Trials@uspto.gov
Tel: 571-272-7822

Paper 9
Entered: February 4, 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SAWAI USA, INC. AND SAWAI PHARMACEUTICAL CO., LTD.,
Petitioners,

v.

NISSAN CHEMICAL INDUSTRIES LTD.,
Patent Owner.

Cases IPR2015-01647
Patent No. 5,856,336 B2

Before JACQUELINE WRIGHT BONILLA, SHERIDAN K. SNEDDEN, and TINA E. HULSE, *Administrative Patent Judges.*

SNEDDEN, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Sawai USA Inc. and Sawai Pharmaceutical Co., Ltd. ("Petitioner") filed a Petition to institute an *inter partes* review of claims 1 and 2 (Paper 1, "Pet.") of U.S. Patent No. 5,856,336 B2 (Ex. 1001, "the '336 patent"). Nissan Chemical Industries, Ltd. ("Patent Owner") filed a Patent Owner Preliminary Response. Paper 8 ("Prelim. Resp.").

Upon consideration of the Petition and Patent Owner Preliminary Response, we conclude that Petitioner has not established that there is a reasonable likelihood that it will prevail with respect to at least one of the challenged claims. For the reasons that follow, we do not institute an *inter partes* review.

A. Related Proceedings

The parties inform us of no related litigation between them involving the '336 patent. Pet. 5–6; Paper 4. Concurrent with the filing of the present Petition, Petitioner also filed a different Petition requesting *inter partes* review of claims 1–2 of the '336 patent (IPR2015-01648).

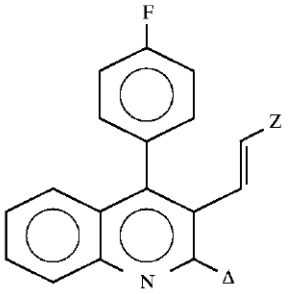
B. The '336 patent (Ex. 1001)

The '336 patent discloses mevalonolactone derivatives having a quinoline ring and their use as a pharmaceutical for reducing hyperlipidemia, hyperlipoproteinemia, or atherosclerosis. Ex. 1001, 1:6–35. The compounds are active against the enzyme HMG-CoA (or 3-hydroxy-3-methylglutaryl-coenzyme A). *Id.* at Abstract.

C. Challenged claims

Challenged claims 1 and 2 are reproduced below:

1. A compound of the formula,



[A]

Z= —CH(OH)—CH_2—CH(OH) —CH_2—COO. ½Ca.

2. A method for reducing hyperlipidemia, hyperlipoproteinemia or atherosclerosis, which comprises administering an effective amount of the compound of formula A as defined in claim 1.

Ex. 1001, 32:20–40.

D. Asserted Grounds of Unpatentability

Petitioner challenges claims 1 and 2 of the '336 patent on the following ground. Pet. 20–57.

References	Basis	Claim[s] challenged
Picard[1] and Kesseler[2]	§ 103(a)	1 and 2

[1] Joseph A. Picard et al., U.S. Patent No. 4,761,419, issued Aug. 2, 1988. Ex. 1009 ("Picard").

[2] Kurt Kesseler et al., U.S. Patent No. 4,925,852, issued May 15, 1990. Ex. 1010 ("Kesseler").

Petitioner relies also on the Declaration of Dr. Milton Brown in support of the proposed ground of unpatentability. Ex. 1012 ("Brown Declaration" or "Brown Decl.").

II. ANALYSIS

A. Claim Interpretation

We interpret claims using the "broadest reasonable construction in light of the specification of the patent in which [they] appear[]." 37 C.F.R. § 42.100(b); *see also* Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,766 (Aug. 14, 2012); *In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1278–79 (Fed. Cir. 2015), *cert. granted sub nom. Cuozzo Speed Techs., LLC v. Lee*, 84 U.S.L.W. 3218 (U.S. Jan. 15, 2016) (No. 15-446). Under the broadest reasonable construction standard, claim terms are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). "Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaim[s] the broader definition." *In re Bigio*, 381 F.3d 1320, 1325 (Fed Cir. 2004). "Although an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity, deliberateness, and precision." *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

We determine that no explicit construction of any specific claim term is necessary to determine whether to institute a trial in this case. *See, e.g., Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011)

("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'") (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc*., 200 F.3d 795, 803 (Fed. Cir. 1999)). At this stage of the proceeding, we have not made a final determination as to the construction of any claim term.

B. Effective Filing Date of Claims 1 and 2 of the '336 Patent

The '336 Patent claims the benefit of Japanese Patent Applications JP 63-193606 ("JP '606," filed August 3, 1988),[3] JP 63-15585 ("JP '585," filed January 26, 1988),[4] and JP 62-207224 ("JP '224," filed August 20, 1987).[5] Petitioner contends that neither JP '585 nor JP '224 provides written description for a ½ calcium salt, as specifically required by claims 1 and 2 of the '336 patent. Pet. 10–15. Thus, Petitioner contends that the earliest effective filing date for the '336 Patent is no earlier than the filing date of JP '606, or August 3, 1988. *Id.*

In its Preliminary Response, Patent Owner does not direct us to any portion of either JP '585 or JP '224 that provides written description for a ½ calcium salt, instead arguing that the Board need not address priority at this time in light of the deficiencies in Petitioner's arguments. Prelim. Resp. 2 n.1. For the purposes of this Decision, we treat Picard and Kesseler as prior art references and consider the patentability challenge set forth in the Petition.

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[3] Certified English translation provided as Ex. 1013.

[4] Certified English translation provided as Ex. 1014.

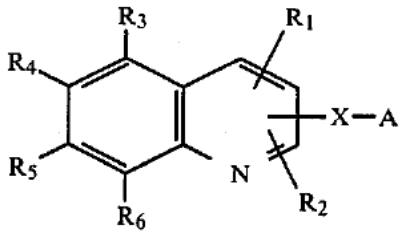
[5] Certified English translation provided as Ex. 1015.

C. Petitioner's Asserted Obviousness Ground

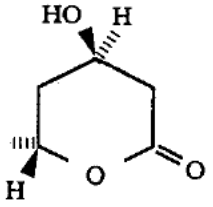
1. Petitioner's Contentions

Petitioner contends that claims 1 and 2 of the '336 patent are obvious over the combination of Picard and Kesseler. Pet. 25–39. Petitioner contends that a person of ordinary skill in the art would have selected Picard's Example 3 compound (Ex. 1009, 17:49–66) as a lead compound and would have found it obvious to change the R2 isopropyl group to a cyclopropyl group in order to achieve the compound of claim 1 of the '336 patent. Pet. 26–30.

In support of this contention, Petitioner directs us to the following teachings of Picard. *Id.* Picard discloses purported compound inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase) having the structure of the following Formula I ("Picard Formula I"):



wherein A is

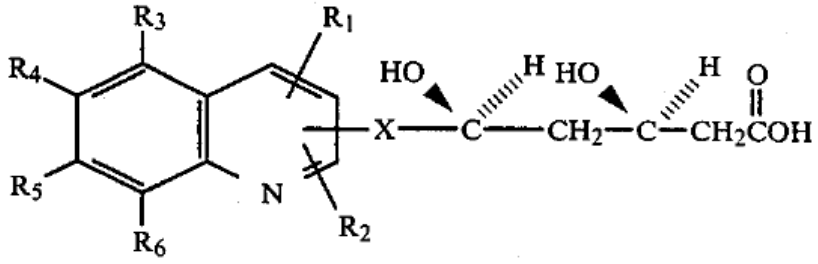


and X is —CH2CH2— or —CH═CH—. Ex. 1009, Abstract, 2:6–29. With regard to R1, R2, R3, R4, R5, and R6, Picard discloses as follows:

> R_1 and R_2 are independently hydrogen; alkyl of from one to six carbons; trifluoromethyl; cyclopropyl; cyclohexyl; cyclohexylmethyl; phenyl; phenyl substituted with fluorine, chlorine, bromine, hydroxy, trifluoromethyl, alkyl of from one to four carbon atoms, or alkoxy of from one to four carbon atoms; phenylmethyl; phenylmethyl substituted with fluorine, chlorine, bromine, hydroxy, trifluoromethyl, alkyl of from one to four carbon atoms, or alkoxy of from one to four carbon atoms; 2-, 3-, or 4-pyridinyl; or 2-, -, or 5-pyrimidinyl; provided that when X is in the 2-position, R_1 is hydrogen and is attached in the 4-position.
>
> R_3, R_4, R_5, and R_6 are independently selected from hydrogen; alkyl of from one to six carbon atoms; trifluoromethyl; cyclopropyl; fluorine; chlorine; bromine; hydroxy; alkoxy of from one to four carbon atoms; cyano; nitro; amino; acetylamino; aminomethyl; phenyl; phenyl substituted with fluorine, chlorine, bromine, hydroxy, trifluoromethyl, alkyl of from one to four carbon atoms, or alkoxy of from one to four carbon atoms; phenylmethyl; or phenylmethyl substituted with fluorine, chlorine, bromine, hydroxy, trifluoromethyl, or alkyl of from one to four carbon atoms.

Id. at 2:30–53.

Picard also discloses compound inhibitors of HMG-CoA reductase having the structure of the following Formula II ("Picard Formula II"):



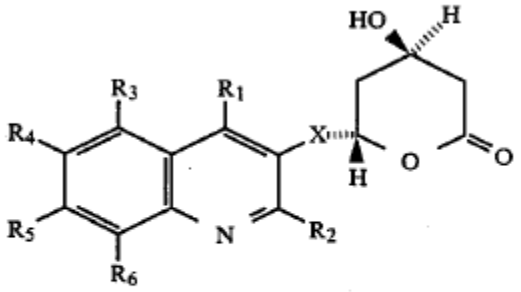
,

where X, R_1, R_2, R_3, R_4, R_5, and R_6 are as defined above. *Id.* at 2:58–67.

Table 1 of Picard ("Picard Table 1"), reproduced below, discloses the

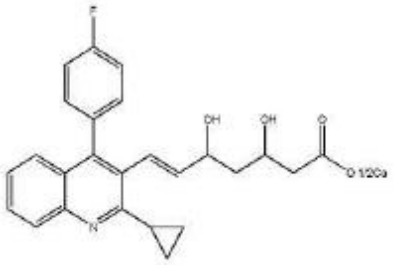
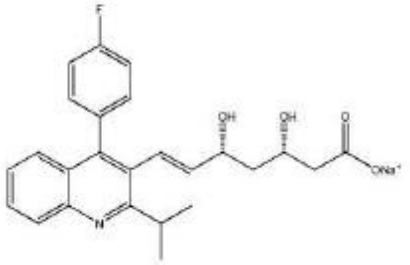
activities of two compounds encompassed by Formula I. *Id.* at 11:25–41.

TABLE 1



X	R_1	R_2	R_3	R_4	R_5	R_6	CSI IC_{50} μMole/Liter
—CH=CH—	4-Fluorophenyl	$-CH_3$	H	Cl	H	H	0.35
—CH=CH—	4-Fluorophenyl	$-CH(CH_3)_2$	H	Cl	H	H	0.032

Example 3 describes the preparation of a compound according to Formula II ("Picard Example 3 Compound"): *Id.* at 17:49–66. Petitioner provides a comparison of the structure of Picard's Example 3 compound and the claimed compound, reproduced in the table below. Pet. at 28.

Claim 1 of the '336 Patent	Picard Example 3 Compound
	

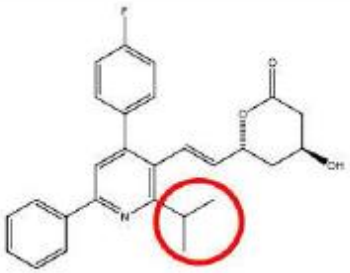
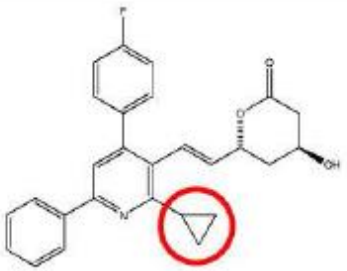
With reference to the above table, Petitioner contends that Picard Example 3 Compound differs from a compound of claim 1 by the presence of an isopropyl at the R_2 position, instead of a cyclopropyl group. *Id.*

Petitioner further contends that the data provided in Picard Table 1 describes preferred lactones in which R_1 is 4-fluorophenyl and R_2 is methyl

or isopropyl. Pet. 27 (citing Brown Decl. ¶ 32). According to Petitioner, Picard indicates in Table 1 that a R_2 isopropyl substituted compound is about 10 times more potent than its methyl-substituted counterpart. Pet. 27. Based on that data, according to Petitioner, a person of ordinary skill in the art would have reasonably expected "that derivatives having an isopropyl group would be more active than those having a methyl group." Pet. 27, 30 (citing Brown Decl. ¶¶ 32, 37.)

Petitioner further contends that Picard discloses "that cyclopropyl is a preferred alternate propyl group at this position, a POSA would naturally have prepared cyclopropyl as the next isomeric propyl alternative." *Id.* at 30 (citing Brown Decl. ¶ 38).

Petitioner further contends that "Kesseler (Ex. 1010) expressly teaches that a cyclopropyl group is ***preferred*** to an isopropyl group at the R_2 position." *Id.* at 30–31 (citing Brown Decl. ¶ 40). With reference to the table reproduced below, Petitioner directs our attention to compounds Ie and Iac disclosed by Kesseler. *Id.* at 31; Ex. 1010, 14:20–47. According to Petitioner, "Kesseler . . . discloses that changing isopropyl to cyclopropyl in the R2 position (circled) results in a nearly threefold increase in the IC_{50} values." Pet. 31 (citing Brown Decl. ¶ 41-42).

Kesseler compound Ie	Kesseler compound Iac
	
IC_{50}/mol/liter: 2.9×10^{-9}	IC_{50}/mol/liter: 1.0×10^{-9}

Petitioner concludes as follows:

> In view of the clear structural similarity between these compounds, a POSA would have understood that each was described as an active HMG-CoA reductase inhibitor, and would have considered Kesseler's ring-cracked compounds (i.e., those of formulae I and II in Kesseler) to be "analogs" of the ring-fused structure of compactin.
>
> Accordingly, a POSA would have expected that the activity of the compound of Picard Example 3 would have been improved by the similar substitution of a cyclopropyl for its isopropyl group.

Pet. 36 (citations omitted); Brown Decl. ¶¶ 46–48, 51–52.

2. Patent Owner's Contentions

Patent Owner contends that the evidence presented by Petitioner shows that there were many potentially beneficial compounds disclosed in the prior art. Prelim. Resp., 14–25 (citing Pet. 15, 17–18; Brown Decl. ¶ 25 n.1; Ex. 1009, 11:39–40 (Table 1); Ex. 1010, 1:35–54, 14:24–45). Patent Owner further contends that Petitioner's rationale fails to establish why the Picard Example 3 Compound would have been an obvious choice of a "lead compound" for an HMGCoA reductase inhibitor and thus "is the epitome of

impermissible hindsight reconstruction." *Id.* at 14.

Patent Owner contends that Picard only provides functional activity data for the compounds provided in Picard Table 1, which does not include the compound disclosed in Example 3 of Picard. *Id.* at 17–18 (citing Ex. 1009, col. 11 (Table 1)). Patent Owner argues that the Petitioner fails to provide a sufficient reason for why a person of ordinary skill in the art would "jump to the conclusion that the compound of Example 3 (for which not a shred of *in vitro* data is provided) would be a better inhibitor of HMG-CoA reductase than the 4-chloro compounds disclosed in Table 1 (for which *in vitro* data is provided)." *Id.* at 20.

With regard to Kesseler, Patent Owner contends that Kesseler discloses "an entire class of *non*-quinoline compounds . . . with *better* activity against HMG-CoA reductase than anything disclosed in Picard." *Id.* at 24. According to Patent Owner, Kesseler discloses at least 14 compounds having IC_{50} values against HMG-CoA reductase between 0.9–5.0 nanomolar, whereas the IC_{50} values disclosed in Picard were between 32 and 350 nanomolar. *Id.* (citing Ex. 1010, 14:24–45; Ex. 1009, 11 (Table 1)). Patent Owner further contends Petitioner fails to provide a sufficient rationale as to why a person of ordinary skill in the art would have equated results from the pyridine and pyrimidine cores of Kesseler to the quinoline cores of Picard. *Id.* at 34–37.

3. Analysis

We generally follow a two-part inquiry to determine whether a new chemical compound would have been obvious over particular prior art

compounds. *Otsuka Pharm. Co. v. Sandoz, Inc*., 678 F.3d 1280, 1291–93 (Fed. Cir. 2012). First, we determine "whether a chemist of ordinary skill would have selected the asserted prior art compounds as lead compounds, or starting points, for further development efforts." *Id.* at 1291. Second, we analyze whether there was a reason to modify a lead compound to make the claimed compound with a reasonable expectation of success. *Id.* at 1292.

A lead compound is defined as "'a compound in the prior art that would be most promising to modify in order to improve upon its . . . activity and obtain a compound with better activity.'" *Id.* at 1291 (citing *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd*., 492 F.3d 1350, 1357 (Fed. Cir. 2007)). Stated another way, "a lead compound is 'a natural choice for further development efforts.'" *Id.* (citing *Altana Pharma AG v. Teva Pharm. USA, Inc*., 566 F.3d 999, 1008 (Fed. Cir. 2009)). The analysis of whether a chemist of ordinary skill would have chosen the prior art compound as a lead compound "is guided by evidence of the compound's pertinent properties" including "positive attributes such as activity and potency," "adverse effects such as toxicity," "and other relevant characteristics in evidence." *Id.* at 1292.

Importantly, "[a]bsent a reason or motivation based on such prior art evidence, mere structural similarity between a prior art compound and the claimed compound does not inform the lead compound selection." *Id*.; *see also Daiichi Sankyo Co., Ltd. v. Matrix Laboratories, Ltd*., 619 F.3d 1346, 1354 ("[P]roving a reason to select a compound as a lead compound depends on more than just structural similarity, but also knowledge in the art of the functional properties and limitations of the prior art compounds").

Establishing that a chemical compound would have been obvious over a structurally similar compound requires "a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention.'" *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd*., 492 F.3d 1350, 1356 (Fed. Cir. 2007) (internal quotations omitted).

In the present case, Petitioner identifies the Picard Example 3 Compound as a "lead compound" and then proceeds to walk us through the steps a person of ordinary skill in the art would have had to perform in order to arrive at the compound of the claims. Pet. 26–36. These steps involve concluding from the data provided in Picard Table 1 that an isopropyl group at position R_2 of Picard Formula I is important for improved compound activity (i.e., IC_{50}). As the Picard Example 3 Compound is not a compound according to Picard Formula I, a person of ordinary skill in the art would have had to predict that this improved activity, attributed to the R_2 substituent, would have also been exhibited by a compound according to Picard Formula II having an isopropyl group at the R_2 position. A person of ordinary skill in the art would then have replaced the isopropyl at the R_2 position of the Picard Example 3 Compound with a cyclopropyl group to achieve the compound of the challenged claims. Petitioner reasons that Kesseler would have informed a person of ordinary skill in the art that such a change would improve the activity of the compound based on a comparison of Kesseler's Ie and Iac compounds. Pet. 31 (citing Brown Decl. ¶¶ 41–42).

We are not persuaded that Petitioner has established that a person of

ordinary skill in the art would have been motivated to perform the necessary modifications to the Picard Example 3 Compound in order to achieve the claimed compound. We note that Picard does not disclose any biological or pharmacokinetic data for the Picard Example 3 Compound, and as such, provides no suggestion that this compound has any particular functional activity to suggest that the compound should serve as a lead compound. Rather, the data disclosed in Picard relates to compounds according to Picard Formula I (Ex. 1009, 11:39–40 (Table 1)), which differs significantly from the Example 3 compound, a compound of Picard Formula II.

Petitioner's asserted obviousness ground is based primarily on the structural similarity of the Example 3 compound and the compound of the challenged claims. As stated in *Otsuka*, structural similarities alone are not enough to inform the lead compound selection. 678 F.3d at 1292. Accordingly, we determine that Petitioner has not provided sufficient reason to show that it would have been obvious to select the Picard Example 3 Compound from the genus of compounds disclosed in Picard.

Moreover, even assuming one would have started with Picard Example 3 Compound (based on its disclosure as an example compound), Petitioner does not persuade us sufficiently that an ordinary artisan would have had reason to substitute the isopropyl at the R2 position in particular in that compound with a cyclopropyl group. Table 1 in Picard, which relates to entirely different compounds, does not disclose a cyclopropyl group at that position. Consequently, Petitioner necessarily relies on Kesseler in its reasoning for the substitution—a reference that also discloses a number of entirely different compounds. Petitioner does not explain adequately why

one would have chosen this particular substitution in relation to Picard Example 3 Compound in particular, in view of the large number of possible substitution options when considering the different compounds disclosed in Kesseler and Table 1 of Picard.

D. Interference Estoppel

Petitioner contends that "[t]he grandparent application of the '336 patent was involved in two interferences," both of which the Patent Owner lost. Pet. 41 (citing Ex. 1005 and Ex. 1006). Petitioner attempts to use arguments made in those interferences to support arguments that the Patent Owner disclaimed or otherwise lost the right to claim the compound of claims 1 and 2 of the '336 patent. *Id.* at 41–60. It thus appears that Petitioner is attempting to rely on estoppel based on prior judgments in the above-mentioned interferences (Ex. 1005 and Ex. 1006), not on asserted unpatentability under 35 U.S.C. §§ 102, 103 based on prior art.

Under 35 U.S.C. § 311(b), a petitioner in an *inter partes* review "may request to cancel as unpatentable 1 or more claims of a patent only on a ground that could be raised under section 102 or 103 and only on the basis of prior art consisting of patents or printed publications." Petitioner has not directed us to any authority that allows this Board to cancel claims in an *inter partes* review based on arguments by a Petitioner that the Patent Owner may have disclaimed the subject matter of challenged claims in a related grandparent application, which is the relief requested by Petitioner (*see* Pet. 41–60).

The '336 patent itself was not involved in the two interference cases cited by Petitioner. Pet. 41–42. Nonetheless, Petitioner relies on alleged

"estoppel" based on judgments in those interferences, and specifically Petitioner's assertion that certain claims at issue in those cases recite subject matter that "is not patentably distinct" from the subject matter recited in the challenged claims. Pet. 46, 48. Thus, Petitioner does not assert unpatentability under 35 U.S.C. §§ 102, 103 based on prior art. *See also W. L. Gore & Associates, Inc. v. LifePort Sciences LLC*, Case IPR2014-01319, Paper 7, slip op. at 14–15 (PTAB Feb. 23, 2015) (addressing a similar type of argument regarding asserted "interference estoppel"). Accordingly, we do not institute an *inter partes* review based on the alleged interference estoppel asserted by Petitioner.

III. CONCLUSION

Petitioner does not persuade us that there is a reasonable likelihood that at least one of the challenged claims is unpatentable based on the asserted ground. We deny the petition for *inter partes* review and decline to institute trial on the asserted ground as to any of the challenged claims.

IV. ORDER

In consideration of the foregoing, it is hereby ORDERED that the petition is *denied* as to all challenged claims and no trial is instituted.

PETITIONER:

Kenneth Burchfiel
kburchfiel@sughrue.com

Travis Ribar
tribar@sughrue.com

Chid Iyer
ciyer@sughrue.com

Michael Dzwonczyk
mdzwonczyk@sughrue.com

Azy Kokabi
akokabi@sughrue.com

PATENT OWNER:

David Conlin
dgconlin@mintz.com

Kathleen Carr
KBCarr@mintz.com

David Cotta
DCotta@mintz.com

Peter Cuomo
PJCuomo@mintz.com