

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

Foresight Diagnostics Inc.,
Petitioner,

v.

Personalis, Inc.,
Patent Owner.

Case No: IPR2023-00546
U.S. Patent No. 10,450,611

PETITIONER'S REPLY TO
PATENT OWNER'S PRELIMINARY RESPONSE

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I. Claim Construction: “personalized genetic testing”

Patent Owner (PO) contends that the preamble, “a method for personalized genetic testing” is “limiting” but offers no explanation of what is required for genetic testing to be “personalized.” See POPR 16-18. In its analysis of the Petition’s grounds, PO then uses the “limiting preamble” to imply claim elements that do not exist. Petitioner submits that review can be instituted without determining whether the preamble is limiting or otherwise construing it because the Petition establishes that the prior art’s methods are “personalized” under any reasonable understanding of the term. *Axalta Coating Sys., LLC v. Ppg Indus. Ohio, Inc.*, No. IPR2022-00676, 2022 WL 4139422, at *3 (P.T.A.B. Sept. 12, 2022). (“The Board is required to construe ‘only those terms ... that are in controversy, and only to the extent necessary to resolve the controversy.’”).

As an example, the specification explains that in a method for “personalized genetic testing, initial information gathered on an individual subject (who may be a medical patient) may be used to design and synthesize chemical reagents,” which “may be used for further testing.” Ex. 1001 at 28:16-22. “By using information from a first operation to synthesize chemical reagents specific to the subject being tested, the subsequent testing may be better focused on the personal characteristics of the subject.” *Id.* 28:22-26. Moreover, the specification describes conducting personalized genetic testing “by sequencing

both the tumor and germline DNA samples with a generic assay (e.g., an exome), to determine which variants are somatic. This may lead to a personalized assay with a smaller footprint.” *Id.* 63:55-62. Similarly, the specification notes that “initial assays which sequence DNA or RNA from the subject’s tumor or a germline sample” may then be “used as the basis for designing nucleic acid sequences to be array synthesized to create a personalized assay.” *Id.* 64:14-18.

The methods for identifying and testing mutations in a particular patient disclosed in the cited art are consistent with how the specification repeatedly describes “personalized” methods. Thus, even if the preamble were “limiting,” the manner in which it limits the claims does not exclude the personalized, patient-specific, genetic testing disclosed in the cited art. In just one example, consistent with the specification’s exemplary “personalized” assays, Ley first performed whole-genome sequencing of tumor and germline DNA and then “us[ed] the identified mutations to design PCR primer probes specific to each selected mutation” identified in the patient thereby “synthesizing chemical reagents *specific to the subject*” to conduct personalized genetic testing. Quackenbush ¶¶83-84; *accord* Ex. 1001 at 28:16-22.

PO fundamentally distorts Ley’s teachings, claiming that it “teaches away from using personalized panels” and instead discloses methods “for discovering mutations that are responsible for initiation and pathogenesis of AML and other types of cancer across entire patient populations.” POPR 19-20. This is

exemplified by PO's use of ellipses to re-draft Ley to appear consistent with its argument. POPR 19 (below).

genes that may respond to targeted therapies.”); *id.* at 71 (“In summary, we have successfully used a next-generation whole genome sequencing approach to identify new candidate genes that may be relevant for AML pathogenesis...the identification of the true somatic mutations in this tumour genome would not have been feasible without this approach.”). Accordingly, Ley does not describe a method

The omitted sentence confirms Ley's methods are personalized: “We cannot overemphasize the importance of parallel sequencing of *the patient's* normal genome to determine which variants were inherited.” Ex. 1012 at 71. A POSA would have understood that Ley actually implemented and advocated for *personalized* testing focused on the characteristics of that patient's cancer, rather than approaches directed to a general population: “Ley's approach ... uses an initial whole-genome sequencing step to understand the nature of the *patient's tumor*, [to] help avoid ‘miss[ing] key mutations,’ and only after that information is collected, a specific set of probes for further sequencing of key mutations can be created.” Quackenbush ¶¶85, ¶¶175-76. *See* Ex. 1012 at 70 (explaining that “most of these genes would not have been candidates for directed re-sequencing on the basis of our current understanding of cancer” absent Ley's initial sequencing of the *patient's* tumor genome); *id.* (analyzing “ten non-synonymous somatic mutations [that] were identified *in this patient's tumour genome.*”).

Additionally, PO acknowledges that Newman's method is called “cancer

personalized profiling by deep sequencing or ‘CAPP-Seq,’” POPR 13, confirming that Newman’s methods are personalized. PO then contends that Newman’s “selectors are designed not from the patient’s tumor samples, and instead correspond to ‘recurrent mutations in potential driver genes.’” POPR 34. This ignores the fact that the Petition specifically relies on Newman’s application of its techniques to a tumor sample “using a 157-kb **personalized** selector followed by sequencing to cover mutations in the tumor that Newman discovered in its patient-level analysis of the tumor tissue.” Quackenbush ¶182 (describing Newman’s creation of a “157-kb **personalized** selector ... that selectively enriched the target sequences of the GBM tumor.”).

PO urges the Board to disregard Newman’s express disclosure of the claimed methods because “this experiment was [] not a method for personalized genetic testing and instead was a validation experiment.” PO bases this contention on Newman’s statement that one purpose of the experiment was “to establish the detection limit of iDES-enhanced CAPP-Seq[.]” POPR 34-35. *See also id.* at 27-28 (arguing that Ley’s express disclosures should be disregarded as a “validation experiment”). Thus, PO’s urging of a “limiting” construction of the preamble appears to also require that one practicing the method have a specific intent to perform the same steps in the future as a so-called “going forward method” or patient-facing diagnostic test. Despite PO’s implications, the specification does not limit “personalized genetic testing” to methods with

patient diagnosis as their sole and only purpose, as discussed above. Nor does the fact that a method that interrogates the genetic signature of an individual may also provide information useful on a more general level (such as to understand population-level cancer genetics) mean that such methods are not “personalized.” And while there is a disputed factual issue regarding how a POSA would have understood the prospective teachings of the references, the actual performance of the claimed methods even a single time – demonstrated by each of Ley and Newman using probes tailored to a particular patient – is sufficient to invalidate the claims.

II. Alleged Secondary Considerations

PO’s allegations regarding secondary considerations are overstated, given the reasonable likelihood that at least one claim is anticipated, and “secondary considerations are not an element of a claim of anticipation.” *Cohesive Technologies, Inc. v. Waters Corp.*, 543 F.3d 1351, 1364 (Fed. Cir. 2008). Moreover, given that PO’s arguments were first raised in the POPR, it would be inappropriate “to hinge the outcome of a Decision to Institute” on an incomplete record, where Petitioner “has not yet been given an opportunity for discovery, much less [to] present evidence at trial in response.” *Invata, LLC v. OPEX Corp.*, No. IPR2022-01604, 2023 WL 2597830, at *4 (P.T.A.B. Mar. 17, 2023).

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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 June 2, 2023, a complete copy of **PETITIONER 'S REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE** was served upon the following, by ELECTRONIC MAIL:

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