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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ANTTI E. SEPPO, FIONA GINTY, KEVIN B. KENNY, DAVID LAVAN HENDERSON, MICHAEL J. GERDES, ADRIANA INES LARRIERA, XIAOFENG LIU, ALEX D. CORWIN, STEPHEN E. ZINGELEWICZ, THOMAS HA, NATALIA R. JUN, AINURA KYSHTOOBAYEVA, DENISE A. HOLLMAN-HEWGLEY, and YING LI[1]

Appeal 2021-004837
Application 14/388,057
Technology Center 1600

Before DONALD E. ADAMS, ERIC B. GRIMES, and JEFFREY N. FREDMAN, *Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a tissue imaging method, which have been rejected for nonenablement. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

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[1] Appellant identifies the real party in interest as the Danaher Corporation. Appeal Br. 2. "Appellant" refers to "applicant" as defined in 37 C.F.R. § 1.42.

STATEMENT OF THE CASE

Claims 1, 2, 7, 12, 17, 19–22, 28, and 34 are on appeal. Claim 1, reproduced below, is illustrative (emphasis added):

> 1. A method of generating a composite image of a region of interest in a human tissue sample comprising the steps of:
>
> 1) generating a first image including said region of interest of said sample having undergone a first protocol but not a second protocol, wherein the first protocol comprises: (i) binding a human target protein-specific *monoclonal antibody labeled with a fluorophore* to the human target protein in the sample, wherein said human target protein is selected from the group consisting of EGFR, Her2, ALK, galactosyl transferase II, neuron specific enolase, proton ATPase-2, acid phosphatase, Ki67, cyclin E, p53 and cMet; (ii) detecting by immunofluorescence the bound fluorophore to generate the first image, and (iii) staining the sample with *a fluorescent marker that provides morphological information*, and;
>
> 2) digesting said sample with a protease after generating the first image but before said sample has undergone the second protocol;
>
> 3) generating a second image including said region of interest of said sample after having undergone the second protocol, wherein the second protocol comprises: (i) hybridizing *a nucleic acid probe labeled with a fluorophore* to a target nucleic acid in the sample, wherein the target nucleic acid encodes a selective portion of the human target protein; and (ii) detecting by immunofluorescence the hybridized probe fluorophore to generate the second image wherein the nucleic acid probe is a DNA or RNA of from 4 to 50 nucleotides; and
>
> 4) generating a composite image that includes at least the region of interest from each of the first and the second images by *registering fluorescent signals* from the first image with fluorescent signals from the second image

> and *aligning and overlaying the first and second images based on the morphological information*.

OPINION

Claims 1, 2, 7, 12, 17, 19–22, 28, and 34 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that "the specification, while being enabling for the method of claim 1 wherein different fluorophores are used in each part of step 1) and 3), does not reasonably provide enablement for use of the same fluorescent label/marker/signal for all steps." Final Action[2] 8.

The Examiner reasons that,

> if the label used for the monoclonal antibodies and the label used on the nucleic acid probes is the same as that which is to provide "morphological information", one would not be able to accurately and reproducibly >>register<<, in a composite image, the fluorescent signals from each of the different binding reactions, as they would all be the same.

Id. The Examiner acknowledges the Specification's Example 1, "teaching the use of different labels," but notes that "narrowing limitations cannot be read into the claims." *Id.* at 9.

In the Answer, the Examiner also "note[s] that an applicant is required to enable the making and use of their invention." Ans. 5. The Examiner states that the Specification's "Examples . . . use[] multiple labels on the different antibodies and nucleic acid probes. The disclosure is silent as to how one is to utilize a composite image where all labels for antibodies and nucleic acid probes all have the same fluorescent label and are thusly indistinguishable." *Id.*

[2] Office Action mailed Sept. 24, 2020.

Appellant argues that the "Examiner acknowledges that Appellant's specification provides an example of using different markers," so the "assertion of lack of enablement is based on matter that is enabled by the specification, but not expressly recited by the claims." Appeal Br. 5. Appellant also argues that "the protease digestion removes the immuno-fluorescence associated with the first image," so "[e]ven if the same label were used, the images of step 1) and of step 3) would be distinguishable, because in step 3), the immunofluorescence associated with the first image is not present in view of the protease treatment of step 2)." *Id.* at 5–6.

Regarding the Examiner's concern about using an image generated with an antibody and nucleic acid probe having the same label, Appellant argues that "composite images generated by the claimed method using the 'same fluorescent label/marker/signal for all steps' are still useful, insofar as they provide data as to the location of the human target protein, morphological information, and target nucleic acid." Reply Br. 3.

Finally, Appellant argues that, "even if the embodiment, in which the 'same fluorescent label/marker/signal [is used] for all steps,' is hypothetically considered to be inoperative . . . [t]he presence of one or more inoperative embodiments within the scope of a claim does not necessarily render the claim invalid for lack of enablement." *Id.* at 4. Rather, Appellant argues, "the presence of inoperative embodiments merely prompts further consideration as to the number of such embodiments and whether identification thereof by a person of ordinary skill in the art would require undue experimentation." *Id.*

We agree with Appellant that the Examiner has not made out a prima facie case that the claimed method is not enabled by the Specification. "[A]s

part of the quid pro quo of the patent bargain, the applicant's specification must enable one of ordinary skill in the art to practice the full scope of the claimed invention." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003).

> That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art.

Id.

Here, the Examiner has posited one variant of the claimed method—in which "the same fluorescent label/marker/signal [is used] for all steps" (Final Action 8)—that in his view would not yield useful information. But the Examiner's reasoning itself suggests that a skilled artisan would *expect* that embodiment to be of limited or perhaps no utility, and thus those of skill in the art would have known to avoid it. *See* Ans. 4 ("It stands to reason that if the label[s] used . . . [are] the same . . . , one would not be able to accurately and reproducibly >>register<<, in a composite image, the fluorescent signals."). The enablement analysis must take into account the knowledge of those skilled in the art. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334 (Fed. Cir. 2003) ("[T]he requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'").

As Appellant has pointed out, the Examiner's reasoning at best identifies a single inoperative embodiment that is encompassed by the claims. As the Court of Appeals for the Federal Circuit has held:

> Even if some of the claimed combinations [are] inoperative, the claims are not necessarily [nonenabled]. . . . Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid. That, however, has not been shown to be the case here.

Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576–77 (Fed. Cir. 1984).

The Examiner has not persuasively shown that undue experimentation would be required to practice the claimed method using appropriate fluorescent labels for the recited monoclonal antibody, morphological staining, and nucleic acid probe. The rejection of claims 1, 2, 7, 12, 17, 19–22, 28 and 34 under 35 U.S.C. § 112, first paragraph, is reversed.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 2, 7, 12, 17, 19–22, 28, 34	112, first paragraph	Enablement		1, 2, 7, 12, 17, 19–22, 28, 34

REVERSED