

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.

Case IPR2012-00006
U.S. Patent 7,713,698

Before SALLY G. LANE, RICHARD M. LEBOVITZ, and DEBORAH
KATZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

**DECISION ON REQUEST FOR REHEARING UNDER 37 C.F.R.
§ 41.71(c) OF DECISION TO INSTITUTE INTER PARTES REVIEW
& SCHEDULING ORDER**

I. REHEARING REQUEST

Illumina requests rehearing of the decision under 35 U.S.C. § 311 (“the ‘698 Decision”) (Paper 28) denying inter partes review of claims 15 and 16 of US 7,713,698 (“the ‘698 patent”) based on Tsien and Dower as anticipatory publications (Illumina Request for Reconsideration under 37 C.F.R. 42.71(c), dated March 26, 2013 (“Illumina Req. Reh’g.”; Paper 30))

Under 37 C.F.R. § 42.71(c), “[w]hen rehearing a decision on petition, a panel will review the decision for an abuse of discretion.” An abuse of discretion occurs when a “decision was based on an erroneous conclusion of law or clearly erroneous factual findings, or . . . a clear error of judgment.” *PPG Indus. Inc. v. Celanese Polymer Specialties Co. Inc.*, 840 F.2d 1565, 1567 (Fed. Cir. 1988). *See also* 37 C.F.R. § 42.71(d) (“The request must specifically identify all matters the party believes the Board misapprehended or overlooked”).

I.A. THE BOARD ERRED IN NOT AUTHORIZING INTER PARTES REVIEW OF CLAIMS 1 AND 11 BASED ON TSIEN & DOWER (ILLUMINA REQ. REH’G 3)

Nucleotides comprise a sugar, phosphate, and nitrogen base (‘698 patent, Fig. 7). Claim 1 is drawn to nucleic acid sequencing method comprising employing at least one nucleotide which comprises a deazapurine as the nitrogen base. Claim 11 is drawn to a primer hybridized to a nucleic acid template, where at least one of the nucleotides in the primer comprises a deazapurine as a base. Neither Tsien nor Dower is said by Illumina to expressly describe a deazapurine base in their written disclosures. Rather, Illumina contends the nucleotides are present by virtue

of the incorporation by reference to the Prober I publication by Tsien and Dower. Dower is said to disclose nucleotides with deazapurine bases (Petition 26 & 39-40). The issue addressed in the '698 Decision with respect to these rejections was whether Illumina met its burden in establishing whether Prober I is incorporated into the host document in a manner that complies with the requirement of 35 U.S.C. § 102 ('698 Decision 10-11).

“To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.” *Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000). When making such determination, the standard “of one reasonably skilled in the art should be” applied. *Id.* at 1283. Illumina contends that we erred by not using “the person of reasonable skill in the art” standard to evaluate whether Tsien (Exhibit 1002) and Dower (Exhibit 1005) incorporated Prober I’s (Exhibit 1003) disclosure of a 7-deazapurine base (Illumina Req. Reh’g 4). Specifically, Illumina contends that we “used a heightened standard that would require recitation of the exact word ‘deazapurine’ (or at least ‘deaza-substituted’) as used in claims 1 and 11” (*id.*). To support their argument, Illumina points to declarations by Dr. Weinstock and Dr. Blanchaud (*id.* at 5).

I.A.1. Dower and Prober I

We agree with Illumina that we erred in not instituting inter partes review of claims 1 and 11 based on Dower as an anticipatory publication.

On page 12 of the '698 Decision, we reproduced the following passage of Dower which referred to Prober I:

(c) An alternative polymer stepwise synthetic strategy can be employed. In this embodiment, the fluorophores need not be removable and may be attached to irreversible chain terminators. Examples of such compounds for use in sequencing DNA include, but are not limited to, dideoxynucleotide triphosphate analogs as described by Prober et al. (1987) *Science* 238:336-341.

Dower, col. 25, ll. 41-47.

On pages 33 and 34-35 of the Petition, Illumina referred to the following additional disclosure:

DNA polymerase, or a similar polymerase, is used to extend the chains by one base by incubation in the presence of dNTP analogs which function as both chain terminators and fluorescent labels. This is done in a one-step process where each of the four dNTP analogs is identified by a distinct dye, such as described in Prober et al. *Science* 238:336-341

Dower, col. 23, ll. 18-24.

Fluorescent chain terminators (analogues of dATP, dCTP, dGTP, and TP, each labeled with fluorophore preferably emitting at a distinguishable wavelength) are added to the reaction at a sufficient concentration and under suitable reaction conditions (time, temperature, pH, ionic species, etc., See Sambrook et al. (1989) *Molecular Cloning*, vols. 1-3, and Prober et al.).

Dower, col. 25, ll. 4-10.

It is evident from the above quoted disclosure from Dower that Dower is referencing Prober I for all its dNTP analogues, at least one of which is a deazapurine. For example, Dower, at column 23, lines 18-24 and column 25, lines 41-47, refers to Prober I's disclosure of nucleotide analogs (dNTP and dideoxynucleotide triphosphate) in DNA sequencing.

To support the position that such disclosure is an adequate incorporation by reference for the purpose of anticipation, Illumina cites *Callaway Golf Co. v. Acushnet Co.*, 576 F.3d 1331 (Fed. Cir. 2009) (Illumina Req. Reh’g 8-9, 10, and 12). Illumina contends that *Callaway* holds that “reference to a **general class of compositions** discussed in prior art is **sufficient to incorporate a specific composition** by reference. *Callaway*, 576 F.3d at 1346-47 (holding reference to a ‘foamable polymeric composition’ sufficient to specifically incorporate polyurethane as the foamable composition)” (*id.* at 10-11). We agree that the holding in *Callaway* is relevant in the circumstances before us.

In *Callaway*, the Federal Circuit wrote:

Nesbitt [the cited anticipatory publication] states broadly that the layers of the golf ball disclosed therein may be made from a “natural or synthetic polymeric material.” [U.S. Patent No. 4,431,193] col. 3 ll. 53-54. Nesbitt goes on to directly indicate that such materials include all of the foamable polymeric materials described in Molitor [U.S. Patent No. 4,274,637]: “Reference is made to [Molitor “637] which describes a number of foamable compositions of a character which may be employed for one or both layers ... for the golf ball of this invention.” *Id.* col.3 ll. 56–61 (emphasis added). Polyurethane is a foamable composition. Nesbitt incorporates the entire list of foamable compounds (“a number of foamable compositions”) disclosed by Molitor “637 as appropriate materials for use in golf ball cover layers, including polyurethane and mixtures of ionomer resins.

Callaway, 576 F.3d at 1347-48.

Dower incorporates all the nucleotide analogues from Prober I, which includes an analogue comprising a deazapurine base. Consistent with *Callaway*, the incorporation by reference to Prober I in Dower is therefore sufficient to establish that Dower describes within its four corners a method

of using a nucleotide comprising a deazapurine base as required by claims 1 and 11.

Columbia in their opposition to Illumina's Rehearing Request argues that Dower refers to Prober I six times, "but not once uses the words 'incorporated herein by reference' whereas Dower refers to other specific references seventeen times using the words 'incorporated herein by reference.'" (Columbia's Opposition 2, dated April 26, 2013; Paper 37.) Columbia has not cited any legal authority that the words "incorporated herein by reference" are necessary to incorporate Prober I's disclosure into Dower. Rather, we find that Dower's reference to Prober I for dNTP analogs in DNA sequencing is sufficient for a person of reasonable skill in the art to have recognized that Prober I is incorporated for this teaching.

Columbia also notes that the Board relied upon the disclosure at column 25, lines 41-47 of Dower in the '698 Decision, but that this passage was not cited by Illumina in their petition (Columbia Opposition 3). We acknowledge this fact to be true, but the disclosure appears on the same column 25 (at lines 4-10 and lines 35-37) cited by Illumina in their petition (Petition 35, 37, 39, and 41), and thus our attention was clearly drawn to column 25 for its pertinence. In addition, the passage at column 25, lines 4-10 expressly cited by Illumina refers to "[f]luorescent chain **terminators**" and the passage at column 25, lines 41-47 appears in the section titled "There are several suitable labeled, **terminator** structures as follows." Thus it was reasonable to consider the disclosure at column 25, lines 41-47 based on the passage expressly cited by Illumina in their petition.

Columbia further argues that even if Dower had incorporated by reference the deazapurines disclosed in Prober I, the '698 Decision "that

Dower did not anticipate the claims at issue would still be correct. The deaza-substituted dideoxynucleotides of Prober I do not contain a removable chemical moiety capping the 3'-OH group of the sugar as required by the claims.” (Columbia Opposition 5, n.4).

Illumina in their petition points to specific passages of Dower which describe modified analogs which “should” be blocked at the 3'-end of elongation (Petition 35). Columbia has not identified a defect in this specific disclosure which teaches utilizing 3'-blocked analogs in DNA sequencing, and we find none.

For the foregoing reasons, we **authorize** an inter partes review of claims 1 and 11 instituted with respect to Illumina’s patentability challenge based on Dower.

Claims 2-7, 11, 12, 14, 15, and 17

With respect to dependent claim 2-7, 11, 12, 14, 15, and 17, Illumina identified specific disclosure in Dower where each limitation is found (Petition 35-39). We find Illumina’s factual assertions to be supported, and authorize an inter partes review of claims 2-7, 11, 12, 14, 15, and 17 to be instituted with respect to Illumina’s patentability challenge based on Dower as an anticipatory publication.

I.A.2. Tsien & Prober I

Contrary to Illumina’s contention, the ‘698 Decision did not ignore how a person of reasonable skill in the art would have viewed Tsien’s incorporation by reference to Prober I. The only evidence of how such a

person would have understood the reference to Prober I in Tsien was the declaration of Dr. George Weinstock.

Dr. Weinstock stated in his declaration (Exhibit 1021):

In discussing sequencing by synthesis methods utilizing a dNTP in which the fluorescent label group is coupled to the base of the dNTP, Tsien references the disclosure of Prober I, *Science* 238, 336-341 (1987) for its teaching of preparing nucleotides with fluorescent tags that can be successfully incorporated by Tsien's preferred polymerase. See Tsien et al., page 5, lines 22- 23, page 19, lines 4-18; and page 28, lines 5-18. Tsien also states that Prober I, and the other references discuss in Tsien, are referenced "for their teaching of synthetic methods, coupling and detection methodologies, and the like." Tsien, p. 3, ll. 11-16 and p. 5, ll. 22-23.

(Weinstock Decl. ¶ 63.)

Based on the cited disclosure in Tsien, Dr. Weinstock concluded that he understood "Tsien to incorporate the teachings of Prober I for its teachings regarding of fluorescent label attachment, and in particular, regarding its teaching regarding attachment of a linker to the 7 position in the 7-deazapurine" (*id.* at ¶ 63).

The '698 Decision did not find Dr. Weinstock's testimony persuasive because "Dr. Weinstock did not provide a factual basis for his testimony as to why this teaching would have been recognized by one of ordinary skill in the art." ('698 Decision 13.) In particular, it was noted in the Decision that "Illumina provided testimony by Dr. George Weinstock that Prober I is incorporated by Tsien for 'its teaching regarding attachment of a linker to the 7 position in the 7-deazapurine,' but these words do not appear in Tsien. Weinstock Decl. ¶ 63." (*Id.* at 13.) Dr. Weinstock's testimony was determined to be inadequate to make up for this deficiency.

Tsien does not indicate that Prober I is being referenced for its teaching of a deazapurine nucleotide. Tsien refers to Prober I for its teaching that fluorescent ddNTPs can be incorporated by two different enzymes, but did not identify the fluorescent ddNTPs as comprising a deazapurine base as recited in claims 1 and 11 ('698 Decision 11-12). Dr. Weinstock's testimony did not bridge the gap. Thus, while the Decision addressed Tsien's failure to specifically identify the deazapurines in Prober I, the Decision found the incorporation defective for the purpose of establishing anticipation because Dr. Weinstock's testimony did not sufficiently explain why the reasonably skilled person would have understood the reference to Prober I to be a reference to deazapurines.

In the Request for Rehearing, Illumina attempts to remedy this deficiency, stating “[s]ignificantly, the only analogs of dATP and dGTP present in the Prober I reference are 7-deazapurines” and explains why this is the case (Illumina Req. Reh'g 6). However, as pointedly stated by Illumina, the determination of “incorporation by reference” for the purpose of establishing anticipation is from the viewpoint of one reasonably skilled in the art. The identification of where Prober I described deazapurines, and the explanation of why Tsien's disclosure “fluorescent ddNTPs” would be understood to be these deazapurines was not discussed in Dr. Weinstock's declaration, but rather is only described in this Request for Rehearing signed by Illumina's attorney. The argument of counsel cannot take the place of evidence lacking in the record. *Estee Lauder Inc. v. L'Oreal, S.A.*, 129 F.3d 588, 595 (Fed. Cir. 1997).

Moreover, 37 C.F.R. § 41.71(d) states a Request for Rehearing “must specifically identify . . . the place where each matter was previously

addressed in a motion, an opposition, or a reply.” Illumina has not cited where in the ‘698 Petition it was argued that the only analogs of dATP and dGTP described in Prober I are 7-deazapurines.

Blanchaud Declaration

Illumina also states that “Blanchaud understood certain features to be included in the incorporation of Prober based on the general description of the incorporated matter in Tsien and Dower, respectively.” (Illumina Req. Reh’g 5.) In fact, Blanchaud only appears in the list of references cited on pages v-vi of the Petition, but was not mentioned in any other place in the Petition. Accordingly, we did not address Blanchaud in the Decision. It is therefore not a matter misapprehended or overlooked by the Board as required by 37 C.F.R. § 42.71(d).

Calloway

Unlike in *Calloway* (reproduced above), Tsien did not disclose that all the materials in Prober I are to be included in their sequencing methods. For example, Tsien does not refer to Prober I for disclosing fluorescent nucleotides that could be used in its method, but rather referred to Prober I for “show[ing] enzymatic incorporation of fluorescent ddNTPs” using two different enzymes (‘698 Decision 25). Illumina did not direct us to adequate factual evidence or testimony by one reasonably skilled in the art that such sentence serves to incorporate the specific ddNTPs described in Prober I.

I.B. DUPLICATIVE REJECTIONS

Citing 37 C.F.R. § 42.108, we denied certain unpatentability challenges to the claims. Illumina contends that “the Board abused its discretion by considering an improper factor when deciding whether to authorize *inter partes* review.” (Req. Reh’g 13.) Illumina contends that the Board’s “discretion is limited to determining whether, in fact, the references render the challenged patent unpatentable. The Patent Rules do not authorize the Board to exercise discretion based on whether or not certain references are cumulative or duplicative of each other.” (*Id.* at 14.)

Under 37 C.F.R. § 42.108(a), the Board has discretion to “authorize the review to proceed on all or some of the challenged claims and on all or some of the grounds of unpatentability asserted for each claim.” The Board also “may deny some or all grounds for unpatentability for some or all of the challenged claims.” 37 C.F.R. § 42.108(b). As stated in the ‘698 Decision, in making such determinations, the Board must also take into account 37 C.F.R. § 42.1(b) which requires “the just, speedy, and inexpensive resolution of every proceeding.”

In this case, the decision not to authorize *inter partes* review on certain unpatentability challenges was based on the finding that the challenges appeared to rely on the same prior art facts as other challenges for which *inter partes* review had been authorized. The determination not to proceed on all of the proposed unpatentability challenges by Illumina was therefore grounded on the determination that the same facts were being applied to the claims, albeit using different publications to establish that a fact was prior art to the claims. The concern was that the redundant unpatentability challenges would impede “the just, speedy, and inexpensive resolution of every

proceeding” as required under 37 C.F.R § 42.1(b). In other words, considering multiple rejections for the same unpatentability issue would unnecessarily consume the time and resources of all parties involved. As Illumina did not provide a meaningful distinction between the different, redundant rejections, we perceived no unfairness by not authorizing what appeared to be redundant challenges because an inter partes review had been instituted on the same factual basis.

Illumina contends:

[A]lthough the references are used to support invalidity contentions regarding the same claims, the references themselves are not identical. Thus, the Patent Owner may assert that a claim element is not present, or would not be obvious to combine with another reference, when that same element is more clearly set forth in a different reference.

(Req. Reh’g 14.)

While it is true that the cited references are not identical, the cited references appear to have been cited for the same facts. Illumina speculates that in certain publications an element may be more clearly set forth in one publication rather than another, but has not provided a persuasive example of such a case.

Dower

Illumina contends that Dower is not duplicative to Tsien, and cites one such difference (Req. Reh’g 14-15). However, Illumina did not provide an adequate explanation as to how this difference would impact the unpatentability challenge.

II. SCHEDULING ORDER

In the conference call on April 16, 2013 between Illumina, Columbia, and the PTAB panel, Columbia requested a change in the Scheduling Order (Paper 29) to provide more time, depending on the outcome of the decision on Illumina's Request for Rehearing. While the '698 Decision on Petition has been modified, the modification is not deemed sufficient to warrant a time extension on any of the dates in the Scheduling Order. Columbia's request is therefore DENIED.

III. SUMMARY

The '698 Decision is modified as follows:

Pursuant to 35 U.S.C. § 314, in addition to challenges I-III identified in the '698 Decision, we authorize inter partes review to be instituted as follows:

IV. Claim 1-7, 11, 12, 14, 15, and 17 under 35 U.S.C. § 102(b) as anticipated by Dower.

GRANTED-IN-PART

Case IPR2012-00006
U.S. Patent 7,713,698

Petitioner:

Robert Lawler
and
James Morrow
Reinhart Boerner Van Deuren s.c.
ipadmin@reinhartlaw.com

Patent Owner:

John P. White
Cooper & Dunham LLP
jwhite@cooperdunham.com

and

Anthony M. Zupcic
Fitzpatrick, Cella, Harper & Scinto
ColumbiaIPR@fchs.com