

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ILLUMINA, INC.,
Petitioner,

v.

THE TRUSTEES OF COLUMBIA UNIVERSITY
IN THE CITY OF NEW YORK
Patent Owner.

IPR2018-00291 (Patent 9,718,852)
IPR2018-00318 (Patent 9,719,139)
IPR2018-00322 (Patent 9,708,358)
IPR2018-00385 (Patent 9,725,480)
IPR2018-00797 (Patent 9,868,985)¹

PATENT OWNER'S ADDITIONAL BRIEF

¹ An identical Paper is being entered into each listed proceeding.

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Introduction

In 2012, Illumina filed petitions challenging certain broad claims of Columbia's U.S. Patent Nos. 7,790,869, 7,713,698, and 8,088,575 ("the prior proceedings"). Exs. 2002-2004. Those challenged claims were found unpatentable. Notably, Illumina did not challenge all of the claims in those patents, such as '869 patent claim 19, which claims a 3'-O-allyl nucleotide, nor did it challenge all of the patents within the same patent family. After those proceedings, Columbia continued to prosecute patent applications within the same family, and pursued claims that were purposefully narrower and more precisely defined the inventors' contributions to the SBS field. Those narrow claims are the subject of the current proceedings, and they present materially different patentability questions than the claims adjudicated in the prior proceedings. The evidence shows that the current claims are non-obvious, and Illumina has failed to meet its burden of demonstrating unpatentability. Thus, even if collateral estoppel applies to Board decisions in IPR proceedings, the Board's prior decisions would not bar consideration of the present claims and would be inapplicable to the underlying factual issues in the current proceedings. Importantly, Columbia has scrupulously avoided relitigating previously-decided issues, and thus, the pertinent issues presently before the Board have not been previously decided.

Columbia now addresses the five questions raised in the Board’s March 19, 2019 Order, which are summarized below.

Question 1: Do principles of collateral estoppel (issue preclusion) preclude relitigation of certain issues based on the affirmance of the prior proceedings?

Answer: No. As explained below, collateral estoppel does not apply to the present claims (Section A, *infra*) or to the underlying factual issues (Section B, *infra*). Moreover, as a threshold matter, collateral estoppel does not apply at all because the USPTO has unambiguously concluded that the doctrine does not apply to IPR proceedings (Section C, *infra*).

A. Collateral estoppel does not apply to the present claims

The issue before the Board is whether the present claims are unpatentable. Designed to prevent litigation of the “same issue” of law or fact more than once, collateral estoppel applies only “[w]hen an issue of fact or law is actually litigated and determined by a valid and final judgment, and the determination is essential to the judgment[.]” *B & B Hardware, Inc. v. Hargis Indus., Inc.*, 135 S.Ct. 1293, 1298-99, 1303 (2015). The doctrine does not apply here because the patentability of the present claims has never previously been litigated or decided.

The prior proceedings decided the patentability of materially different claims (the “prior claims”). Unlike the prior claims, the present claims contain negative limitations and other features that restrict which capping groups can be used on the claimed nucleotides. For example, these limitations require that (i) the capping group

R “does not contain a ketone group,” and that OR does not form (ii) a “methoxy group” or (iii) “an ester group.” *E.g.*, Ex. 1001 at claim 1. There can be no question that these negative limitations materially alter the patentability questions before the Board, particularly the questions of motivation to combine and reasonable expectation of success. Illumina conceded these new claims recite a distinct invention—stating “[t]hese *negative limitations are carve-outs that Columbia added to avoid the prior art.*” Petition at 41 (emphases added throughout);² *see also Inphi Corp. v. Netlist, Inc.*, 805 F.3d 1350, 1353 (Fed. Cir. 2015) (noting that addition of negative limitations overcame an obviousness rejection). Prior art teachings avoided by these limitations include Tsien’s teaching to use groups excluded by the negative limitations. *E.g.*, Ex. 1013 at 21 (teaching use of methoxy (-OCH₃) capping group, and listing many ester capping groups as preferred embodiments); Ex. 1009 at 18 (Columbia explaining during prosecution that the claimed negative limitations are “contrary to the teachings of Tsien that such groups could be used in [SBS]”).

“With the newly added limitations[,] the [claims] require new and additional findings *because the ‘issues’ change with the scope of the claims.*” *Henkel Corp.*

² With similar papers having been filed in various proceedings, Columbia refers to the papers filed in IPR2018-00291, except where otherwise indicated.

v. Coral, Inc., 754 F. Supp. 1280, 1313 (N.D. Ill. 1990), *aff'd*, 945 F.2d 416 (Fed. Cir. 1991). In the prior proceedings, the question decided by the Board and Federal Circuit was whether Tsien disclosed the use of capping groups in general. *See* Ex. 1005 at 22 (relying on Tsien’s disclosure that “[t]he coupling reaction generally employs 3' hydroxyl blocked dNTPs,” *i.e.*, nucleotides with a capping group); Ex. 1008 at 21 (finding that Tsien “invites use” of a “3'-blocked dNTP analogue”). The addition of the negative limitations to the present claims presents an entirely different question—whether it would have been obvious to use a particular capping group, *i.e.*, one which does not contain a methoxy, ester, or ketone and also meets all the other claim limitations.

Out of the “perhaps hundreds or more potential blocking groups” disclosed in Tsien (Ex. 2009 at 15), the **only** one Illumina identified as falling within the scope of the present claims is the allegedly-described -CH₂-CH=CH₂ capping group (the “allyl capping group”). By raising new arguments based on the allyl capping group, rather than simply presenting again the same arguments as before, Illumina has acknowledged that the present claims materially differ from the prior claims. *See* 6 Annotated Patent Digest (Matthews) § 38.46 (“Collateral estoppel requires that the ‘identical’ issue have been litigated in the previous suit. Logically, this would suggest that if different theories of invalidity are presented in the second suit ... the requirement for identity is not satisfied.”). Indeed, the patentability question

presently before the Board turns on entirely new issues related to the allyl capping group, such as (i) whether Tsien describes the allyl capping group (it does not), and if Tsien describes this group, (ii) whether a POSA would have been *motivated* to select it for SBS despite the fact that the prior art discouraged such use (he/she would not have), and (iii) whether a POSA would have had a *reasonable expectation of success* in achieving the claimed invention by using the allyl capping group (he/she would not have). *See* Patent Owner Response; Sur-reply.

Furthermore, additional new limitations are present in the claims, including that (i) the capping group R “is stable during a DNA polymerase reaction,” (ii) the claimed nucleotide is “recognized as a substrate by a DNA polymerase,” and (iii) the claimed nucleotide “produces a 3'-OH group on the deoxyribose upon cleavage of R.” Ex. 1001 at claim 1. These limitations contribute to the narrow scope of the present claims, which required Illumina to make different obviousness arguments in the present proceedings, *i.e.*, those focusing on the allyl capping group.

In addition, the present method claims ('985 patent claims 1-2) include further new limitations, for example, (i) “[a] method for sequencing a nucleic acid” and (ii) “[a] method for simultaneously sequencing a plurality of different nucleic acids.” Ex. 1075 at claims 1-2. These limitations raise new issues, as demonstrated by Illumina’s challenge to claim 2, based on the combination of Tsien, Prober, *and Pallas*—a combination not asserted in the prior proceedings. IPR2018-00797,

Petition at 51-54 (arguing that a POSA “would have been motivated to use Tsien’s SBS methods” in “Pallas’s system for [] sequencing”).

Still further, the scope of the present claims is narrowed by combining limitations not previously combined. For example, the present claims require (i) the use of a small capping group (ii) on a deazapurine nucleotide that (iii) has a label which is fluorescent, wherein (iv) the capping group is cleaved by chemical means. Ex. 1001 at claim 1. Individually, these elements may be found in earlier claims, but no prior claim combined all of these limitations in a purposefully narrower claim.

For the preceding reasons, collateral estoppel cannot apply to the patentability of the present claims, which raise materially different questions of patentability. *See SK Hynix Inc. v. Netlist, Inc.*, IPR2017-00561, Paper 36, at 13 (July 5, 2018) (“Because the differences between [the claims] materially alter the question of unpatentability, collateral estoppel does not apply.”).

B. Collateral estoppel does not apply to the underlying factual issues

Collateral estoppel is also inapplicable to the underlying factual issues before the Board. Although the prior proceedings made numerous findings, such as that Tsien suggests to use a cleavable linker (Ex. 1005 at 10, 21-22), and that Prober teaches the use of a deazapurine (Ex. 1005 at 26-29), those findings are immaterial to the resolution of the present proceedings because Columbia has been vigilant not to relitigate already-decided issues. Instead, Columbia has contested only issues of

first impression, including those pertaining to the allyl capping group. *See* Question 1, *supra*; Question 5, *infra*. The “same issues” are not being relitigated.

C. Collateral estoppel does not apply to IPR proceedings

As to the broader question of the applicability of common law collateral estoppel in IPR proceedings, the USPTO has already concluded that collateral estoppel does not apply. In a Federal Circuit brief, the USPTO explained that “[e]stoppel within administrative agency proceedings is a question for Congress to specify,” and that Congress dictated a limited scope of estoppel for IPR proceedings. Brief for Intervenor, *BioDelivery Sciences Int’l, Inc. v. Monosol Rx, LLC*, Nos. 2017-1265, -1266, -1268, 2017 WL 2666499 (Fed. Cir. 2017), at *12 (hereinafter “Brief”).

Congress articulated the scope of IPR estoppel in 35 U.S.C. §§ 315(d), (e) and 325(d). Section 315(e)(1) limits estoppel to circumstances not applicable here. Earlier versions of that statutory section contemplated estoppel similar to the common law principle. *See* H.R. 2795 Sec. 9, § 336, 109th Cong. (2005) (applying estoppel to “any issue of fact or law actually decided by the panel and necessary to the determination of that issue”). Ultimately, Congress limited the scope of estoppel in § 315(e)(1), evidencing its intent that common law collateral estoppel not apply.

The Brief noted that the term “may” in §§ 315(d) and 325(d) (a departure from the prior inter partes reexamination statute) granted the USPTO discretion to introduce additional estoppel, beyond the narrow estoppel mandated in § 315(e)(1).

Brief at *14-15. However, “[h]aving not implemented any rules, issued precedential decisions, or taken any other action on the issue, [] ***the USPTO currently applies estoppel only to the extent that Congress has explicitly outlined in the Patent Act.***”

Brief at *16; *see also Westlake Services LLC v. Credit Acceptance Corp.*, CBM2014-00176, Paper 28 (May 14, 2015) (precedential) (acknowledging (i) the limits of estoppel under the specific language of the statute and (ii) the discretion granted the USPTO under § 325(d)).

That position comports with both *XY, LLC* and *B & B Hardware*. *XY, LLC* considered whether a ***district court*** could apply common law collateral estoppel based on a Board decision. *XY, LLC v. Trans Ova Genetics*, 890 F.3d 1282, 1294-95 (Fed. Cir. 2018). *B & B Hardware* also involved the application of estoppel by a district court. *B & B Hardware*, 135 S. Ct. at 1302 (2015). Neither case addressed Congress’ intent regarding agency action. *See* Brief at *13-18; *but see MaxLinear, Inc. v. CF Crespe LLC*, 880 F.3d 1373, 1377-78 (Fed. Cir. 2018) (remanded to the Board for consideration of whether dependent claims were materially different from independent claims found unpatentable; but not addressing Congress’ legislative intent). *B & B Hardware* acknowledges that Congress may legislate away collateral estoppel. 135 S. Ct. at 1306; *see also Astoria Fed. Sav. & Loan Assn. v. Solimino*, 501 U.S. 104, 108 (1991).

For these reasons, the USPTO's decision not to expand the scope of IPR estoppel beyond that articulated in the statute, either through a rule or precedential decision, forecloses the application of collateral estoppel in this IPR proceeding. Nevertheless, to answer fully the Board's specific questions, Columbia addresses the following questions assuming, for the sake of argument, that collateral estoppel may apply in one IPR proceeding based on a decision in an earlier IPR proceeding.

Question 2: Although the instant proceedings are based on different issued patents and claims than the previous proceedings, would that be a meaningful distinction here for patents that are in the same patent family and based on common antecedents?

Answer: Yes. “[I]t can not be presumed that related patents rise and fall together” because “[s]eparate patents describe ‘separate and distinct [inventions.]’” *Comair Rotron, Inc. v. Nippon Densan Corp.*, 49 F.3d 1535, 1539 (Fed. Cir. 1995) (reversing district court's finding of collateral estoppel based on prior litigation of related patent); *see also Kearns v. Gen. Motors Corp.*, 94 F.3d 1553, 1556 (Fed. Cir. 1996) (“Issue preclusion ... requires that the identical issue was decided on the merits In the case at bar it is not possible to show that the identical issue was presented in the [newly asserted patents] as in the [previously asserted patents]; for each patent, by law, covers a[n] independent and distinct invention.”).

The pertinent issue is not the relationship between the patents but whether the “same issues” are being relitigated. For example, in *MaxLinear*, a prior finding that independent claims were unpatentable did not necessarily give rise to collateral

estoppel of dependent claims *in the same patent*, despite there being no evidence that those dependent claims were separately patentable. *MaxLinear*, 880 F.3d at 1377-78, n.4. Instead, the Federal Circuit remanded back to the Board to determine whether the dependent claims “present materially different issues that alter the question of patentability[.]” *Id.*

As explained in response to Question 1, the present claims are narrower than the prior claims and therefore present entirely new questions of patentability not addressed in the prior decisions, including questions regarding the allyl capping group. The finding that broader claims in different patents of the same family were unpatentable does not detract from the overwhelming evidence demonstrating the non-obviousness of the present narrower claims. *See Hewlett-Packard Co. v. Bausch & Lomb, Inc.*, 882 F.2d 1556, 1565 (Fed. Cir. 1989) (recognizing that narrower claims can be valid even if broader claims are not); *see also Henkel*, 754 F. Supp. at 1313 (“The Court also finds that the narrowed claims of the [new] patent distinguish over the same prior art which invalidated the claims of the [original] patent. Application of collateral estoppel is inappropriate here [because the] prior decision ... did not consider the ... invention with all the narrowing limitations added[.]”).

Question 3: Is a patentable distinction under 37 C.F.R. § 42.73(d)(3)(i) necessarily a material difference for purposes of applying *B & B Hardware*?

Answer: Yes. The Federal Circuit acknowledged this in *MaxLinear*, where as noted above, the decision touched upon the issue of collateral estoppel with respect

to certain dependent claims, where the independent claims were previously found unpatentable. *MaxLinear*, 880 F.3d at 1377-78. When remanding the matter, the Federal Circuit explained that the issue could turn on whether the dependent claims “present *materially different* issues that alter the question of patentability, making them *patentably distinct*” from the previously-invalidated independent claims.

Thus, claims that are patentably distinct present materially different issues. *Id.* Even if a patentable distinction is not *necessarily* a material difference, it is in this case. As explained in response to Question 1, the present narrower claims materially alter the question of patentability. Thus, collateral estoppel does not apply.

Question 4: Is it proper for the Board to reweigh obviousness for the claims as a whole, e.g., considering any narrowing of the claims at issue, without relitigating issues common to the previous proceedings?

Answer: Yes. It is necessary for the Board to weigh obviousness of the claims “as a whole.” 35 U.S.C. § 103; *see MaxLinear*, 880 F.3d at 1377-78. Otherwise, it would be using the prior claims as prior art to the present claims, which has been rejected by the Federal Circuit:

The original claim is not prior art against the [new] claim. It is not correct to weigh the [new] claim against the original claim. It is not correct to weigh the changes in the [new] claim against the original claim. It is the [new] claim alone that is to be analyzed in accordance with the *Graham* guidelines, and the differences to be considered are the differences between the [new] claim *as a whole* and the prior art.

Interconnect Planning v. Feil, 774 F.2d 1132, 1141 (Fed. Cir. 1985).

While the Board must consider the invention “as a whole,” it need not relitigate issues common to the previous proceedings because, as explained above and below, Columbia has not contested previously-decided issues.

Question 5: If collateral estoppel applies, what issues have been decided and how do they apply to the current proceeding?

Answer: If collateral estoppel applies, its application would be limited to previously-decided issues that were essential to the prior judgement. Since Columbia is not relitigating any prior findings, those findings are immaterial to the resolution of these proceedings.

Question 5(a): Is there collateral estoppel for the conclusion that Tsien/Prober would have rendered obvious the use of nucleotide analogues, including that a POSA would have had a reasonable expectation of success in achieving cleavability of a 3'-O-allyl blocking group from a nucleotide analogue and incorporation of a nucleotide analogue with a 3'-O-allyl blocking group, for purposes of SBS?

Answer: No. In the prior proceedings the Board did not decide *any* issue regarding the allyl capping group. Therefore, collateral estoppel cannot apply to any issue pertaining to the allyl capping group. This includes the issue whether a POSA would have reasonably expected success in achieving cleavability of the allyl capping group. Previously, the Board merely noted that Tsien’s methods use “removable” blocking groups (Ex. 1005 at 22); it did not address cleavability of the allyl capping group. Nor did it address the pertinent question here—cleavability of the allyl capping group under SBS-compatible conditions (*e.g.*, quantitative, rapid

cleavage under mild, aqueous conditions) as required for Tsien's and Dower's SBS methods. *Compare* Patent Owner Response at Section V(B) *with* Ex. 1005 at 22.

Similarly, in the prior proceedings the Board did not decide whether a POSA would have expected success in incorporating a nucleotide analogue with the allyl capping group for purposes of SBS. *See* Ex. 1005 at 33-34 (not addressing the allyl capping group). As such, collateral estoppel cannot apply to either of Columbia's two key arguments regarding incorporation presently before the Board, (i) that a POSA would not have been *motivated to select the allyl capping group* for use in Tsien's and Dower's SBS methods (which require efficient incorporation) because it had been shown to result in inefficient incorporation at best (*see* Patent Owner Response at Section V(A)), and (ii) that inefficient incorporation of a 3'-O-allyl adenine provided no *expectation* that a guanine, thymine, or cytosine nucleotide with the same capping group would be incorporated at all (*see* Patent Owner Response at Section V(E)).

Question 5(b): Is there collateral estoppel for the conclusion that Tsien/Prober would have rendered obvious the use of nucleotide analogues in SBS, including that a POSA would have had a reasonable expectation of success in using the same with a label attached via a cleavable chemical linker to the 7-position of an adenine or guanine base, or attached to a thymine or cytidine base, into a growing DNA strand via a polymerase?

Answer: No. The Board in the prior proceedings made no finding that Tsien (alone or further in view of Prober) provided a reasonable expectation of

incorporating *any* nucleotide analogue into a growing DNA strand via a polymerase. Instead, the Board's findings on this issue relied on Anazawa, Stemple, Prober, and expert testimony. *See* Ex. 1005 at 33-34, 18-19, 14. Furthermore, the Board in the prior proceedings merely found an expectation that "a nucleotide analogue with a label on the base and a capping group on the 3'-OH" could be incorporated (*id.*), which differs from and does not answer whether there would be an expectation of successful incorporation (i) of a nucleotide as described in Question 5(b) (*i.e.*, one with a cleavable chemical linker attached to the 7-position), or (ii) of a nucleotide as described in the present claims (*e.g.*, one in which the capping group is not a methoxy, ester, ketone and meets all the other limitations).

Question 5(c): Were any conclusions of obviousness in the previous proceedings based on the specific blocking group, *i.e.*, a 3'-O-allyl (2-propenyl) blocking group, *e.g.*, that Petitioner argues Tsien discloses, or rather on a genus of blocking groups without a conclusion as to any specific blocking group?

Answer: No conclusion of obviousness in the prior proceedings was based on the allyl capping group. As noted above, the Board and Federal Circuit previously considered whether Tsien disclosed the use of capping groups in general. *See* Ex. 1005 at 22; Ex. 1008 at 21. The findings were not based on the allyl capping group. *See also* Ex. 1005 at 8-9 (citing Tsien at 21:9-33 and 23:28-25:25, which encompasses numerous capping groups, such as "ester blocking groups," "ether blocking groups," "phosphate blocking groups," "carbonate blocking groups," *etc.*).

In its Reply, Illumina argued that the Board previously “reject[ed] a claim specifically reciting the 3-carbon allyl protecting group over Tsien.” Reply at 27. That argument is disingenuous. Illumina is referring to the ’869 patent, which has a dependent claim to a 3'-O-allyl nucleotide (claim 19). Illumina ***never challenged*** the 3'-O-allyl nucleotide claim 19 in the prior proceedings and it remains valid today. *See* Ex. 2002, Certificate (not cancelling claim 19). During those proceedings Columbia sought to rewrite dependent claim 15 as an independent claim, and in the process, merely ***renumbered*** the unchallenged 3'-O-allyl nucleotide claim to depend from the resulting independent claim. Ex. 1005 at 46-47 (noting that claim 19 was “identical” to proposed amended claim except for renumbering); *see also* IPR2012-00007, Paper 79, Motion to Amend, Appendix A at 4 (August 30, 2013) (proposed amended claim). Those amendments had nothing to do with the obviousness of a 3'-O-allyl nucleotide, and the Board denied the motion to amend and never decided the patentability of that claim.

Conclusion

Collateral estoppel does not foreclose consideration of any of the issues currently before the Board in these proceedings.

Respectfully submitted,

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