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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/777,842	02/26/2013	BRIAN JON PETER	20100165-01	2560

22878 7590 05/29/2018

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EXAMINER
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ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
05/29/2018	ELECTRONIC

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte BRIAN JON PETER

Appeal 2017-008386[1]
Application 13/777,842[2]
Technology Center 1600

Before TONI R. SCHEINER, ULRIKE W. JENKS, and JAMES A. WORTH, *Administrative Patent Judges*.

WORTH, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellant appeals under 35 U.S.C. § 134(a) from the Examiner's Final Rejection of claims 1–20, which are all pending claims. We have jurisdiction under 35 U.S.C. §§ 134 and 6(b).

We reverse.

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[1] Our Decision refers to Appellant's Appeal Brief ("Appeal Br.," filed June 9, 2016) and Reply Brief ("Reply Br.," filed May 15, 2017), and the Examiner's Final Office Action ("Final Act.," mailed Feb. 1, 2016) and Answer ("Ans.," mailed Mar. 16, 2017).

[2] According to Appellant, the real party in interest is Agilent Technologies, Inc. Appeal Br. 3.

Statement of the Case

Background

Appellant's application "relates, in part, to a method for genome partitioning." Spec. 1:7. "Methods for genome partitioning, i.e., separating selected regions of a genome from other regions, find use in a variety of genomic analysis applications, including, but not limited to SNP analysis, sequencing, mutation detection and the detection of chromosomal rearrangements." *Id.* at 1:4–7.

A C-probe is an oligonucleotide, consisting of RNA, DNA, or a combination of RNA and DNA, and is called a "C-probe" because it forms a "C" shape when it hybridizes to a target nucleic acid. *See* Spec. 14:13–19. In one embodiment, C-probe 2 contains oligonucleotide sequence 18 (a sequence of defined length), first region 10' and second region 12', where the first region 10' hybridizes to a first genomic sequence 10 and the second region 12' hybridizes to a second genomic sequence 12. *Id.* at 14:6–9, Fig. 1. According to the disclosure, exonuclease T may be used to trim the 3' end of the target nucleic acid. *Id.* at 16:17. After the 3' end of the target nucleic acid has been trimmed, the 3' end of the first sequence is extended using the C-probe as a template. *Id.* at 16:24–25. The target sequence may be further processed, e.g., by removing the 5' end of the target sequence and ligating the resulting ends of the DNA containing the target sequence, i.e., into a covalently closed circular DNA molecule. *Id.* at 17:6–7, 19:11–15. The C-probe may be used in this manner to capture the target sequence. *See id.* at 20:6–7, Figs. 2A, 2B. In one further embodiment, the methylation status of the target sequence can be compared from different samples. *Id.* at 21:1–2.

The Claims

Claims 1 and 20 are the independent claims on appeal. Claim 1, reproduced below, is illustrative of the subject matter on appeal:

> 1. A method of processing a nucleic acid, comprising:
>
> (a) hybridizing a C-probe to a strand of a target nucleic acid to produce a complex, wherein:
>
> (i) said strand comprises a target sequence that is flanked by a first sequence and a second sequence, and
>
> (ii) said C-probe comprises a first region that hybridizes to said first sequence, a second region that hybridizes to said second sequence, and an oligonucleotide sequence between said first and second regions,
>
> (b) enzymatically removing any 3' overhang from the target nucleic acid of said complex to produce a 3' hydroxyl group at the 3' end of said first sequence;
>
> (c) extending the 3' end of said first sequence using the oligonucleotide sequence of said C-probe as a template, wherein said extending results in a 3' hydroxyl group that is adjacent to the 5' end of said second sequence;
>
> (d) enzymatically removing any 5' overhanging from the target nucleic acid, either before or after said extending of step (c), to produce a 5' phosphate group at the end of said second sequence; and
>
> (e) ligating the 5' phosphate group at the end of the second sequence to the 3' hydroxyl group that is adjacent to the 5' end of said second sequence to produce a circular DNA molecule that contains said target sequence and the complement of said oligonucleotide sequence.

Appeal Br., Claims App.

The Issues

A. The Examiner rejected claim 20 under 35 U.S.C. § 101 as being directed to patent ineligible subject matter.

B. The Examiner rejected claims 1–20 under pre-AIA 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

C. The Examiner rejected claims 1–20 under pre-AIA 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.[3]

A. 35 U.S.C. § 101

The Examiner determines that claim 20 is directed to a kit that comprises a C-probe as well as a "one or more enzymes that remove 5' and 3' single stranded overhangs; and a DNA ligase." Final Act. 2. The Examiner determines that "one or more enzymes that remove 5' and 3' single stranded overhangs" as well as DNA polymerase and DNA ligase, are all recognized as being products of nature without significantly more, and therefore fall under the laws of nature or natural phenomena exceptions. *See id.* at 2–3. The Examiner determines that no evidence has been presented showing that the presence of the probe will result in markedly different characteristics to either the "one or more enzymes" or to the "DNA ligase." *Id.* at 3.

Appellant argues, *inter alia*, that "[t]he inclusion in the kit of additional components, even components derived from a natural source, in no way negates that clearly statutory C-probe component of the kit (which

[3] Certain other rejections, i.e., under 35 U.S.C. §§ 102 and 103, have been withdrawn. Ans. 18–19.

the Examiner has acknowledged does not occur in nature)." Appeal Br. 4. Appellant also contends that the Examiner has failed to comply with the recently published guidelines entitled "Subject Matter Eligibility Examples: Life Sciences" (May 2016). *Id.* at 5.

The statutory provision at issue, 35 U.S.C. § 101, states that "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."

"Laws of nature, natural phenomena, and abstract ideas are not patentable." *Mayo Collaborative Services v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1293 (2012) (citation omitted). The Supreme Court articulated a two-step test for patent eligibility under § 101 that "distinguish[es] patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014) (citing *Mayo*, 132 S. Ct. at 1296–97). "First," Alice instructs a court to "determine whether the claims at issue are directed to one of those patent-ineligible concepts." *Id.* (citation and quotations omitted). If the claims are directed to a patent ineligible concept then the court must proceed to the second step of the test—the "search for an inventive concept—i.e., an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the ineligible concept itself." *Id.* (quotations and alterations omitted).

Turning to the first step of the *Alice* test, although certain of the individual elements of claim 20 are naturally occurring, we are persuaded by

Appellant's contention that the C-probe and the combination of elements, as recited in the kit of claim 20, are not naturally occurring. In particular, we agree with Appellant that the recited C-probe has not been shown to be a product of nature. Independent claim 20 recites that "the 3' end of said C-probe is blocked to prevent the addition of nucleotides by a polymerase or a ligase." Appeal Br. 19, Claim App. As defined in the Specification,

> [t]he term "blocked", in the context of an oligonucleotide that is blocked at its 3' end when it is annealed to a target nucleic acid, refers to an oligonucleotide that cannot be extended by a template-dependent polymerase, either because the 3' end of the oligonucleotide has a non-natural nucleotide at the 3' end (e.g., by a dideoxy nucleotide or any of a multitude of nucleotides that are not substrates for the polymerase) or because the 3' end of the oligonucleotide is mis-matched with the target, i.e., because one or more nucleotides at the 3' end of the oligonucleotide are not complementary to correspondingly positioned nucleotides in the target sequence). In certain cases, blocked oligonucleotides cannot be digested by a 3' to 5' exonuclease, e.g., because one or more phosphodiester linkages has been altered to become, for example, a phosphothioate linkage.

Spec. 13:23–14:2. Accordingly, the C-probe either contains a non-natural nucleotide or contains one or more non-complementary nucleotides at the 3' end such that the 3' end is functionally blocked. The Examiner has not shown such a C-probe to be naturally occurring, neither alone nor with the correspondingly-recited enzymes, i.e., as in the kit of independent claim 20.

Accordingly, we reverse the Examiner's rejection based on that ground.

B. 35 U.S.C. § 112 (Enablement)

> The Examiner determines, *inter alia*, that:
>
> [t]he nucleotide sequence for the genome of any given species of bacteria is highly unpredictable.
> . . . In order to practice the full scope of the invention, one would have to first determine the nucleotide sequence for each and every organism, much less any gene of interest, in order to identify the correct nucleotide sequences for all probes and/or primers essential to the claimed invention. Such information is neither provided by the disclosure nor the art of record.

Final Act. 10–11. Thus, as we understand it, the Examiner's rejection is based on the fact that the claims encompass, prospectively, the detection of any and all target nucleic acids, in any and all types of organisms, for which the nucleotide sequences, as well as the sequences of suitable probes, have not yet been determined. Therefore, the Examiner reasons, practicing the full scope of the claimed method requires sequencing any and all organisms, which would take a significant amount of time and effort. *See id.* at 11 ("In order to determine the appropriate primers for the tens of millions of bacteria that are not known yet encompassed by the claimed method, one would need to determine the nucleotide sequence of the various target sequences.").

Appellant asserts that "the specification provides a detailed description of how the method can be implemented and that several 76 million individual sequences from over 260,000 named organisms (including the entire human and mouse genomes) were publicly available from NCBI's Genbank database at the time of filing (*see*, e.g., Nucl. Acids Res. 2008 36: D25-D30)." Appeal Br. 7.

The issue with respect to this rejection is: Does a preponderance of the evidence of record support the Examiner's conclusion that there is a lack of enablement for claims 1–20?

We are persuaded by Appellant that a preponderance of the evidence of record does not support the Examiner's conclusion of non-enablement.

As our reviewing court has explained, the Examiner "bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application." *In re Wright*, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993).

"The scope of enablement . . . is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation." *National Recovery Technols., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1196 (Fed. Cir. 1999).

While the Specification must enable the skilled artisan to practice the full scope of the claimed subject matter, "[i]t is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art." *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991). Moreover, a claim does not lack enablement merely because it encompasses inoperative embodiments. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984).

Rather, as the Federal Circuit has explained:

> [T]here must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill [in the art] how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue

> experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility.

Vaeck, 947 F.2d at 496 (footnote omitted).

In the present case, Appellant's claims are directed to a method and a kit for capturing a target sequence of DNA by hybridizing a C-probe to a target nucleic acid and extending the target sequence using the C-probe as a template. *See* Spec. 16:8–10, 16:24–25, 20:5–7, Figs. 1, 2A, 2B.

We agree with the Examiner that, given its broadest reasonable interpretation consistent with the Specification, Appellant's claim 1 encompasses detecting numerous target nucleic acids in addition to those exemplified in the Specification. The Examiner does not, however, advance specific persuasive evidence demonstrating sufficiently that an ordinary artisan (*see* Appeal Br. 7 (discussing knowledge in art); Ans. 25), would have needed to experiment unduly to determine suitable probe and target sequences for practicing the claimed invention.

We do not agree, with the Examiner's implication (*see* Final Act. 11) that Appellant must draft its claims in a manner that excludes application of the claimed process to such as yet undiscovered target sequences. *See In re Anderson*, 471 F.2d 1237, 1242 (CCPA 1973) ("It is always possible to put something into a combination to render it inoperative. It is not the function of the claims to exclude all such matters but to point out what the combination is."). In the present case, the claims are not directed to methods of sequencing every known organism. Rather, the claims are directed to a method and kit for capturing a target sequence using a C-probe and DNA processing enzymes. As noted above, Appellant's Specification describes how to perform the claimed process.

Accordingly, for the reasons discussed, we agree with Appellant that a preponderance of the evidence does not support the Examiner's prima facie case of lack of enablement. We, therefore, reverse the Examiner's rejection on that ground.

C. 35 U.S.C. § 112 (Written Description)

The Examiner determines, *inter alia*, that "[f]or purposes of examination, the claimed method (claims 1-19) as well as the claimed kit (claim 20), which is to comprise the C-probe, have been construed as encompassing probes that will hybridize to any conceivable target." Final Act. 23. The Examiner further states: "[i]n addition to no teaching of any actual and useful nucleic acid probes sequences (35 USC 101; specific, substantial, and credible utility), the disclosure has not been found to teach those nucleotide sequences that are useful in the bacteria, plants, viruses, etc., that are fairly encompassed by the claims yet not known to the public." *Id.* at 25.

Appellant argues that "the written description requirement does not require a specific description of every species encompassed by a claim." Appeal Br. 9. Appellant further asserts that the written description requirement is satisfied because "the specification provides a detailed description of how the method can be implemented and that several 76 million individual sequences from over 260,000 named organisms (including the entire human and mouse genomes) were publicly available from NCBI's Genbank database (see, e.g., Nucl. Acids Res. 2008 36: D25-D30)." *Id.* at 10.

The issue with respect to this rejection is: Does a preponderance of the evidence of record support the Examiner's conclusion that the Specification fails to provide descriptive support for the claims?

The Federal Circuit has explained:

> [T]he determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.

Capon v. Eshhar, 418 F.3d 1349, 1359 (Fed. Cir. 2005).

We find Appellant has the better position. The instant invention is not in the target sequences themselves, but rather the method of capturing target sequences using a C-probe and DNA processing enzymes.

The Specification refers to the deposit of sequences at NCBI's Genbank database for reference genomic regions. Spec. 8:13–30, 10:28–30. The instant facts are therefore also similar to those in *Falko-Gunter*, which teaches that "where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here 'essential genes'), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences." *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1368 (Fed. Cir. 2006) (footnote omitted).

We recognize, but find unpersuasive, the Examiner's finding that the Specification does not teach probe sequences. Final Act. 25. The Specification discloses the use of substantially complementary sequences and optionally, particular mismatches, e.g., G-A mismatches. *E.g.*, Spec., 5:24–6:20, 9:28–10:2, 18:9–17. We, therefore, conclude that the evidence of

record does not support the Examiner's conclusion that the Specification fails to provide descriptive support for the claims. Accordingly, we reverse the Examiner's rejection on that ground.

DECISION

The Examiner's decision to reject claims 1–20 is reversed.

REVERSED