping claims were not enabled in similar circumstances. *Wyeth*, 720 F.3d at 1385-86; *ALZA Corp. v. Andrx Pharm., LLC*, 603 F.3d 935, 941 (Fed. Cir. 2010); *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365-68 (Fed. Cir. 1997).

Enzo attempts to manufacture an intra-circuit split by asserting that this Court's earlier decisions required "proof of unworkable species" to establish undue experimentation. Pet.17. Not so. Enzo's argument

fundamentally misunderstands the enablement inquiry, which has never required "actual proof of inoperability within a genus" to establish undue experimentation. Pet.3

Indeed, none of the cases Enzo cites suggest otherwise or support its novel rule. Enzo relies primarily on *Wyeth*, 720 F.3d at 1384-86, which the panel discussed extensively in its opinion. *See* Op.10-11. The idea that the panel created a split with *Wyeth* strains credulity. Not only did the panel conclude that *Wyeth* "controls this case," but it also found "the facts in this appeal largely mirror those in *Wyeth*." Op.10. The panel unsurprisingly did not contradict the very case it treats as the most relevant precedent.

It is Enzo's arguments—not the panel's decision—that conflict with *Wyeth*. There, this Court *affirmed the grant of summary judgment* and held that practicing the full scope of a patent covering "any structural analog" of rapamycin "that exhibits immunosuppressive and antirestenotic effects" required undue experimentation. *Wyeth*, 720 F.3d at 1384. *Wyeth* gave two reasons for its decision. *Id.* at 1385-86. *First*, the specification was "silent" about how to modify rapamycin "in a way that would preserve the recited utility." *Id.* at 1385. *Second*, to practice

the full scope of the claims, a skilled artisan would need to create and test "*each* of at least tens of thousands of compounds" in an "unpredictable and poorly understood field." *Id.* at 1385-86. This need to engage in a "systematic screening process" to confirm whether claimed compounds possessed the desired characteristics amounted to "excessive—and thus undue—experimentation." *Id.* at 1384, 1386. The decision never mentioned inoperative embodiments, much less held inoperability is a threshold requirement.

The panel correctly held that *Wyeth* controls. Op.10. As in *Wyeth*, the asserted claims use functional language to encompass a broad genus of potential compounds. But the undisputed evidence demonstrates that a skilled artisan, even after reading the specification, would not be able to identify in advance which—if any—phosphate-labeled polynucleotides are hybridizable and detectable. Appx8542(148:9-21); Appx4254(145:16-19); Appx5965(83:5-19). Instead, as Enzo's expert conceded, the skilled artisan would have to "actually make" and "test" each of the polynucleotides Enzo claims, one at a time, to determine which would work as a probe. Appx8454(150:11-15); Appx6490(144:4-13) (inventor testifying that whether an attached label is actually detectable requires

"case-by-case" experimentation). When there are "an extremely large number of possible embodiments," Op.15, this trial-and-error testing is the epitome of undue experimentation.

Just as *Wyeth* does not require proof of inoperable embodiments, neither does *Alcon Research Ltd. v. Barr Laboratories, Inc.*, 745 F.3d 1180 (Fed. Cir. 2014). Under that decision, a defendant must "put forward evidence that *some experimentation* is needed to practice the patented claim." *Id.* at 1188 (emphasis added). That evidence need not be proof that the claims cover inoperable embodiments, as *Wyeth* and *ALZA* make clear. Both held the challenged claims were not enabled because practicing the full scope of the claims required "an iterative, trial-and-error process" *without mentioning inoperative embodiments*. *ALZA*, 603 F.3d at 941; *Wyeth*, 720 F.3d at 1385-86. So too here: Enzo's witnesses concede one would need to "make" and "test" each claimed compound to determine which would work. Appx8454(150:12-13); Appx6490(144:4-13). That evidence far exceeds *Alcon*'s "some experimentation" threshold.

Enzo also relies on *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293 (Fed. Cir. 2015), but that decision again does not require evidence of inoperative embodiments. *It does not mention inoperative embodiments*

at all. *Id.* at 1309-11. Instead, the defendant challenged whether a skilled artisan would believe the claimed composition actually had the claimed efficacy and reduction in side effects. *Id.* at 1310. This Court rejected that argument because the specifications "disclose[d] actual *in vitro* and *in vivo* data." *Id.* The '180 and '405 patents do not offer any similar data proving the claimed polynucleotides will actually work as probes, much less data that would eliminate the need for trial-and-error experimentation across the full scope of these astonishingly broad claims.

What Enzo really wants is a stricter rule than this Court has previously adopted, effectively forcing patent challengers to engage in undue experimentation to prove a claim invalid. This Court has never required the kind of heightened and expensive proof that Enzo seeks, and there is no conflict warranting this Court's *en banc* review to resolve. In any event, this would be a particularly poor case in which to consider such a requirement given the extraordinary size of the genus Enzo claimed and its admission that case-by-case experimentation would be required.

II. En Banc Review Is Not Warranted Because The Panel's Decision Was Correct.

The rest of Enzo's petition offers three reasons the panel should have reversed, but those case-specific arguments do not warrant *en banc* review. Regardless, the panel properly concluded that no *genuine* issues of *material* fact precluded finding the late-added claims of the '180 and the '405 patents were not enabled. Based on undisputed evidence, the panel correctly determined that the limited disclosure in the 1982 application could not enable the full scope of a broad genus in an unpredictable art.

A. The Undisputed Evidence Proves A Skilled Artisan Would Have Been Required To Engage In Undue Experimentation

Enzo first asserts that there was no evidence about "how much experimentation would have been required to practice claims" or about "what skilled artisans at the time would have considered a typical amount of experimentation." Pet.10. But the Court's decision shows that, based on undisputed evidence, the amount of experimentation would have been undue.

The panel quoted testimony by *Enzo's expert* that a skilled artisan "would need to actually make the compound and test it in a hybridization

experiment" to feel comfortable that a particular polynucleotide would work as a probe. Op.14 (quoting Appx8454(150:8-15)). The panel also relied on testimony from *Enzo's expert* that a skilled artisan "motivated to make" a "non-Ward labeled probe" would "have to make it and assure against the prevailing wisdom that it could work." Op.14 (quoting Appx8456(152:3-11)). Relying on that testimony, the panel concluded "each labeled polynucleotide would need to be tested to determine whether it is hybridizable and detectable upon hybridization." Op.14-15.

Other evidence in the record confirms the art was unpredictable and lacked guiding principles for identifying which combinations would create a working probe and which would not. *Enzo's* inventors, experts, and other witnesses testified repeatedly that "figuring out what does and doesn't work" required "trial and error." Appx6509 (Waldrop); *see, e.g.*, Appx4253-4254, Appx6488 (Kline); Appx6451-52 (Backman); Appx8452-8455 (Sherman). Such case-by-case experimentation was necessary, according to Enzo's witnesses, because labeling at the phosphate position could interfere with or disrupt hybridization, and one could not predict *ex ante* whether a label would be detectable when attached to a polynucleotide. Appx4718-4730; Appx4457; Appx4254; Appx4249.

Performing this case-by-case experimentation is neither quick nor straightforward. To create *three* non-radioactively labeled probes, the Ward group spent "six to eight months" synthesizing precursor compounds and over a year testing potential non-radioactive labels before identifying "two or three" that could be incorporated into the nucleic acid. Appx4223(147:16-22); Appx4226(168:22-25). The Ward group then performed "a lot of experiments" over many months to identify three locations on the base where one label could be attached without interfering with hybridization or detectability. Appx4227(169:3-13). Enzo's own expert gave a more optimistic estimate that it could take a week to test each compound. Appx6438-6439 (Backman). But either way, the amount of testing required was immense. There are *at least* "tens of thousands" of possible nucleotides that would need to go through similar testing. Op.15 (citing Appx6438(120:20-121:11)). Nothing about this was a "typical amount of experimentation." Pet.10. Unsurprisingly, this Court has previously held similar case-by-case testing constitutes undue experimentation. *Wyeth*, 720 F.3d at 1385; *ALZA*, 603 F.3d at 941.

B. The Panel Did Not Overlook Evidence That The Art Was Supposedly Predictable

Enzo's related assertion—that the panel "overlooked" evidence that "the hybridizability and detectability of labeled polynucleotides was not … unpredictable"—is likewise meritless. Pet.11. The snippet from the specification Enzo quotes describes desired functionality, not *how to achieve* that functionality. As the panel concluded, "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." Op.12. The panel also gave Enzo the benefit of the doubt that varying "the length and sequence of the polynucleotide do[es] not give rise to separate embodiments" that must be tested. Op.15. It simply found that holding the length and sequence constant "still result[s] in an extremely large number of possible embodiments" that a skilled artisan must test individually. *Id.*

Enzo mischaracterizes the record in other ways as well. Abbott's expert never testified that the "disclosure of a non-radioactively labeled polynucleotide *necessarily discloses* a polynucleotide that is detectable when hybridized." Pet.12. Instead, the expert testified that if a labeled oligonucleotide is detectable before hybridization, it will also be

detectable *if it successfully hybridizes*—not that it will necessarily hybridize. As the undisputed evidence shows, hybridization can be disrupted by many variables, none of which are controlled for by the claims or taught in the specification. *E.g.*, Appx4484-4485. Nothing about this testimony required a different decision, and nothing in the panel's decision somehow shifted the burden to Enzo to prove enablement.

C. The Panel Viewed The Evidence In The Light Most Favorable To Enzo

Finally, the panel did not misapply the summary judgment standard or fail to draw all reasonable inferences in Enzo's favor. Enzo asserts that "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." Pet.13. But Enzo offers no *evidence* to support its speculation, which would be legally irrelevant even if it were true. Enzo's witnesses admitted there was "no ability to predict" which labeled polynucleotides would work as probes in 1982, Appx8455(151:12-18), so a skilled artisan would still have to make and test each one to practice the full scope of the invention.

Enzo's additional arguments do not raise genuine disputes of *material* fact. Example V in the specification does not disclose "phosphate-labeled polynucleotides capable of hybridization and subsequent detection." Pet.13. Enzo's experts could not identify the sequence or length of DNA used in Example V, admitted there was no disclosure of hybridization and detection, and could not predict whether a labeled polynucleotide created using the same chemistry would work as a hybridization probe. Appx5943(127:8-17); Appx6441(140:12-141:22); Appx8453-8454(149:17-150:6). But even if Enzo had disclosed a single example of a working probe, the asserted claims would still be invalid because "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." Op.15.

None of Enzo's criticisms of how the panel read the summary judgment record raise questions of exceptional importance. The panel engaged in routine review of a summary judgment decision invalidating claims of exceptional breadth, nothing more. Whatever disagreements Enzo may have with the conclusions the panel reached, those objections have no importance beyond the parties and this case, and provide no

occasion for *en banc* review. Regardless, the panel's unanimous decision was correct.

CONCLUSION

Enzo's petition should be denied.

October 11, 2019

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on the 11th day of October, 2019, a true and correct copy of the foregoing document was filed with the clerk of court using the CM/ECF system, which will send notice of electronic filing to all CM/ECF participants, resulting in service upon all counsel of record.

/s/ Jason M. Wilcox
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ECF-3(B)(2) REPRESENTATION

Pursuant to this Court's Administrative Order Regarding Electronic Case Filing, the undersigned represents under ECF-3(b)(2) that counsel for Roche Molecular Systems, Inc., Roche Diagnostics Corporation, Roche Diagnostics Operations, Inc., Roche Nimblegen, Inc., Becton, Dickinson and Company, Becton Dickinson Diagnostics Inc., and Geneohm Sciences Inc. have consented to their signatures on this filing.

Dated: October 11, 2019

/s/ Jason M. Wilcox
Jason M. Wilcox

CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATION

The undersigned hereby certifies that this brief complies with the type-volume limitation of Fed. Cir. R. 35(e)(4).

1. Exclusive of the exempted portions of the brief, as provided in Fed. R. App. P. 35(c)(2), the response contains 3,898 words.

2. The brief has been prepared in proportionally spaced typeface using Microsoft Word 2016 in 14 point Century Schoolbook font. As permitted by Fed. R. App. P. 32(g), the undersigned has relied upon the word count feature of this word processing system in preparing this certificate.

Dated: October 11, 2019

/s/ Jason M. Wilcox
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