

UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

FORESIGHT DIAGNOSTICS INC.,
Petitioner,

v.

PERSONALIS, INC.,
Patent Owner.

IPR2023-00317
U.S. Patent No. 11,408,033

**PETITIONER'S AUTHORIZED RESPONSE
TO PATENT OWNER'S NEW SUR-REPLY
EVIDENCE AND ARGUMENTS**

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Chicago Manual of Style (EX2178): EX1216 puts “capture” in quotes to highlight it as a scientific term, after stating in the preceding sentence, without the use of quotes, that “[t]he major differences with all the platforms [including “traditional multiplex PCR”] are the way in which *multiple loci are captured and amplified*.” EX1216.1. “[O]ligo-probes,” i.e., hybrid capture baits, are then listed as a quote/unquote “capture” mechanism right after PCR. *Id. See also* EX1220 at 24:2-4 (Personalis Executive describing pulldown probes having “a physical, often referred to as a, *quote/unquote*, pull-down that occurs.”).

Dudley 2021 (EX2181): There is no dispute that PCR primers comprise “a nucleic acid sequence that hybridizes to target DNA...in solution,” and Personalis’s witnesses confirmed that they “can physically capture and isolate the target DNA.” Reply 15-16. Thus, PCR primers satisfy even Personalis’s (incorrect) construction. Personalis responded that “Foresight has no reply to” (new exhibit) EX2181’s statement that “hybrid capture-based workflows” can take longer than PCR (days instead of hours)¹ and can be more expensive. Sur-Reply 15. This is a strawman: there is no dispute that there are different types of capture probes and that each may have pros and cons in certain situations, none of which are recited in the claims. Moreover, none of the considerations

¹ Such timing differences are immaterial to the claims. *See e.g.*, EX1030, Fig. 4. Indeed, delays for materials to be shipped are not uncommon. *See* EX1220 at 18:17-23:1.

mentioned in 2021 by EX2181 – which emphasizes the overlapping applicability of PCR capture probes (referencing Forshew) and hybrid capture baits (referencing Newman) for MRD detection and tumor genotyping of various types of polymorphisms – teach away from using either approach. EX2181.201.

Chadhuri 2015 (EX2185) / Bratman 2015 (EX2186): In Ground 3, Personalis suggests that a POSA would not have been motivated to repeat Wagle’s assay on a subsequent plasma sample. POR78-79.² Personalis did not introduce EX2185 or EX2186 with its POR. It now raises the new argument that these exhibits’ mention of an ongoing desire in the art for improved sensitivity and specificity of cfDNA monitoring techniques for *clinical* use would have negated a POSA’s motivation to analyze cfDNA. Sur-Reply 25. But the claims do not require clinical applications or recite minimum sensitivities. Indeed, Personalis’s NeXT is “used in research only.” EX2001.2; EX2012.031, ¶10. Moreover, as Dr. Quackenbush explains, the cited articles note “challenges” because “[t]he way scientists typically write papers is to point out what a challenge is and then describe how one overcomes that challenge,” usually to highlight what they see as an advance of their paper. EX2188 at 263:2-10. This in no way undermines the motivation raised in the Petition.

² Ground 3 established the obviousness of repeating the claimed assay on either (i) additional tumor samples; or (ii) plasma samples. This belated sur-reply argument relates only to subpart (ii).

Moreover, Personalis's counsel has elsewhere advanced positions directly at odds with its characterizations of EX2185 and EX2186. *See NeoGenomics Labs., Inc. v. Natera, Inc.*, No. IPR2024-00346, Paper No. 1 (PTAB Dec. 19, 2023). In *Neogenomics*, relying on Forshew (Ex. 1030), counsel asserted that “sequencing tumor DNA to identify tumor-specific mutations, followed by collecting a cfDNA sample from the blood stream of the cancer patient and then amplifying and sequencing the cfDNA to check if the tumor-specific mutations are present...*is, on its face, not remotely inventive*.” *Id.* at 1. Consistent with Foresight's position, Personalis's counsel further stated that Forshew “teaches that mutations had long since been detected, including in ctDNA, *by a slew of different methods* down to a level of 1 in 10,000, which corresponds to a sensitivity of 0.01%.” *Id.* 44.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify, pursuant to 37 C.F.R. section 42.6, that on February 29, 2024, that a complete copy of the foregoing document is being served via electronic mail upon:

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