

Filed on behalf of: ILLUMINA

By: Robert A. Lawler
rlawler@reinhardtllaw.com
(608) 229-2217

James G. Morrow
jmorrow@reinhardtllaw.com
(414) 298-8136

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ILLUMINA, INC.

Petitioner,

v.

Patent of THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF

NEW YORK

Patent Owner.

Case No. IPR2012-00007
U.S. Patent No. 7,790,869

PETITIONER ILLUMINA'S OPPOSITION TO
PATENT OWNER COLUMBIA'S MOTION TO AMEND

Illumina Ex. 1127 Illumina v. Columbia IPR2018-00291, -00318, -00322, -00385, and -00797

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I. INTRODUCTION

Patent Owner's motion to amend requested cancellation of original Claims 12- 33 from U.S. Patent No. 7,790,869. Petitioner does not oppose Patent Owner's request to cancel the original claims. Patent Owner's motion also requested entry of proposed amended Claims 3. Despite the Board publishing detailed requirements for filing motions to amend (*see, e.g.*, IPR2012-00027, Paper 26), Patent Owner's motion failed to comply with nearly every regulation and requirement governing the motion. In particular, Columbia: (1) failed to show why the proposed claims are patentable; (2) improperly attempted to incorporate statements from its Response and expert declaration into its motion to amend; (3) failed to address other known prior art references; and (4) did not show that the proposed claims are enabled. In addition to the numerous flaws in Patent Owner's motion, the proposed claims are still anticipated and/or obvious. The Board should therefore deny entry of Patent Owner's proposed amended claims.

II. LEGAL STANDARDS FOR A MOTION TO AMEND THE CLAIMS

In a motion to amend, "[t]he burden is not on the petitioner to show unpatentability, but on the patent owner to show patentable distinction over the prior art of record and also prior art known to the patent owner." IPR2012-00027, Paper 26 at 7. Thus, the patent owner should submit evidence "about the specific technical disclosure of the closest prior art known to the patent owner, and not just

a conclusory remark that no prior art known to the patent owner renders obvious the proposed substitute claims.” *Id.* at 7. “A mere conclusory statement by counsel, in the motion to amend, to the effect that one or more added features are not described in any prior art, and would not have been suggested or rendered obvious by prior art, is on its face inadequate.” *Id.* at 8.

The Board has also reminded patent owners that “the motion itself should set forth the arguments and explanations with appropriate pinpoint citations to the expert declaration, rather than incorporating by reference the expert declaration.” IPR2013-00099, Paper 19, at 2. Indeed, the final rules expressly prohibit incorporation by reference of an argument from another paper. 37 C.F.R. § 42.6(a)(3) (“Arguments must not be incorporated by reference from one document into another document. Combined motions, oppositions, replies, or other combined documents are not permitted”). The final rules also explain that “the prohibition against incorporation by reference minimizes the chance that an argument would be overlooked and eliminates abuses that arise from incorporation and combination.” 77 Fed. Reg. 157, p 48617.

III. COLUMBIA CANCELED ALL OF THE ORIGINAL CLAIMS AT ISSUE IN THIS PROCEEDING

Columbia unambiguously requested cancellation of all original claims at issue in this proceeding, essentially conceding unpatentability of the cancelled original claims. Paper 79 at 4. Columbia did not make its request to cancel the

original claims contingent upon substitution of any amended claim. *Id.*; *see also* IPR2012-00027, Paper 26 at 10. Neither Columbia nor its expert, Dr. Trainor, have presented any argument regarding the validity of original claims. Illumina does not oppose Columbia's request to cancel the original claims. Therefore, original Claims 12- 33 should be canceled.

IV. COLUMBIA HAS NOT MET ITS BURDEN TO SHOW THAT THE PROPOSED AMENDMENTS SHOULD BE ENTERED

Patent Owner proposed a single new independent claim 34 having three substantive amendments: addition of the limitation "wherein the base is a deazapurine" to original independent claim 12 (proposed claim 34) from original dependent claim 15; deletion of "light" from the Markush group describing the cleaving means for the cleavable linker; and deletion of "light" from the Markush group describing the cleaving means for the cleavable 3' blocking group.

A. Patent Owner Improperly Incorporated Material by Reference to Attempt to Show that the Proposed Claims Are Patentable

Patent Owner's motion was required to "come forward with technical facts and reasoning" to explain why the proposed claims are patentable over prior art of record and prior art not of record but known to Patent Owner. IPR2012-00027, Paper 26 at 7. It failed to do so. Patent Owner's Motion summarizes its argument for the patentability of proposed independent claim 34 in a single conclusory statement:

This amendment responds to two grounds of unpatentability, satisfying the requirement of rule 37 C.F.R. §42.121. Proposed claim 34 now includes all limitations of claim 15. Because grounds I and III did not include claim 15, proposed claim 34, and all the claims which depend from it, are free of grounds I and III.

Paper 79, page 10. The Motion to Amend is conspicuously silent, however, as to Grounds II¹ and IV. Patent Owner asserted patentability of Claim 34 based on the conclusory statement that Tsien and Stemple III “[do] not disclose the features of [original] claim 15.” Paper 79 at 9-10. Patent Owner did not indicate what feature of original Claim 15 is missing from Tsien and Stemple III. Patent Owner makes no representations regarding obviousness over Tsien in view of Prober I (Ground II), or Stemple III in view of Anazawa (Ground IV), and does not address patentability of the proposed claims over Stemple III in view of any other prior art reference. Thus, the Patent Owner, at a minimum, failed to provide evidence or reasoning supporting the non-obviousness of the claims over two of the specific grounds at issue in this proceeding. Moreover, the proposed claims are anticipated and/or obvious over this prior art. *See* Part VI below.

Likewise, Patent Owner provided only a single sentence regarding all other

¹ Although Section V.B. is captioned "Ground II" (Tsien in view of Prober I) the argument is directed to Columbia's position regarding Ground III, Stemple alone.

references known to Patent Owner: “Further, Patent Owner is not aware of any other prior art over which these claims would not be patentable.” Paper 79, page 10. This statement provides no evidence or reasoning, and does not even provide an indication that the Patent Owner considered other prior art. Patent Owner’s assertion is precisely the type of statement the Board has deemed to be “on its face inadequate.” IPR2012-00027, Paper 26 at 8.

Patent Owner’s motion does not include any technical facts or reasoning to support the proposed substitute claims being “patentable over the prior art of record, and over prior art not of record but known to the patent owner.” IPR2012-00027, Paper 26 at 8. Therefore, Columbia’s motion to amend should be denied.

At best, Patent Owner argued for the patentability of the new claims by inappropriately incorporating arguments from its Response and expert declaration into the motion to amend. *See* Paper 70 at 10-11. Such incorporation by reference is clearly impermissible. 37 C.F.R. § 42.6(a)(3) (“Arguments must not be incorporated by reference from one document into another document. Combined motions, oppositions, replies, or other combined documents are not permitted”). Patent Owner cannot be permitted to use its 43 page Response (Paper 78) and its 121 page expert declaration (Ex. 2033) to circumvent the 15 page limit on its motion to amend. The technical facts and reasoning supporting the proposed substitute claims must be in the motion itself. They are not in the motion, and thus

Patent Owner failed to meet its burden of showing that the amended claims are patentable. Patent Owner cannot use incorporation by reference to rehabilitate their facially inadequate motion to amend.

B. Columbia's Motion Failed to Address Several Known Prior Art References

Even if Columbia's incorporation by reference were proper, however, Columbia still failed to meet its burden because it did not show that the proposed claims are patentable over known prior art. IPR2012-00027, Paper 26 at 6 ("in all circumstances [patent owner should] make a showing of patentable distinction over the prior art"). Patent Owner did not explain how the proposed claims are patentable over several highly relevant prior art references, such as Prober II (Ex. 1004 at 18:58-68 & 19:4-7) (teaching incorporation of 7-deazapurines in polymerase-mediated, template directed, DNA sequencing reactions) and Hobbs (Ex. 1013 at 11:1-4) (teaching that attachment of a label to the 7-position of a 7-deazapurine with a linker is advantageous for DNA sequencing). These references were clearly known to the Patent Owner because they were submitted as exhibits with Illumina's Petition. Paper 5 at 29-31, 40-41, & 57-59.

Dr. Trainor's declaration does not cure Patent Owner's omission because Dr. Trainor made no attempt to show that the proposed claims are patentable over the particular teachings of Prober II or Hobbs. Ex. 2033. Indeed, Dr. Trainor admitted at his deposition that he made no effort to independently evaluate any potential

references for validity other than the grounds of rejection authorized by the Board in this proceeding. Trainor Tr. 385:16-386:16 & 176:9-14.

Dr. Trainor also failed to address obviousness in view of at least the following known prior art references: Ex. 1029, Herman; Ex. 1030 - Rosenblum et al.; Ex. 1032 – Ward; and Ex. 2015 - Metzker.

The Patent Owner has clearly failed to explain how the proposed claims are patentable over the prior art of record, and Patent Owner's motion should be denied for at least this reason. IPR2012-00027, Paper 26 at 7.

C. Patent Owner Failed to Show that the Proposed Claims are Definite Under 35 U.S.C. § 112(b)

Proposed Claim 34 amends two means-plus-function clauses. Paper 79 at Appendix A. Patent Owner, however, failed to identify any structure in the specification that could perform the specified functions of the two amended means-plus-function clauses. Regarding the base cleaving means-plus-function clause in particular, the only structure provided in the specification is a xenon lamp for photocleavage of a 2-nitrobenzyl cleavable linker. Ex. 1001 at 23:57-24:31. But Patent Owner has amended both means-plus-function clauses to delete the word “light.” When a specification lacks corresponding structure as required by 35 U.S.C. § 112(f), the claims fail to comply with 35 U.S.C. § 112(b). *Cardiac Pacemakers, Inc. v. St. Jude Med., Inc.*, 296 F.3d 1106, 1115-18 (Fed. Cir. 2002). Claim 34 can only comply with § 112(b) if the “physical means” and/or “physical

chemical means” of the proposed linker cleaving means is construed to encompass the only structure taught in the specification for this function – photocleavage with a xenon lamp. Absent this construction, Claim 34 is indefinite.

Moreover, even if proposed Claim 34 does not invoke 35 U.S.C. § 112(f), the claim is still indefinite. The specification provides no explanation for the terms “physical means,” “chemical means,” or “physical chemical means”; they are simply provided in a list, without any examples. ’869 patent at 10:45-56 and 14:1-

6. Dr. Trainor testified that this type of listing of cleavage mechanisms without examples is not sufficient to show possession of the claimed subject matter.

Trainor Tr. at 366:9-374:4; *see* Stemple III at 3:31-35; 9:55-10:3. Moreover, Patent Owner’s expert declarant did not know the meaning of any of these terms.

Trainor Tr. 397:8-404:11. If a purported expert cannot understand these terms, neither would an ordinarily skilled artisan. Thus, proposed Claim 34 is indefinite.

D. Patent Owner Failed to Show that the Proposed Claims Are Enabled Under 35 U.S.C. § 112(a)

Patent Owner failed to establish that the proposed claims are enabled under 35 U.S.C. § 112(a). In fact, Dr. Trainor admitted in deposition that he was not asked to and did not consider whether the proposed amended ’869 claims are enabled. Trainor Tr. 397:16-398:14.

Furthermore, Dr. Trainor’s declaration repeatedly asserted that making and using the claimed nucleotide analogs was extremely difficult and unpredictable.

For example, Dr. Trainor stated that there were “no reports of successful incorporation” by a polymerase of a 3’-OH removably capped nucleotide with a base having a cleavable linker. Ex. 2033 at ¶ 50. In addition, Dr. Trainor asserted that it would have required “multiple changes, each of which was associated with unknown and unpredictable outcomes” to arrive at the proposed claims. *Id.* at ¶ 64. Dr. Trainor indicated that “major obstacles” had to be overcome (*id.* at ¶ 76), that making the claimed nucleotide analogs would require “new chemical procedures” that would be “complex and fraught with difficulties” (*id.* at ¶ 82), that success would have been “totally speculative and unsupported by any scientific reason or literature” (*id.* at ¶ 84), and that the results of making an enzymatic incorporation could not have been predicted with any reasonable certainty (*id.* at ¶¶ 87. 136).

Despite Patent Owner’s various arguments of difficulty and unpredictability to make and use the claimed nucleotide analogs, Patent Owner did not provide evidence or explain why the proposed claims could have been made and used without undue experimentation. Accordingly, Patent Owner’s own evidence indicates that the proposed claims are *not* enabled under 35 U.S.C. 112(a), and Patent Owner’s motion should be denied for at least this reason.

V. SUBSTITUTE CLAIM 34 IS NOT “SUBSTANTIALLY IDENTICAL TO ORIGINAL CLAIMS 12 AND 15”

The Board should deny Columbia’s request to make a determination that

claim 34 is “substantially identical to original claims 12 and 15” (Paper 79, p. 10.), and instead make a determination that the proposed claims are “not substantially identical.” Columbia’s proposed claim 34 does not, as argued by Columbia, simply rewrite “claims 12 and 15 in independent form in substitute claim 34.” (Paper 79, p. 10.) Instead, Columbia has affirmatively removed an element from the two Markush groups of cleavage “means” – for both the 3’ OH group and the cleavable linker. (See Paper 79, App. A at 3.)

In fact, Columbia admits that the removal of the “light” limitations from the Markush groups of cleavage means are narrowing amendments: “Deletion of a member of a Markush group *is a narrowing amendment* so that the patent owner can no longer seek to enforce the patent against that alternative method.” (Paper 79, p. 11 (citation omitted; emphasis supplied).) Narrowing a claim through amendment in a post-issuance proceeding constitutes a “substantive change” to the scope of the claim and gives rise to intervening rights. 35 U.S.C. §§ 252 and 328(c); *Marine Polymer*, 672 F.3d 1350 (Fed. Cir. 2012). Accordingly, the Board should deny Columbia’s request, and instead make a determination that proposed claim 34 and the original patent claim 12 and 15 are *not* “substantially identical” within the meaning of 35 U.S.C. § 252.

Patent Owner does not argue that any original claims of comparable scope to substitute claims 35-54 exist. As such, the Board should find that claims 35-54 are

not substantially identical to any original claim.

VI. COLUMBIA'S PROPOSED CLAIMS ARE ANTICIPATED AND/OR OBVIOUS

A. Dr. Trainor's conclusion regarding the obviousness of claim 34 fails to consider the actual language of the claims

To the extent Dr. Trainor's declaration statements regarding the combination of Tsien and Prober I, and Stemple III and Anazawa, are considered for purposes of this Motion to Amend, they should be given little weight. Dr. Trainor's opinions are based on the incorrect premise that the claims require that the claimed nucleotide analogue is able to be incorporated by a polymerase. *See, e.g.*, Ex. 2033, ¶¶ 59(6); 67(8); 100(6); and 108(4). No such requirement exists in proposed independent claim 34, and neither Columbia's motion nor Dr. Trainor separately address any dependent claim with respect to this feature.

Proposed claim 43 requires that the nucleotide is "incorporated onto a primer," but the claim does not specify that the incorporation is performed by means of a polymerase, or that the nucleotide is incorporated into a growing primer extension strand instead of being a component of a primer before it is hybridized to a nucleic acid template. Similarly, proposed claim 49 requires only that the "cleavable chemical group does not interfere with the recognition of the nucleotide by a polymerase." Dr. Trainor admitted that this property is met by any 3' blocking group that allows incorporation by a polymerase. Ex. 2094 at 154:10-

156:22. For example, Tsien discloses an allyl 3'-OH blocking group, which would not interfere. Ex. 1002, at 24:29-30; Ex. 2094 at 106:14-108:21.

Because Dr. Trainor's conclusions regarding obviousness are based in part on features that do not appear in the claims, the Board should disregard the declaration testimony of Dr. Trainor regarding the combination of Tsien and Prober I, and Stemple III and Anazawa with respect to proposed claim 34, and the claims depending therefrom.

B. Proposed Claim 34 Is Obvious

Proposed Claim 34 is original Claim 15 rewritten in independent form. Petitioner supplied a detailed element-by-element analysis demonstrating the obviousness of original Claim 15 by Tsien in view of Prober I, and Stemple III in view of Anazawa (Paper 5 at 21-28 & 47-55), in addition to other references.

Neither Patent Owner's motion to amend nor Dr. Trainor explain why it would be nonobvious to use a deazapurine base in the nucleotide analogues of Tsien and/or Stemple III. Patent Owner's general citation to a broad swath of the Trainor Declaration (Paper 79 at 10, *citing* Ex. 2033 at ¶¶ 48-140) fails to provide sufficient specificity. Dr. Trainor does not assert that the limitation is missing from the combination of either Tsien in view of Prober I, or Stemple III in view of Anazawa. *See* Ex. 2033, ¶¶ 49-87 & 88-140, respectively. In particular, Dr. Trainor's declaration acknowledges the Anazawa discloses a deazapurine base; he

asserts only that the feature cannot be combined. *See* Ex. 2033, ¶ 138.

Thus, Patent Owner has not provided evidence to support its conclusory assertion of patentability. Paper 79 at 10. Likewise, the Patent Owner makes no citation to any specific argument of the Response, and merely asserts without explanation that an argument is “set forth.” *Id.* Patent Owner has failed to rebut the *prima facie* case for invalidity set forth in Illumina’s Petition; therefore, proposed Claim 34 is not patentable over the prior art of record in this proceeding. IPR2012-00027, Paper 26 at 7.

C. Proposed Claim 34 is Anticipated

The amended means-plus-function clauses do not provide a patentable feature to proposed Claim 34. As discussed *supra*, the only structure in the specification for a base cleaving means is a xenon lamp for photocleavage of a 2-nitrobenzyl cleavable linker. Ex. 1001 at 23:57-24:31. Accordingly, if the recited “means” are to have any meaning, they must encompass photocleavage with a xenon lamp. Dr. Trainor, however, confirms that at least Stemple III teaches a photocleavable linker between the label and the base, and a photocleavable 3’-OH cap. Ex. 2033 at ¶¶ 108, 111, 138. As such, if any of “a chemical means, a physical means, [or] a physical chemical means” are to have any meaning at all, they must encompass the prior art admitted by Dr. Trainor.

Furthermore, if even if proposed Claim 34 does not invoke 35 U.S.C. § 112(f), Patent Owner fails to establish Claim 34 is not anticipated. In particular, Patent Owner fails to provide reasoning or evidence that “a chemical means, a physical means, [or] a physical chemical means” excludes light. Dr. Trainor confirms that at least Stemple III teaches a photocleavable linker between the label and the base, and a photocleavable 3'-OH cap. Ex. 2033 ¶¶ 108, 111, 138. However, Dr. Trainor never argues the patentability of the actual language of Claim 34. Ex. 2033 ¶¶ 59, 67, 85, 100, 104, 108, 111, 112, 125, 133, 136, 138, 139. Claim 34 recites “a chemical means, a physical means, [or] a physical chemical means”. Dr. Trainor never asserts that these “means” exclude light. Thus, Patent Owner has not distinguished Claim 34 over Stemple III.

D. Patent Owner Has Not Shown That The Proposed Dependent Claims Are Patentable

Patent Owner adds various claims dependent from independent Claim 34. However, Patent Owner makes no assertion that any such dependent claim adds a patentable feature relative to the independent claim from which it depends. Claims 35-54 are new, narrower claims added by the motion to amend. Neither Patent Owner's motion nor Dr. Trainor's declaration address the obviousness of any of proposed dependent Claims 35-54 in light of the known prior art. In a motion to amend, absent “meaningful reasons” supporting the patentability of dependent claims, dependent claims are not separately patentable over the prior art relative to

the independent claim from which it depends. *See* IPR2012-00027, Paper 26 at 9-10 (*citing* 37 C.F.R. § 42.121(a)(2) and (a)(3)). Patent Owner has not provided any such “meaningful reasons;” therefore, Patent Owner has not carried its burden of showing patentability for any of the proposed dependent claims.

VII. CONCLUSION

Based on the foregoing, Columbia’s Motion to Amend the claims of the ’869 Patent, and that claim 34 is “substantially identical” claim 15, should be denied.

Dated: September 27, 2013

Reinhart Boerner Van Deuren s.c.
P.O. Box 2965
Milwaukee, WI 53201-2965
Telephone: 414-298-1000

Respectfully submitted,

/Robert A. Lawler/

Counsel for Petitioner

Robert A. Lawler (Reg. No. 62,075)
rlawler@reinhartlaw.com

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent of: Jingyue Ju et al.
Title: MASSIVE PARALLEL METHOD FOR DECODING
 DNA AND RNA
Patent No.: 7,790,869
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Customer No.: 22922

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P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF SERVICE

Copies of the following were served electronically this 27th day of
September 2013 to Columbia at jwhite@cooperdunham.com,
ColumbiaIPR@fchs.com and dthibode@nsf.gov:

1. Petitioner Illumina's Opposition to Patent Owner Columbia's Motion
to Amend.

Dated this 27th day of September 2013.

Reinhart Boerner Van Deuren s.c.
1000 North Water Street
Suite 1700
Milwaukee, WI 53202
Telephone: 414-298-1000
Facsimile: 414-298-8097

Nicole A. Wilson
nwilson@reinhartlaw.com

BY: /Nicole A. Wilson/
Reg. No. 66,672

Mailing Address:
P.O. Box 2965
Milwaukee, WI 53201-2965