

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GUARDANT HEALTH, INC.,
Petitioner,

v.

COLD SPRING HARBOR LABORATORY,
Patent Owner.

Case IPR2025-01355

Patent 10,947,589

**PATENT OWNER'S DISCRETIONARY DENIAL OF INSTITUTION
BRIEF**

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EXHIBIT LIST

Exhibit No.	Description
2001	Intentionally left blank
2002	Prosecution File History of U.S. Patent No. 9,404,156
2003	March 26, 2025 Memorandum from Acting Director Coke Morgan Stewart titled “Interim Processes for PTAB Workload Management”
2004	Intentionally left blank
2005	Intentionally left blank
2006	<i>Foundation Medicine, Inc., v. Guardant Health, Inc.</i> IPR2019-00130, Paper 7 (June 5, 2019)
2007	Petition for <i>Inter Partes</i> Review of U.S. Patent No. 12,234,510, IPR2025-01353
2008	Plaintiffs’ First Amended Complaint for Patent Infringement, <i>Guardant Health, Inc., v. Tempus AI, Inc.</i> 1:24-cv-00687-RGA (D. Del. filed November 4, 2024)
2009	Third Amended Scheduling Order, <i>Cold Spring Harbor Laboratory v. Guardant Health, Inc.</i> , C.A. No. 25-263-JCG (July 1, 2025 D. Del.) (No. 37)
2010	Defendant’s Opening Brief in Support of Partial Motion to Dismiss for Failure to State a Claim, <i>Cold Spring Harbor Laboratory v. Guardant Health, Inc.</i> , C.A. No. 25-263-JCG (May 1, 2025 D. Del.) (No. 25)
2011	Defendant’s Initial Invalidity Contentions, <i>Cold Spring Harbor Laboratory v. Guardant Health, Inc.</i> , C.A. No. 25-263-JCG (September 19, 2025 D. Del.)
2012	November 10, 2016 Information Disclosure Statement by Applicant filed in connection with Guardant Patent Application No. 14/712,754

I. INTRODUCTION

Patent Owner Cold Spring Harbor Laboratory (“PO” or “CSHL”) respectfully requests that the Director discretionarily deny institution of this IPR filed by Petitioner Guardant Health, Inc. (“Petitioner” or “Guardant”) against U.S. Patent No. 10,947,589 (“the ‘589 Patent”). Institution should be denied because this IPR would cause the parties and the Board to incur significant inefficiencies and wasted efforts for multiple reasons explained below, and additional reasons that will be more fully elaborated in CSHL’s forthcoming Patent Owner Preliminary Response (“POPR”).

First, this Petition is one of two (IPR2025-01355 and IPR2025-01353) filed by Guardant challenging related CSHL Patents that are asserted in *Cold Spring Harbor Laboratory v. Guardant Health, Inc.*, C.A. No. 25-263-JCG (D. Del.) (the “Litigation”). In this Petition Guardant challenges the validity of all claims of the ‘589 Patent asserted by PO in the Litigation, but in the related proceeding IPR2025-01353, Guardant declined to challenge the validity of claims 16 and 27 of related U.S. Patent No. 12,234,510 (“the ‘510 Patent”) (*See* EX2007, p. 1), despite both those claims being asserted in the Litigation. Thus, the Litigation will continue even if these IPRs are instituted and regardless of their outcomes.

Second, the Petition is deficient on its face for multiple reasons, and the interests of efficiencies and preservation of Board resources favor denial. The Petition relies on cumulative references that add nothing new beyond art already

considered during prosecution. Both the primary and secondary references are relied upon by the Petitioner for substantially the same teachings as art that was considered during prosecution. Petitioner and their expert *admit* that the method described in their primary reference “*had been previously applied*” in two publications (Chiang and Wang) considered by the Examiner during prosecution.¹ Similarly, the Petition *admits* that it relies on two secondary references that were considered during prosecution (Brenner and McCloskey), and that an additional two newly-cited secondary references (Chee and Porreca) are relied upon for the *same* teachings as the references considered during prosecution. Despite these admissions, the Petition fails to even attempt to articulate any reason why the Examiner erred when previously considering the same references and cumulative art. Petitioner also repeatedly fails to specify with particularity the reasons and evidence supporting their obviousness assertions and instead relies on the bare assertions of their expert to supply missing claim features as allegedly obvious.

Third, Guardant has been aware of the ‘589 Patent family since at least 2016, when it started citing it in their own applications. And then in 2019, Guardant directed an Opposition against the European counterpart of the ‘589 Patent, and

¹ All emphasis added unless otherwise indicated.

knew or should have known of the ‘589 Patent when it issued on March 16, 2021. Yet, Guardant did not promptly bring an IPR (or a PGR) against the ‘589 Patent.

Fourth, Guardant’s arguments in the Petition are contradicted by positions Guardant previously took to defend and enforce its own patents. The Board should deny institution of this IPR predicated on contradictory positions.

II. INSTITUTION SHOULD BE DENIED BECAUSE IT WILL NOT OBVIATE PARALLEL DISTRICT COURT LITIGATION

The Litigation has an April 19, 2027 trial date (EX2009, p. 27), which is shortly after the February 1, 2027 deadline for the issuance of a final written decision in this IPR. Nonetheless, several factors weigh in favor of denying institution of this IPR.

First, the Litigation is not stayed, and Guardant has not even moved for a stay. Instead, Guardant began motion practice, seeking a limited dismissal of only CSHL’s claim of pre-suit willful infringement. That motion is fully briefed and will require the Court’s attention, and even if granted would only slightly narrow the Litigation. EX2009, p. 26. The assigned Judge, Judge Choe-Groves, previously denied (without explanation) a stipulated stay where the PTAB had instituted an IPR for two out of three patents-in-suit—leaving one patent not subject to an IPR. *Data Health Partners, Inc. v. Teladoc Health, Inc.*, C.A. No. 23-160-JCG, D.I. 38 (D. Del. Oct. 7, 2024). In that case, because an IPR was not instituted on one of the three

patents, the litigation needed to continue regardless of the IPR outcomes. Similarly here, Guardant declined to challenge the validity of two claims of the related ‘510 Patent (claims 16 and 27) (EX2007, p. 1) that PO has asserted in the Litigation. EX1020, p. 2. Thus, even if these IPRs were instituted, the Litigation will need to continue, regardless of the IPR outcomes.

Second, since the March 6, 2025 filing of the Litigation the parties have invested substantial resources in the case. In addition to Guardant’s motion, CSHL has served its initial infringement contentions, and Guardant has served its initial invalidity contentions. *See* EX2011. Further, by the February 1, 2026 Institution Decision deadline, the parties will be proceeding through claim construction briefing. *See* EX2009, p. 26.

Third, there is substantial overlap between the issues raised in the Petition and the Litigation. All claims challenged in the Petition are also at issue in the Litigation, and Guardant has not filed any stipulation agreeing to not re-raise the same arguments it makes here. To the contrary, in its invalidity contentions Guardant advanced the *exact same* prior art and arguments presented in this IPR—even incorporating these IPRs *in their entirety* into those contentions (EX2011 at 24)—in addition to invalidity contentions based on 35 U.S.C. § 112 and § 101. *See id.*, pp. 7-23 and 40-41. CSHL will be required to defend the validity of its patents in the Litigation, including against the exact same grounds asserted in this Petition.

III. INSTITUTION SHOULD BE DENIED UNDER 35 U.S.C. § 325(d) BECAUSE THE PETITION RAISES ONLY CUMULATIVE ART

The Petition relies on art that is substantially the same as the art considered by the Examiner, but Petitioner does not demonstrate material error by the Examiner. Where a petitioner (1) asserts art or arguments that were previously presented, and (2) fails to demonstrate that the Office erred in a manner material to patentability, denial is appropriate. *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GMBH*, IPR2019-01469, Paper 6, 10 (PTAB Feb. 13, 2020).

Under § 325(d), “[p]reviously presented art includes art made of record by the Examiner, and art provided to the Office by an applicant, such as on an Information Disclosure Statement (IDS).” *Advanced Bionics*, Paper 6, 7-8. “[C]hallenging the claims using the same prior art that was previously presented on an IDS is sufficient to satisfy the first part of the *Advanced Bionics* framework.” *Ecto World, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13, 4 (PTAB May 19, 2025).

If the “same or substantially the same prior art or arguments previously were presented to the Office,” then there must be a showing that the Office erred in evaluating the art or arguments. *See, e.g., Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8, p. 24 (PTAB Dec. 15, 2017). If the Petition fails to sufficiently identify a material error by the Office, then discretionary denial of the Petition is appropriate. *Ecto World*, Paper 13 at 6. As explained in *Ecto World*,

“a petitioner *must* provide an analysis even when the asserted prior art is on an IDS, but the Examiner did not apply the reference.” *Id.* at 5; *see also TankLogix, LLC v. SitePro, Inc.*, IPR2025-00761, Paper 10 (PTAB Sept. 3, 2025) (Denying institution in part because the art relied on in the Petition was either cited by the Examiner *or* cited in an IDS and Petitioner did not identify any error by the Examiner).

Here, all of the Petition’s Grounds rely on the same or substantially the same art as considered by the Examiner, and the Petition fails to meet its burden of showing that the Office erred in evaluating the art. The petition should be denied under § 325(d). Consolidated Trial Practice Guide, 64 (PTAB Nov. 2019).

A. The art presented in the Petition is the same or substantially the same as art previously presented during prosecution

1. The art cited in the Petition

a. US 2009/0029377 (“Lo”)

The Petition alleges that the ‘589 Patent claims are obvious over Lo “in view of the knowledge of a POSA” as allegedly reflected in a variety of other references discussed below.

Lo is cited for its teaching of “a method for determining copy number information based on sequencing DNA from a sample, mapping the sequence reads to a reference genome, and counting the number reads that correspond to a location in the genome.” Paper 1 at 12. The Petition alleges that “[t]o the extent any aspect of the independent claims is missing in Lo, it is tagging DNA sequences to generate

unique tagged nucleic acid molecules followed by amplification of these tagged nucleic acid molecules.” Paper 1 at 22.

b. McCloskey, Chee, Brenner, or Porreca

When attempting to supply the missing claim limitation of “tagging DNA sequences to generate unique tagged nucleic acid molecules followed by amplification of these tagged nucleic acid molecules,” the Petition relies on *any* one of McCloskey, Chee, Brenner, or Porreca *in the alternative* for the *same* teachings: “This Petition relies upon four references that teach the use of tagging, amplification, and sequencing for molecular counting: McCloskey, Chee, Brenner, and Porreca.” Paper 1 at 10; *see also* Paper 1 at 23 (alleging that “it would have nonetheless been obvious to perform this step in combination with Lo in view of the knowledge of the skilled artisan, as reflected in McCloskey, Porreca, Chee, *or* Brenner”).

Petitioner’s expert, Gregory Cooper, Ph.D., similarly relies upon McCloskey, Chee, Brenner, or Porreca for the same teachings regarding the “general approach of tagging, amplification, and sequencing for molecular counting.” *See* EX1002 at ¶¶95, 101, 110 and 117. (Dr. Cooper states that these four references all teach “the general approach of tagging, amplification, and sequencing for molecular counting”). As discussed below, Brenner and McCloskey were well considered.

2. The art that was considered during prosecution of the parent ‘156 Patent

The ‘589 Patent is a continuation of U.S. Patent No. 9,404,156 (“the ‘156 Patent”), issued August 2, 2016. During prosecution of the ‘156 Patent, the same Examiner who examined the ‘589 Patent applied Brenner (US 2007/0172873)² in a rejection in an April 30, 2014 Office Action (EX2002, p. 363-364).

Further, PO’s first IDS in the ‘156 Patent, containing only 14 references, included Brenner (U.S. Patent No. 7,537,897, EX1014) and McCloskey (EX1008). Finally, McCloskey and Brenner are both also discussed in the Background section of the specification. EX1001, 2:23-26 and 2:16-20.

In the Examiner’s Reasons for Allowance, having considered the disclosure of Brenner, McCloskey and the other references provided by PO in its IDSs, the Examiner noted that “[n]o prior art in the record teaches a combination of steps a) to f) of claim 1 and a combination of steps a) to e) of claim 9. No prior art either alone or in combination with other art in the record teaches or reasonably suggests a

² US 2007/0172873 is the publication corresponding to U.S. Patent No. 7,537,897 (EX1014), cited by Petitioner in this IPR as one of the four secondary references that allegedly teaches “molecular counting based on tagging, amplification, and sequencing.” Paper 1, at 10; EX1002 at ¶101.

method for obtaining copy number information [] which comprise all limitations recited in claim[] 1.” EX2002, p. 692.

3. The art that was considered by the Examiner during prosecution of the ‘589 Patent

During prosecution of the ‘589 Patent, the PO disclosed in IDSs the references previously disclosed in connection with the ‘156 Patent, including Brenner and McCloskey. EX1009, pp. 207-210 (Brenner and McCloskey cited as Cite Nos. 13 and 38, respectively). The same Examiner examined the ‘589 Patent and the ‘156 Patent.

During prosecution of the ‘589 Patent, PO also disclosed in an IDS an Opposition filed against the European counterpart of the ‘589 Patent, along with the references cited therein.³ EX1009, p. 318. The Opposition alleged that the claims of the European counterpart were anticipated or not inventive over a variety of references including Brenner (US2007/0172873, the publication of U.S. Patent No. 7,537,879), McCloskey 2007, and Chiang 2009. PO also disclosed subsequent briefing and additional evidence filed by the opponent in the Opposition, including

³ The Opposition was filed on behalf of Guardant. *See* EX2010, p. 2 (Guardant characterizing arguments by the opponent in the anonymously-filed Opposition as “*Guardant’s* arguments”).

Wang (EX1012). EX1009, p. 540. The Examiner considered Brenner and McCloskey, the Opposition and subsequent briefing, and each of the references cited in the Opposition before allowing the ‘589 Patent. *See* EX1009, p. 255 (Brenner cited as Cite ID 13), p. 257 (McCloskey cited as Cite ID 38), p. 532 (Chiang cited as Cite ID 6); and p. 605 (Wang cited as Cite ID 6).

4. The art cited in the Petition is substantially the same as art that was considered during prosecution

a. The teachings relied upon by Petitioner in McCloskey, Brenner, Chee and Porreca are cumulative

As noted above, both McCloskey and Brenner were repeatedly cited during prosecution of the ‘589 Patent and parent ‘156 Patent. The Petition and Dr. Cooper now cite to *any* one of McCloskey, Brenner, Chee or Porreca in the alternative for the same teaching: “This Petition relies upon four references that teach the use of tagging, amplification, and sequencing for molecular counting: McCloskey, Chee, Brenner, and Porreca.” Paper 1 at 10. Thus, the Petition *admits* that its two newly cited secondary references (Chee and Porreca) are being relied upon for the *same* “use of tagging, amplification, and sequencing for molecular counting” teaching as the art that was considered during prosecution (McCloskey and Brenner).

b. Lo is cumulative of Wang et al. and Chiang et al.

Although the primary reference Lo was not cited during prosecution of the ‘589 Patent, the teachings of Lo relied upon in the Petition are substantially the same

as art that was considered during prosecution. Indeed, the Petition itself admits that the “*method described in Lo [] had been previously applied* to other sources of DNA to detect copy number information” (Paper 1 at 16), citing to Wang et al. “Digital Karyotyping” (2002) (“Wang”, EX1012) and Chiang et al. “High Resolution Mapping of Copy Number Alterations with Massively Parallel Sequencing” (2008) (“Chiang”, EX 1013) as two examples where the method described in Lo had been previously applied.

Both Wang and Chiang were disclosed to the Examiner during prosecution in IDSs. The Petition’s citation to Lo is a transparent attempt by Petitioner to avoid relying on the *same art* (i.e. Wang and Chiang) that was already considered by the Examiner during prosecution. However, by Petitioner’s own admission, Lo is *substantially the same* as Wang and Chiang because both Wang and Chiang relate to the “method described in Lo.” Paper 1 at 16.

B. The petition fails to identify any error by the Examiner

Despite relying on art that it *admits* is substantially the same as art considered by the Examiner during prosecution, the Petition fails to explain why or how the Examiner erred.

While the Petition alleges that “[d]uring prosecution, the Examiner made no rejections based on prior art, instead focusing solely on §§101 and 112 rejections” (Paper 1 at 10), the Petition ignores the examination of the parent patent by the same

Examiner, where there is a clear record of Brenner (US 2007/0172873 A1) being applied in a rejection, and cited in the IDSs in this ‘589 Patent (including as part of the cited European Opposition documents). Either way, the Petition ignores the *Ecto World* requirement that the Petition provide an analysis if art was disclosed in an IDS, even if not applied.

Despite the Petition relying on the teachings of previously presented art, or art that is substantially the same as previously presented art, the Petition fails to identify *any* error by the Office in examining the subject patent. Denial of institution is appropriate for that reason alone.

IV. THE WEAKNESS OF THE UNPATENTABILITY CHALLENGE WEIGHS IN FAVOR OF DENIAL

The Director’s March 26, 2025 Memorandum identifies “[t]he strength of the unpatentability challenge” and “[t]he extent of the petition’s reliance on expert testimony” as two relevant factors. EX2003 at 2. The Petition’s extensive reliance on expert testimony to impermissibly fill gaps in the prior art, and the presentation of arguments that contradict previous arguments advanced by Guardant, further evidence the weakness of the Petition.

A. The Petition’s reliance on expert testimony evidences its weakness

The Petition improperly relies solely on the bare assertions of its expert to fill in pieces of its alleged obviousness rationale, as will be detailed in the POPR.

As an example, supported solely by its expert's bare assertions, the Petition alleges that a POSA would have been motivated to combine the tagging of McCloskey, Porreca, Chee, or Brenner with the method described in Lo because "[i]t offered a known solution to a known problem: the need to improve the accuracy of counting molecules, particularly in situations where few sample DNA molecules are provided" (Paper 1 at 26, citing EX1002 at ¶¶154-155) and because "this technique was one of only a small number of options available for improving the accuracy of counting and was well within the technical grasp of a skilled artisan." *Id.*

These opinions by the expert lack any substantiating evidence and contradict Lo, who nowhere mentions any "need to improve the accuracy of counting molecules" in its methods. Notably, Lo does not cite to McCloskey, Porreca, Chee, or Brenner, let alone their tagging methods as a solution despite these techniques being allegedly "only a small number of options available for improving the accuracy of counting."

Further, again supported solely by its expert's bare assertion, the Petition alleges that "Lo is based on counting, and therefore a POSA would naturally think to include tagging as an extension of Lo's method because tagging was specifically intended for improving the accuracy of molecular counting." *Id.* at 27, citing EX1002 at ¶156. Here too, the expert's opinion lacks any substantiating evidence regarding a need "for improving the accuracy of counting molecules" in the methods

of Lo, or how tagging would improve the accuracy of counting in the methods of Lo.

Finally, and again supported by nothing more than its expert's bare assertion, the Petition alleges that because "Lo explains that 'fetal DNA is present in low absolute concentration' in maternal plasma, creating a low signal problem [] a POSA would have been motivated to combine the tagging techniques known in the art with the amplification techniques described below in step [1C] to increase the signal-to-noise ratio." *Id.* at 29, citing EX1002 at ¶158. Beyond lacking evidence, Petitioner's expert fails to explain how the "tagging techniques known in the art" would even accomplish the goal of "increas[ing] the signal-to-noise ratio" in the context of Lo.

B. The Petition fails to specify the grounds with particularity

Discretionary denial is also appropriate because the Petition fails to identify "with particularity, each claim challenged" (35 U.S.C. § 312(a)(3)). Where a petition fails to meet the particularity requirement, the Board may exercise its discretion to deny the entire petition. *Adaptics Ltd. v. Perfect Co.*, IPR2018-01596, Paper No. 20 at 24 (PTAB Mar. 6, 2019) (informative).

First, the Petition inexplicably cites four secondary references McCloskey, Chee, Brenner, or Porreca *in the alternative* for the *same* teachings: "This Petition relies upon four references that teach the use of tagging, amplification, and sequencing for molecular counting: McCloskey, Chee, Brenner, and Porreca." Paper

1 at 10; *see also* Paper 1 at 23. Citing four secondary references for the same teaching without (1) any stated reason for why one reference would not have been sufficient and (2) any indication of what possible combinations are actually asserted, is a clear failure of the Petition to present its challenges with particularity.

Second, Dr. Cooper's declaration is 139 pages long with 290 paragraphs. The Petition repeatedly incorporates argument from the declaration rather than providing them in the Petition. *See e.g.* Paper 1 at 42 (citing 6 paragraphs from Dr. Cooper in support of the assertion that "Lo in combination with the knowledge of the skilled artisan teaches and renders obvious claim 3" without explanation); *Id.* at 43 (citing 6 paragraphs from Dr. Cooper as support for the assertion that "cutoff values" in Lo are based on comparison to counts obtained from the "same location" on a "reference sample" without explanation); and *Id.* at 44 (citing 4 paragraphs from Dr. Cooper in support of the assertion that the approach in Lo "entails the summing of claim 6" without explanation).

This conclusory approach fails to specify the grounds with particularity, and improperly attempts to incorporate arguments from the expert declaration rather than providing them in the Petition itself. *See Cisco Systems, Inc. v. C-Cation Techs., LLC*, IPR2014-00454, Paper 12 (PTAB Aug. 29, 2014) (informative).

C. The Petition impermissibly relies on expert testimony to supply missing claim elements

37 CFR § 42.104(b)(4) requires that a petition “specify where each element of the claim is found in the prior art patents or printed publications relied upon,” and per 35 U.S.C. § 312(a)(4), the Board shall deny a petition that fails to comply with the regulations promulgated by the director, including 37 CFR § 42.104(b)(4). Here, the Petition alleges throughout that the claims “are obvious in further view of the *knowledge of the skilled artisan.*” The Petition’s failure to comply with 37 CFR § 42.104(b)(4) will be discussed in more detail in the POPR, but the Petition’s impermissible reliance on Dr. Cooper to supply missing claim elements is particularly stark in Grounds 3 and 5.

In Ground 3, Petitioner relies solely on the opinion of Dr. Cooper to supplement the insufficient disclosure in the references, stating without reference to any patent or printed publication that “a POSA [] *would have understood that he or she could easily analyze multiple species in the population at the same time* using the available sequencing technology by using sample tagging.” Paper 1 at 53. Ground 5 similarly relies solely on the opinion of Dr. Cooper for the claim element of “summing counts,” where, by Petitioner’s own admission, the reference relied upon taught “computing a median and *not a sum of the counts.*” Paper 1 at 59.

By relying on the “knowledge of a POSA” solely from Dr. Cooper’s opinions, the Petition plainly goes beyond the teachings of prior art patents and publications.

D. Petitioner’s central arguments in this IPR are inconsistent with the positions it has previously taken

Central arguments in the Petition are contradicted by positions Petitioner has taken elsewhere while defending and enforcing its own *later filed* patents, as explained below and as will be described in more detail in the POPR.

The claims here recite a step of “counting the number of unique tagged nucleic acid molecules that have been assigned to the same location on the reference genome based on the mapping step.” EX1001, 35:39-41. The recited “unique tagged nucleic acid molecules” each comprise “a segment of [...] the genomic nucleic acids” and “a nucleic acid tag.” EX1001, 35:22-24. Thus, the step of “counting the number of unique tagged nucleic acid molecules” includes counting molecules that have a combination of (i) a “*nucleic acid tag*” sequence and (ii) a sequence of a “*segment*” assigned to “*a location* ... by mapping.” EX1001, 35:33-36; *See, also* 15:5-14.

In the Petition, Guardant along with their expert acknowledge that a “difference between this claim step” and the prior art “is that this claim step involves counting ‘unique tagged nucleic acid molecules.’” Paper 1 at 40. However, they allege that “a skilled artisan would have found it obvious to include tagging and amplification with Lo’s method. Having been motivated to modify Lo’s method to

use tagging and amplification, a POSA would have naturally counted the ‘unique’ molecules.” *Id.* at 40.

Yet, when asserting its own *later-filed* patents in a District Court litigation, Guardant has argued that “grouping sequencing reads into families based on sequence information of the molecular barcodes,” i.e. using *nucleic acid tags*, “and beginning and end base positions of the mapped portion of progeny polynucleotides,” i.e., a *segment* sequence, “*was not routine, well-understood, or conventional*, as it leverages a *combination of barcode sequence* and *mapping location* [] to provide unique grouping to families using non-unique tagging.” EX2008 at 25 (Plaintiffs’ First Amended Complaint for Patent Infringement, *Guardant Health, Inc., v. Tempus AI, Inc.* 1:24-cv-00687-RGA (D. Del. filed November 4, 2024)).

Additionally, in IPR2019-00130, relying on an analogous argument, Guardant avoided institution of an IPR against its own U.S. Patent No. 9,598,731 (with an earliest priority date of September 4, 2012) in part because it persuaded the Board that it would not have been obvious to use “non[-]unique *barcodes*”, which “*in combination with sequence data at the beginning (start) and end (stop) portions* of individual sequencing reads [] may allow for the assignment of *a unique identity* to individual sequences.” EX2006, pp. 5 and 27 (*Foundation Medicine, Inc., v. Guardant Health, Inc.* IPR2019-00130, Paper 7 (March 6, 2019)).

Thus, while defending and enforcing its later-filed patents, Guardant had argued that “grouping sequencing reads into families based on sequence information of the molecular barcodes and beginning and end base positions of the mapped portion of progeny polynucleotides” was not routine, not well-understood, and not conventional because it “leverages a *combination of barcode sequence and mapping location* [] to provide unique grouping to families” EX2008 at 25. However, in this attempt to attack CSHL’s patents that were filed years *before* those Guardant patents, Guardant takes the opposite position. Such contradiction further shows the weakness of the Petition and counsels against institution.

V. GUARDANT’S LONG AWARENESS OF THIS FAMILY OF PATENTS WEIGHS IN FAVOR OF DENIAL OF THE PETITION

Guardant has been aware of this family of Patents since at least November 2016, when it began citing in the prosecution of its own, later-filed, patent applications CSHL’s U.S. Application Publication (US 2014-0065609) whose disclosure is shared by each of the ‘156, ‘589 and ‘510 Patents. *See* EX2012.

Moreover, in January 2019, an Opposition was filed at the EPO against counterpart EP Patent No. 2,630,263 by James Poole Limited. Guardant has since admitted in the Litigation that they were behind the Opposition. *See, e.g.,* EX2010, p. 2 (Guardant characterizing arguments by the opponent in the Opposition as “*Guardant’s* arguments”). The EPO Opposition ended in June 2021 when the EPO

upheld CSHL's European patent in amended form. Guardant certainly knew or should have known of the issuance of the counterpart '589 Patent three months earlier in March 2021. Despite being sufficiently concerned to bring an EP Opposition, Guardant chose to not promptly bring an IPR or PGR against the '589 Patent upon its issuance. Instead, Guardant waited over 4 years to challenge its validity.

In the EPO Opposition, the counterpart European Patent was maintained in amended form and was found to be novel and inventive over many of the same prior art references cited by Petitioner in this IPR. As discussed above, the Opposition Request filed on behalf of Guardant outlining its arguments for unpatentability, as well as the references cited in the Opposition, were provided to and considered by the Examiner during prosecution of the '589 Patent.

VI. CONCLUSION

Numerous factors favor discretionary denial. Patent Owner respectfully requests that the Director deny institution of this IPR.

Respectfully submitted,

/Gary J. Gershik/

Dated: October 1, 2025

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CERTIFICATE OF COMPLIANCE

Pursuant to the Interim Director Discretionary Process, the undersigned hereby certifies that this brief complies with the type-volume limitation of Section II.C.iii because this brief contains 20 pages.

/Darren Haber/

Dated: October 1, 2025

Darren Haber (Reg. No. 80,964)

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GUARDANT HEALTH, INC.,
Petitioner,

v.

COLD SPRING HARBOR LABORATORY,
Patent Owner.

Case IPR2025-01355

Patent 10,947,589

CERTIFICATE OF FILING AND SERVICE

The undersigned hereby certifies that true and correct copies of PATENT OWNER'S DISCRETIONARY DENIAL OF INSTITUTION BRIEF, and EXHIBITS 2002-2003 and 2006-2012 are being electronically filed via The Patent Trial and Appeal Case Tracking System (P-TACTS) system and served this 1st day of October 2025 by electronic service by agreement between the parties pursuant to 37 C.F.R. §42.6(e)(1), via electronic mail at the email addresses listed below:

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Dated: October 1, 2025

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