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Paper No. 43
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

HUBEI GRAND LIFE SCIENCE AND TECHNOLOGY CO., LTD,
Petitioner,

v.

VITAWORKS IP, LLC,
Patent Owner.

IPR2018-01766
Patent 9,428,450 B2

Before ERICA A. FRANKLIN, JENNIFER MEYER CHAGNON, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

MAJORS, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining All Challenged Claims Unpatentable
35 U.S.C. § 318(a)

I. INTRODUCTION

Hubei Grand Life Science and Technology Co., Ltd. ("Petitioner"),[1] on September 28, 2018, filed a Petition to institute *inter partes* review of claims 1 and 3–7 of U.S. Patent No. 9,428,450 B2 (Ex. 1001, "the '450 patent"). Paper 2 ("Pet."). Vitaworks IP, LLC ("Patent Owner") filed a timely Preliminary Response to the Petition. Paper 6 ("Prelim. Resp.").[2]

On April 9, 2019, we instituted *inter partes* review. Paper 10. After institution, Patent Owner filed Patent Owner's Response. Paper 17 ("PO Resp."). Petitioner filed a Reply to Patent Owner's Response. Paper 25 ("Pet Reply"). Patent Owner filed a Sur-Reply to Petitioner's Reply. Paper 30 ("PO Sur-Reply").

Oral argument took place on January 15, 2020. A transcript of that argument is entered into the record. Paper 42 ("Tr.").

We have jurisdiction under 35 U.S.C. § 6, and we issue this Final Written Decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. As explained below, we conclude that Petitioner has established by a preponderance of the evidence that claims 1 and 3–7 of the '450 patent are unpatentable for obviousness.

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[1] Petitioner identifies a number of entities as the real parties-in-interest in this proceeding. *See* Pet. 4.

[2] We also permitted Petitioner and Patent Owner to file, respectively, a *pre-institution* Reply (Paper 8) and Sur-Reply (Paper 9). The purpose of those papers was to allow the parties further briefing about alleged inconsistent positions taken by Patent Owner on certain prior art, and whether the challenged claims require a "second" ammonolysis step.

II. BACKGROUND

A. Related Matters

Petitioner states that it is a named defendant in *Vitaworks IP, LLC v. Hubei Grand Life Science and Technology Co., Ltd.*, No. 2:17-cv-12358-CCC-MF (D.N.J. filed Dec. 1, 2017), a case in which the '450 patent is asserted. Pet. 4. According to Petitioner, however, Plaintiff/Patent Owner has not served the complaint from that case on Petitioner. *Id.* Petitioner also identifies two other litigations related to the '450 patent. *Id.* at 5.

Petitioner identifies two other petitions for *inter partes* review that were filed concurrently with the present Petition. Pet. 5. Those other petitions challenged U.S. Patent No. 9,428,451 B2 ("the '451 patent") (IPR2018-01767) and U.S. Patent No. 9,573,890 B2 ("the '890 patent") (IPR2018-01768). *Id.* The '451 and '890 patents issued, respectively, from child and grand-child applications to the '450 patent. The Board instituted *inter partes* review in IPR2018-01767 and IPR2018-01768. Patent Owner, however, subsequently requested that the Board cancel the challenged claims of the '451 and '890 patents, and filed a Request for Adverse Judgment under 37 C.F.R. § 42.73(b)(2) in both cases, which requests the Board granted. *See* Paper 19 in IPR2018-01767 and IPR2018-01768 (cancelling the challenged claims, entering adverse judgment against Patent Owner, and terminating those two proceedings).

B. Background Technology and the '450 Patent

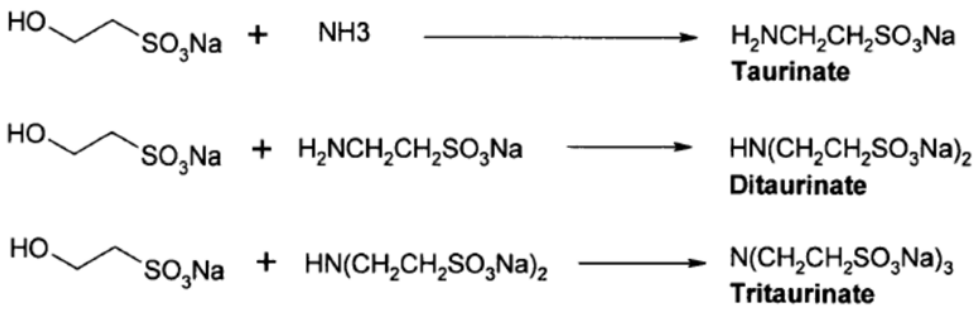
According to the '450 patent, the "invention relates to a cyclic process for the production of taurine from alkali isethionate and from alkali vinyl sulfonate in a high overall yield . . . by continuously converting the byproducts of the ammonolysis reaction, alkali ditaurinate and alkali tritaurinate, to alkali taurinate." Ex. 1001, 1:6–11.

As explained in the ’450 patent, “[t]aurine . . . is one of the amino sulfonic acids found in the tissues of many animals.” *Id.* at 1:15–17. “Taurine is an extremely useful compound because it has such pharmacological effects as detoxification effect, [and a] fatigue-relieving effect.” *Id.* at 1:18–21. Thus, “taurine finds wide applications as an essential ingredient for human and animal nutrition.” *Id.* at 1:21–22.

As background, the ’450 patent describes a pre-existing method of producing taurine called the “ethylene oxide process,” which is also known and referred to in this Decision as the “EO process.” *Id.* at 1:23–31, 1:53–56 (citing prior art (e.g., Ex. 1016) process.). In this process, ethylene oxide is reacted with sodium bisulfite to produce sodium isethionate, which is then subjected to the ammonolysis reaction to produce, among other compounds, sodium taurinate; sodium taurinate, when neutralized with an acid (e.g., sulfuric acid), converts to taurine. *Id.* at 1:23–31.

According to the ’450 patent, this EO process is “well established and widely practiced in commercial production.” *Id.* at 1:32–33. Nevertheless, the ’450 patent states, “overall yield is not very high,” and “the process generates a large amount of waste stream that is increasingly difficult to dispose of.” *Id.* at 1:34–36.

Byproducts of the EO process include, among other compounds, alkali ditaurinate and alkali tritaurinate. Indeed, as the ’450 patent explains, “[f]rom these prior arts, it is therefore concluded that the ammonolysis of sodium isethionate invariably yields a mixture of sodium taurinate, sodium ditaurinate, and sodium tritaurinate.” *Id.* at 2:9–12. This ammonolysis is summarized below, and may be catalyzed by a basic alkali salt (e.g., sodium hydroxide or sodium carbonate).



Ex. 1003 ¶ 46 (Declaration of Dr. Mark A. Lipton); Ex. 2001 ¶ 45 (Declaration of Dr. Robert E. Maleczka, Jr.); Ex. 1001, 1:54–2:3 (identifying prior art that describes the use of catalysts, including sodium carbonate or sodium hydroxide, in the ammonolysis reaction). As depicted, sodium isethionate reacts in the presence of ammonia (NH_3) to produce a mixture of sodium taurinate, as well as sodium ditaurinate and sodium tritaurinate.[3]

Subsequently, by neutralizing the mixture with an acid, the sodium taurinate is converted to taurine and then filtered out. Ex. 1001, 2:23–26 (describing a known technique wherein "[c]rude taurine is easily obtained [(following neutralization of sodium taurinate in acid)] by filtration from a crystalline suspension of taurine after cooling"); Ex. 1003 ¶¶ 33, 46; Ex. 2001 ¶ 46. The remaining waste supernatant, also known as the "mother liquor," includes, *inter alia*, sodium ditaurinate and sodium tritaurinate, and sulfate waste products. Ex. 2001 ¶ 49.

With this background in mind, the '450 patent proposes that the above-mentioned byproducts—particularly sodium ditaurinate and/or

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[3] As Dr. Lipton explains, "[b]ecause ammonia has three hydrogen atoms that can be replaced by a substituent group, the amine formed in the ammonolysis reaction can be a primary, secondary, or tertiary amine, and a mixture of the three amines is usually formed." Ex. 1003 ¶ 41. Also, "[t]he presence of excess ammonia in the ammonolysis reaction will favor the production of monoalkylated amines, or primary amines." *Id.* ¶ 42.

sodium tritaurinate—can be recycled and subjected to further ammonolysis to increase the production of sodium taurinate and, hence, taurine. *See, e.g.*, Ex. 1001, 2:32–49. The '450 patent discloses that "the mother liquor, consisting of taurine, monosodium ditaurinate, and monosodium tritaurinate, is suitable for recycling to the ammonolysis step to prepare sodium taurinate." *Id.* at 2:59–62.

Recycling the byproducts, the '450 patent explains, provides for a "cyclic process" for making additional sodium taurinate (and ultimately taurine). According to the patent, "to achieve the cyclic process, the present invention discloses a novel finding and process for converting sodium ditaurinate and sodium tritaurinate, byproducts of the ammonolysis of sodium isethionate, to sodium taurinate under the ammonolysis conditions." Ex. 1001, 3:18–23. More specifically, "[w]hen sodium ditaurinate and sodium tritaurinate are reacted with aqueous ammonia under ammonolysis reaction conditions, a mixture of similar compositions of sodium taurinate, ditaurinate, and tritaurinate is formed in an equilibrium state. This novel finding renders the cyclic process possible." Ex. 1001, 2:44–49. Further, the patent discloses:

> When sodium ditaurinate and sodium tritaurinate are subjected to the ammonolysis reaction in aqueous ammonia under the same conditions at a temperature of 220°C. for 2 hours, a mixture of similar compositions, i.e., sodium taurinate (74%), sodium ditaurinate (23%), and sodium tritaurinate (3%), is obtained. Clearly, an equilibrium state is reached among the three taurinates, irrespective of the starting materials.

Id. at 3:57–64; *see also id.* at 3:67–4:3 ("[T]he inevitable byproducts of the ammonolysis step, i.e., sodium ditaurinate and sodium tritaurinate, can be continuously converted to sodium taurinate in each successive cycle.").[4]

C. Illustrative Claim

Petitioner challenges claims 1 and 3–7. Claim 1, the only independent claim, reads as follows:

> 1. A process for the production of taurine from alkali ditaurinate, or alkali tritaurinate, or their mixture, comprising:
>
> (a) adding an alkali hydroxide to a solution of alkali ditaurinate, or alkali tritaurinate or their mixture, to prepare a solution of dialkali ditaurinate, or trialkali tritaurinate or their mixture,
> (b) adding an excess amount of ammonia to a solution of dialkali ditaurinate, or dialkali[5] tritaurinate, or their mixture, and subjecting the solution to ammonolysis reaction to yield a mixture of alkali taurinates,
> (c) removing excess ammonia from (b) and neutralizing alkali taurinates with an acid to form a crystalline suspension of taurine, and
> (d) recovering taurine by means of solid-liquid separation.

Ex. 1001, 8:6–20.

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[4] Although the '450 patent discloses a cyclic process, the patent states that the "invention can be carried out discontinuously, semi-continuously, and continuously." Ex. 1001, 5:44–46. The patent further indicates that its examples are not intended to be limiting. *Id.* at 5:50–51.

[5] Petitioner notes that step (b) recites "dialkali tritaurinate" but asserts, in context (*see* step (a)), the term in step (b) should be "trialkali tritaurinate." Pet. 28 n.3. This issue is not decisive because, as explained herein, we find that at least dialkali ditaurinate would be present based on the asserted art.

D. Prosecution History

During prosecution, the Examiner rejected the then-pending claims as obvious over German patent DD 219023 ("DD '023" (Ex. 1007)). Ex. 1002, 149–150. According to the Examiner, DD '023 taught ammonolysis of sodium isethionate (as in the EO process), which produces alkali ditaurinate and alkali tritaurinate in a reaction mixture with ammonia, and "those of ordinary skill would expect at least a portion of the ditaurinate . . . would convert to taurinate." Ex. 1002, 150; *see also id.* at 151–152 ("[T]he recited ammonolysis step is inherent in DD 023 since the taurinate, ditaurinate, and tritaurinate species were in the reaction mixture with ammonia at the recited reaction conditions and any observed outcome or benefit from this step is an invariable aspect of DD 023.") (emphasis omitted).

The applicant responded by amending claim 18 (issued claim 1) to add what is presently step (a) of claim 1. Ex. 1002, 160. Applicant acknowledged that "ammonolysis of the byproducts is inherent in the process [of DD '023] as you [i.e., the Examiner] clearly point out," yet applicant argued the inherent ammonolysis does not result in sodium taurinate "in an amount significant to increase production yield under known reaction conditions." *Id.* at 162.[6] Applicant argued the claims, as amended, included an "extra step [that] is introduced before the ammonolysis . . . to

[6] Applicant's response cited previously "undisclosed results" related to "failed attempts to prepare taurinate from ditaurine and tritaurine under the ammonolysis conditions," but no testing conditions or methodology were actually described. Ex. 1002, 162–163; Ex. 1003 ¶¶ 51–52; Ex. 2001 ¶ 34; Pet. 10. Given the lack of supporting details (or records) about applicant's results cited during prosecution, Patent Owner does not, and agreed it would not, rely on them in this proceeding and states "the Board is encouraged by the parties to do the same." PO Resp. 9 n.1.

convert alkali ditaurinate to di-alkali ditaurinate . . . by mixing the available starting materials with a solution of alkali hydroxide or alkali carbonate." Ex. 1002, 163. With this "extra step," applicant argued, the claims were "distinguished from the inherent ammonolysis of the byproduct." *Id.*

The Examiner then indicated that the claims were allowable. Ex. 1002, 196. According to the Examiner, "the applied references fail to teach or suggest the required steps of adding an alkali hydroxide to a solution of alkali ditaurinate . . . to prepare a solution of dialkali ditaurinate [i.e., step (a)] . . . , and adding an excess amount of ammonia to this to preform [*sic*, perform] an ammonolysis reaction." *Id.*

E. The Instituted Grounds of Unpatentability

The Petition challenges claims 1 and 3–7 based on the grounds in the table below. Pet. 13–14.

Claims Challenged	35 U.S.C. §	Reference(s)/Basis
1, 3–7	102	WO '071[7]
1, 3–7	103	WO '071
1, 3–7	103	Wu,[8] WO '071

[7] Heuer, WO 01/77071 A1, published Oct. 18, 2001 (Ex. 1009) (hereafter "WO '071"). WO '071 (Ex. 1010) is the English translation of the international patent application filed by Bayer Aktiengesellschaft and published in German. Ex. 1008 (Certification of translation for WO '071). As with other translated exhibits, Patent Owner does not contest the accuracy of the translations or sufficiency of the supporting certifications. For the citations to the relied-upon prior art, we refer to the page numbers on the exhibit copies rather than the original pagination of the references.

[8] Wu Jiang et al., *Optimization on Ammonolysis in Manufacturing Method of Taurine*, 19:1 JOURNAL OF HUBEI POLYTECHNIC UNIVERSITY 23–26 (2004) (Ex. 1011) (hereafter "Wu"). Wu (Ex. 1012) is the English translation of Wu. Ex. 1013 (Certification of translation for Wu and Liu).

Claims Challenged	35 U.S.C. §	Reference(s)/Basis
1, 3–7	103	Liu,[9] WO '071

Petitioner also relies on the Declarations of Mark A. Lipton, Ph.D. (Exs. 1003 and 1069), and the Declaration of Joe P. Foley, Ph.D. (Ex. 1070), among other evidence. Patent Owner relies on the Declarations of Robert E. Maleczka, Jr., Ph.D. (Exs. 2001 and 2007), among other evidence.

III. ANALYSIS

A. Overview of the Asserted References

We provide overviews of WO '071, Wu, and Liu below. Pet. 14–19.

1. WO '071 (Ex. 1010)

WO '071 relates generally to "a method for producing ditaurine and salts thereof from taurine or its salts" in a reaction medium. Ex. 1010, 1. As background, WO '071 describes other processes for producing ditaurinate, including the process wherein "[d]itaurinate is [] formed in the reaction of hydroxyethyl sulfonate [i.e., isethionate] with ammonia under pressure [(i.e., the EO process)]." *Id.* at 2.

Citing some downsides with other processes (e.g., low yields) for producing ditaurine, WO '071 discloses a "surprisingly simple method . . . [that] makes it possible to obtain ditaurinate from taurine in a targeted manner and with high yield." *Id.*; *see also id.* at 5 ("It is advantageous in the method . . . that it is possible to produce ditaurine and its salts with good yields in a targeted manner and in a simple fashion."), 6–8 (Examples 1–6

[9] Liu Fuming, *Process Design of Taurine Ammonolysis*, 5:8 CHINA CHEMICAL TRADE 120 (2013) (Ex. 1014) (hereafter "Liu"). Liu (Ex. 1015) is the English translation of Liu. Ex. 1013 (certification).

and Table 1), 9 (claim 2, reciting a method for the preparation of ditaurine and its salts "carried out to yield a conversion of taurine from 1 to 70%").

WO '071 discloses a preferred temperature for the reaction of "from 150 to 270°C" and especially "the range from 190 to 230°C." Ex. 1010, 3. WO '071 further discloses that the reaction medium may include water, and preferably aqueous sodium hydroxide or aqueous potassium hydroxide. *Id.* WO '071 teaches that it is necessary or advantageous to add alkali hydroxide to the reaction mixture. *Id.* (describing addition of 0.1 to 15 moles of alkali hydroxide per mole of taurine); *see also id.* ("If taurine salts, for example sodium or potassium salts, are used . . . it is not absolutely necessary to add alkali hydroxide but it is advantageous."). WO '071 also discloses that the reaction may be performed at various pressures, including atmospheric pressure, and pressures ranging from 0.9 to 40 bar. *Id.* at 4.

WO '071 teaches that ammonia, produced in the conversion of taurine (or taurinate) to ditaurinate, may be separated from the reaction mixture. *Id.* at 3. WO '071 discloses that the method "may also be carried out only up to partial conversion of taurine from e.g. 1 to 70%." *Id.* Further, WO '071 teaches, "[s]ince the equilibrium reaction may be displaced on the product side [i.e., toward ditaurinate] by the removal of the ammonia so formed, the conversion is dependent *inter alia* on the ammonia content in the reaction mixture." *Id.* According to WO '071, "[a]fter carrying out the method . . . and separating the ammonia so formed, there is generally a mixture [] yielded which contains ditaurinate, taurinate, perhaps excess alkali hydroxide, perhaps water, perhaps free taurine, and perhaps other components in small amounts." *Id.* at 4. WO '071 teaches that "[t]he reaction mixture may also be purified, e.g., neutralized or acidified, e.g. using mineral acids such as hydrochloric acid and sulfuric acid." *Id.*

2. Wu (Ex. 1012)

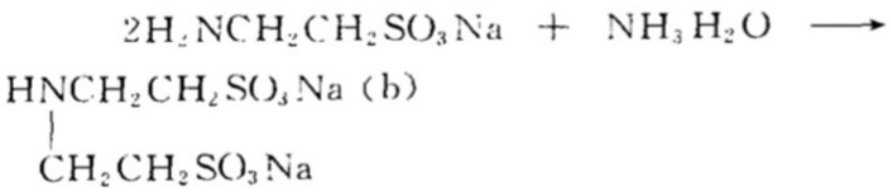
Wu relates to manufacturing of taurine by ammonolysis of sodium hydroxyethyl sulfonate (i.e., sodium isethionate) and subsequent acidification of the reaction mixture. Ex. 1012, 4.

According to Wu, taurine "is the most abundant sulfur-containing free amino acid in body cells" and it "plays a vital role in the development of the brain, nerves, [and] internal organs," among other body systems. *Id.* Moreover, taurine "helps enhance physical fitness, prevent disease, and relieve fatigue," and it "has been added extensively to a variety of foods, particularly in infant formula." *Id.*

Wu describes an initial reaction of ethylene oxide combined with sodium bisulfite to synthesize sodium isethionate. *Id.* Wu then describes an ammonolysis reaction, wherein the sodium isethionate reacts with aqueous ammonia to generate sodium taurinate, which Wu calls "sodium aminoethanesulfonate [] expressed using the symbol (a)." *Id.* Sodium taurinate, upon addition of an acid (i.e., concentrated sulfuric acid), forms taurine. *Id.* Wu states that "the average yield of product taurine is 41%." *Id.* at 7.[10]

Wu further describes a "[s]ide reaction" of the ammonolysis, shown below, which produces "sodium ditaurinate [] expressed using the symbol (b)." *Id.*

[10] According to Dr. Lipton, "with certain of [Wu's] ammonolysis conditions, the taurine yield can reach above 97%." Ex. 1003 ¶ 96; Ex. 1012, 6–7. Wu's 97.6% rate appears to correspond to percent of conversion (consumption) of starting material. Ex. 2075 (Lipton Dep.), 96:1–97:17; Ex. 1012, 6 (Table 5).



Ex. 1012, 4 ("Side reaction"); Ex. 1003 ¶ 93. The above chemical equation shows sodium taurinate forming sodium ditaurinate (product/symbol "(b)") in aqueous ammonia. Wu teaches that "[i]f (a) [sodium taurinate or taurine] can be independently separated and residues consisting primarily of (b) [sodium ditaurinate] are fed again into the ammonolysis system, the total yield of the product [i.e., taurine] may very well increase." Ex. 1012, 7; Ex. 2001 ¶ 72.

Wu also teaches adding sodium carbonate to the reaction environment as a "universal" catalyst for ammonolysis. Ex. 1012, 6 ("As a universal catalyst of high-pressure ammonolysis, the feeding amount of sodium carbonate is certain to be another factor in the reaction.").[11] Wu teaches that "[t]he basic reaction temperature was around (140-260)°C." Ex. 1012, 5. Wu further teaches that, after the ammonolysis reaction occurs in an autoclave, "the ammonia is expelled," then concentrated sulfuric acid is used to adjust the pH of the mixture to acidic (e.g., pH of 3.5), and a sample is taken to determine the sample's taurine content. *Id.* at 4.

[11] Sodium carbonate is a strong base that forms sodium hydroxide in water. Ex. 1003 ¶ 97; Ex. 1067 (Maleczka Dep.), 50:20–51:18 (testifying that sodium carbonate and sodium hydroxide are basic alkali salts that function as catalysts for the ammonolysis reaction), 95:21–96:3 (testifying that a POSA would regard sodium hydroxide as a strong base), 97:6–19 (testifying that a POSA would consider a pH greater than 9 as being "strong basic").

3. Liu (Ex. 1015)

Liu relates to a method for large-scale production of taurine, a product Liu describes as having "been applied extensively in the pharmaceutical and food industries." Ex. 1015, 6. Liu further "explains the process of producing taurine using the ethylene oxide method [i.e., the EO process], the theoretical analysis of ammonolysis, [and] the applications of the mother liquor in production." *Id.*

Liu describes the reaction of ethylene oxide and sodium bisulfite under alkaline conditions (30% sodium hydroxide) to produce 2-sodium isethionate. Ex. 1015, 6. The sodium isethionate then undergoes ammonolysis at high temperature and pressure (18–19.5 MPa, 265–270°C) to generate 2-sodium aminoethanesulfonate (i.e., sodium taurinate). *Id.* Liu teaches that neutralization of sodium taurinate with sulfuric acid generates sodium sulfate and taurine, which may then be extracted from the mixture. *Id.* ("After neutralization, the mother liquor remains after separating the crude taurine and sodium sulfate."). According to Liu, "[c]omponent analysis of the mother liquor indicates that it contains many components," including remaining 2-sodium isethionate and sodium sulfate, as well as "sodium ditaurinate." *Id.* Liu teaches that the mother liquor, if released, "becomes highly concentrated contaminated emissions, damaging and polluting the environment." *Id.*

Liu then describes an "Application of Mother Liquor Recycle in Production." Ex. 1015, 6 (bold-font omitted). Liu teaches that "[t]he 2-sodium isethionate that does not participate in ammonolysis follows the production system into the next process." *Id.* According to Liu, "[e]xcluding a small amount that undergoes a secondary reaction, the majority exists in the mother liquor in the form of 2-sodium isethionate,"

and "[t]he mother liquor can undergo the corresponding processing and purification to participate again in ammonolysis in the form of sodium isethionate." *Id.* Moreover, Liu teaches, "sodium ditaurinate is also generated during the ammonolysis process." *Id.* According to Liu, "[t]his sodium ditaurinate also exists in the mother liquor system," and "[i]f this sodium ditaurinate is fed again into ammonolysis, the proportion of 2-sodium isethionate in the reaction product can be increased, increasing generation yield" of taurine. *Id.*

Liu teaches that "[a]mmonolysis process reaction yield [of taurine] can be increased from 70%–80% to 85%–95%." Ex. 1015, 6. And, Liu discloses, the "equipment operations are stable, reducing the discharge of waste liquids and overall production costs." *Id.*

B. Person of Ordinary Skill in the Art

Petitioner proposes the following qualifications for the person of ordinary skill in the art (or "POSA"):

> [A] POSA at the time of the alleged invention . . . would have an advanced degree, such as a Master's or Ph.D., in the field of organic chemistry or a closely related field. (Ex. 1003, ¶ 17). A POSA would also have at least five years of experience with organic synthesis of nitrogen-containing compounds, and would understand basic chemistry principles and organic synthesis techniques. *Id.*

Pet. 12. Patent Owner agrees. PO Resp. 12; Ex. 2001 ¶¶ 20–22.

We find that the above qualifications are consistent with the cited prior art. *Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required where the prior art itself reflects an appropriate level and a need for testimony is not shown) (internal quotation marks and citation omitted).

We, thus, apply the parties' agreed-upon qualifications for the person of ordinary skill in the art in this Decision.

C. Claim Construction

In this *inter partes* review, we interpret claim terms based on the broadest reasonable construction in light of the specification of the patent in which those terms appear. 37 C.F.R. § 42.100(b) (2018); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming the broadest reasonable construction standard in *inter partes* review proceedings).[12] Under that standard, we presume a claim term carries its "ordinary and customary meaning," which "is the meaning that the term would have to a person of ordinary skill in the art in question" at the time of the invention. *In re Translogic Tech., Inc*., 504 F.3d 1249, 1257 (Fed. Cir. 2007). "[W]e need only construe terms in controversy, and only to the extent necessary to resolve that controversy." *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

"first" and "second" ammonolysis

The terminology of a "first" or "second" ammonolysis reaction is not language that appears in the '450 patent or its claims. And neither party has proposed any express construction for the limitations in the claims. Pet. 12

[12] The Final Rule changing the claim construction standard in IPR proceedings does not apply to the claims here, as the Petition was filed before the rule's effective date, November 13, 2018. *See* Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340, 51,340, 51,344 (Oct. 11, 2018); *see also* Paper 3 (according a filing date of September 28, 2018 to the Petition).

("[N]o claim terms or phrases require specific construction for the purpose of this IPR."); Prelim. Resp. 11; PO Resp. 10–11.

We, nevertheless, explained at institution, after receiving additional briefing from the parties (Papers 8 and 9), why independent claim 1 did not *require* a "second" or "subsequent" ammonolysis reaction as Patent Owner's preliminary arguments may have suggested. Paper 10, 15–18. As we noted at that time, claim 1 recites only one ammonolysis step, in step (b). *Id.* at 17. And, we explained, the ditaurinate recited in claim 1's step (a) and (b) *may* have been generated by an earlier ammonolysis (e.g., by ammonolysis of sodium isethionate in the traditional EO process, which "invariably" produces a mixture of mono-, di-, and tritaurinates (Ex. 1001, 2:9–12)), but such an earlier ammonolysis reaction was not necessarily required to be the source of the ditaurinate (or tritaurinate) in claim 1.[13] Paper 10, 17–18.

To the extent an issue remains, it stems from terminology Patent Owner has used in its arguments to address what Patent Owner regards as a distinction between reactions that *start* with at least some ditaurinate in the mixture (as in claim 1's steps), and those that do not (e.g., the EO process starting with sodium isethionate but no ditaurinate). To that point, Patent Owner contends "[t]his should be clarified further." PO Resp. 10.

According to Patent Owner, "[a] 'first' ammonolysis includes a reaction mixture that does NOT contain a ditaurinate when the reaction is begun," and "[a] 'second' ammonolysis . . . is one that begins with a reaction

[13] We also noted dependent claim 3, which specifies that the source of the ditaurinate (or tritaurinate) in claim 1 be a byproduct from an earlier ammonolysis of alkali isethionate or alkali vinyl sulfonate. Paper 10, 18; Ex. 1001, 8:24–27. In that respect, claim 3 may be characterized as requiring an earlier (first) and a subsequent (second) ammonolysis.

mixture containing ditaurinate." *Id.* at 10–11 (asserting that a "second" ammonolysis "is also often an ammonolysis run after a prior ammonolysis was run, but does not need to be"). In other words, Patent Owner urges, "the difference is primarily a matter of whether there is ditaurinate present at the start of the reaction irrespective of the source of the ditaurinate." *Id.* at 11.

We understand Patent Owner's position. We also do not consider our initial analysis on claim construction at institution as inconsistent with that position. Insofar as Patent Owner is suggesting that claim 1 requires ditaurinate (and/or tritaurinate) be present when the steps recited in the claim are carried out (e.g., "adding an alkali hydroxide to a solution of alkali ditaurinate"), we agree. That is supported by a plain reading of the claims, and the prosecution history. *See, e.g.*, Ex. 1002, 160–162 (amending claims to include step (a) in an effort to distinguish from inherent reaction of byproducts in the mixture left after ammonolysis of sodium isethionate (i.e., the EO process)). By contrast, merely running the traditional EO process—with no ditaurinate at the start, and assuming no further processing of ditaurinate produced by the EO process in a manner that performs claim 1's steps—would not satisfy all the limitations of the method claimed.

D. Principles of Law

A claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious to the person of ordinary skill in the art at the time of the invention. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence

of obviousness. *Graham v. John Deere Co*., 383 U.S. 1, 17–18 (1966). "[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. "[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine elements in the way the claimed new invention does." *Id.*

E. Anticipation by WO '071

Petitioner contends that claim 1 and 3–7 are unpatentable as anticipated by WO '071. Pet. 20–37.

In the Institution Decision, we explained the problems with Petitioner's anticipation challenge. Paper 10, 19–24. As we saw it, the anticipation challenge relied on a POSA's understanding that the reaction described in WO '071 could and would be driven in reverse and, from that, modifying the WO '071 reaction by, for example, adding excess NH_3 to ditaurinate to displace the reaction toward production and recovery of taurine—a theory, we explained, better reserved for obviousness not anticipation. *Id.* at 22–24.

Notwithstanding the problems with the anticipation challenge, and our skepticism that Petitioner was reasonably likely to succeed on it, the anticipation challenge was included in the trial. We included that challenge because we determined that Petitioner had shown it was reasonably likely to succeed on other grounds raised in the Petition. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359 (2018).

During trial, Petitioner, citing the Institution Decision and the Board's expressed skepticism, represented that it "no longer contends that claims 1 and 3–7 are anticipated by WO 071 (Ground 1 of Petition)." Pet. Reply 1 n.1. Petitioner confirmed the same at oral argument. Tr. 8:21–9:6

(Q: "Petitioner is now abandoning, or has abandoned its anticipation challenge based on the WO'071 reference, correct? Mr. Yang [Petitioner's counsel]: Yes, ... I do need to make that clarification. The Petitioner started with four grounds. Petitioner is no longer pursuing Ground 1.").

Petitioner provided no further response to the Board's initial findings on the problems with the anticipation challenge, and instead has abandoned that challenge as noted. So, for the reasons given in the Institution Decision, which we apply here, we find that the preponderance of the evidence on this record does not establish that claims 1 and 3–7 of the '450 patent are anticipated by WO '071. Paper 10, 19–24.

F. Obviousness over WO '071 and POSA's Knowledge

Petitioner contends that claim 1 (and dependent claims 3–7) are unpatentable for obviousness over WO '071 in combination with the skilled artisan's knowledge. Pet. 37–42; *see also id.* at 39–40 (cross-referencing discussion of relevant teachings for the anticipation challenge); *id.* at 26–32 (chart and analysis for claim 1), 33–37 (chart and analysis for claims 3–7).

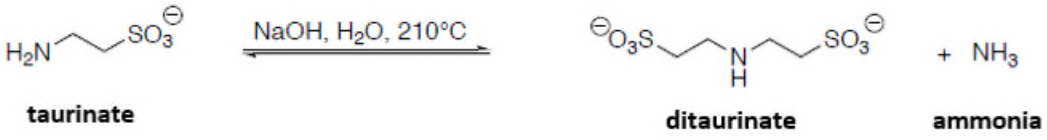
1. Claim 1

As explained above, WO '071 generally describes the production of ditaurinate from taurine (or its salts). Ex. 1010, 1; *supra* Section III(A)(1).

Although the focus of WO '071 is on making ditaurinate (not taurinate or taurine, like claim 1), Petitioner cites WO '071's teaching that the reaction is an "equilibrium reaction." Pet. 23; Ex. 1010, 3 ("Since the *equilibrium reaction* may be displaced on the product side [ditaurinate] by the removal of the ammonia so formed, the conversion is dependent . . . on the ammonia content in the reaction mixture.") (emphasis added). Petitioner reasons and its declarant, Dr. Lipton, testifies that "a POSA would have understood that an equilibrium reaction necessarily proceeds both ways –

forward and reverse." Pet. 23; Ex. 1003 ¶¶ 66–67. Thus, according to Petitioner, the skilled artisan would have understood WO '071 as disclosing not only the forward reaction, where ditaurinate and ammonia are produced from taurinate at the cited reaction conditions, but a *reverse* reaction as well—such that taurinate is also being produced from ditaurinate and ammonia. Pet. 22–23; Ex. 1003 ¶¶ 56–59.

Petitioner contends that "[t]he POSA would understand that this reaction can therefore be represented in the schematic diagram below:"



Pet. 23; *see also* Ex. 1003 ¶ 57. As Dr. Lipton testifies, the above diagram illustrates the reaction at equilibrium, with two reactions proceeding at the same time: one proceeding in one direction (right-facing arrow) where ditaurinate and ammonia are produced from taurinate, and another proceeding in the reverse direction (left-facing arrow) where taurinate is produced from ditaurinate and ammonia. Ex. 1003 ¶¶ 57–59. As depicted, and consistent with WO '071's teachings, the reaction occurs in a medium comprising sodium hydroxide (NaOH) and water, and at a temperature of 210°C. Ex. 1003 ¶¶ 57–59; Ex. 1010, 2 (disclosing reaction media, addition of alkali hydroxides, and temperatures), 6–7 (Examples and Table 1).

Petitioner explains that inclusion of alkali hydroxide (e.g., sodium hydroxide in WO '071) "ensures the reaction environment is basic," and that "a POSA would have readily understood that this [basic] reaction medium accelerates the forward and reverse reactions of an equilibrium by the same factor." Pet. 27. In support, Dr. Lipton testifies that "conditions disclosed in

WO 071, including the presence of the catalyst sodium hydroxide in the reaction medium, apply to both the forward and reverse reactions with equal effect." Ex. 1003 ¶ 63 (citing, for example, Ex. 1020 (excerpts of a textbook on organic chemistry), 81, as disclosing that a catalyst "accelerates the forward and reverse reactions of an equilibrium by the same factor"); *see also* Ex. 1003 ¶¶ 43 ("[A]s reflected in the prior art, a POSA would know that ammonolysis reactions must proceed in a basic environment."), 70 (testifying "reaction conditions . . . , such as alkalinity of the reaction environment in the presence of sodium hydroxide, accelerate the forward and reverse reactions of that equilibrium by the same factor").

Furthermore, Petitioner contends, "[a] POSA would also understand that an equilibrium reaction can be shifted to increase yield of either product or reagent" using "[w]ell-established chemistry principles." Pet. 40; *see also id.* at 23–24; Ex. 1003 ¶¶ 58–63, 86–87. Petitioner cites Le Châtelier's Principle: "whenever the concentration of a component changes, *the equilibrium system reacts to consume some of the added substance or produce some of the removed substance*." Pet. 23–24, 40 (quoting Ex. 1019 (excerpts from a textbook on chemistry), 45–46) (Petitioner's emphasis). Also, according to the Principle of Microscopic Reversibility, "if a reaction occurs by a certain mechanism, the reverse reaction under the same conditions occurs by the exact reverse of that mechanism." Ex. 1020, 81; Pet. 23–24, 40. Hence, Petitioner proposes that the skilled artisan would recognize that the WO '071 reaction can be shifted in direction by removing or adding components to either side of the reaction. Pet. 17, 24–26, 39–40; Ex. 1003 ¶¶ 32, 45–46, 50, 59–63, 67. For example, removing ammonia would cause more taurinate to convert to ditaurinate—a greater shift to the right. And, conversely, adding ammonia to shift the reaction toward the

production of taurinate/taurine—a shift to the left. Reading WO '071 in light of these established principles, Petitioner contends "a POSA would have understood that this equilibrium reaction can also be predictably displaced towards the reagent side [i.e., toward taurinate] by adding ammonia into the reaction system." Pet. 25; Ex. 1003 ¶¶ 61–63, 87–89.

Applying this understanding of WO '071, fundamental principles of chemistry, and other knowledge in the prior art, Petitioner contends the skilled artisan would have had reasons to displace the reaction suggested in WO '071 in a reverse direction—to favor production of taurinate/taurine through the addition of excess ammonia to ditaurinate. Pet. 41–42; Ex. 1003 ¶¶ 42 (testifying that excess ammonia will tend to favor the primary amine), 89–90. Petitioner contends the skilled artisan "would be drawn to the fact that ditaurinate is a standard byproduct from the widely-practiced taurine synthesis process through ammonolysis [i.e., of sodium isethionate in the EO process]." Pet. 41 (citing, e.g., Ex. 1001, 2:9–12; Ex. 1003 ¶ 89). And Dr. Lipton testifies it would have been obvious for a POSA to subject the ditaurinate byproduct in particular to the same ammonolysis reaction, and a POSA "would have been motivated to increase the yield of taurine, especially when, taurine is an important supplement that is very beneficial to a person's well-being." Ex. 1003 ¶ 89.[14] Based on WO '071's disclosed conversion rates, Dr. Lipton testifies a POSA would have been further

[14] As discussed above, at least Wu (Ex. 1012) and Liu (Ex. 1015) describe known benefits of taurine (e.g., as a food supplement) and suggest the byproducts of the EO process, ditaurinate in particular, be recycled for a further round of ammonolysis to produce additional taurine. *See supra* Section III(A)(2)–(3); *see* Pet. 14–15; Ex. 1003 ¶ 48 (describing Wu and Liu in relation to the state of the art knowledge).

motivated to drive the reaction toward making additional taurinate and increasing taurine yield. Ex. 1003 ¶ 89 (opining that a 1–70% taurine conversion rate means "this equilibrium can be made to significantly favor the reagent side, to produce up to 99% taurine or its salt"); Pet. 41 (asserting "a POSA would understand to mean that this equilibrium can be significantly displaced . . . to produce up to 99% taurine or its salt").

The skilled artisan would, according to Petitioner, have also had a reasonable expectation of success in driving the reverse reaction, and generating taurinate from ditaurinate in high yield because the equilibrium reaction consumes ammonia under the same conditions (e.g., reaction media) in WO '071. Pet. 41–42; Ex. 1003 ¶¶ 86–90. Moreover, Petitioner contends, applying well-known techniques, such as those recognized as prior art in the '450 patent itself, the skilled artisan would have easily and predictably neutralized sodium taurinate with an acid to produce and recover crystalline taurine through solid-liquid separation. Pet. 31–32; Ex. 1001, 2:21–26; Ex. 1003 ¶¶ 74–76.

Patent Owner disagrees. According to Patent Owner, Petitioner's challenge hinges on a flawed equilibrium reaction theory that reverses WO '071's reaction to produce, rather than consume, taurinate or taurine. PO Resp. 1–4, 16–22, 31–38. Without an equilibrium and reversibility, however, Patent Owner contends there is no reason to consider WO' 071 as part of a method for making taurine as claimed. *Id.* at 40–41. Further, Patent Owner contends, "reversed or not," the "claims could not be obvious" because WO '071 does not disclose all the limitations of the claims, such as adding and removing "excess ammonia" as in steps (b) and (c) of claim 1. *Id.* at 40.

We address Patent Owner's arguments (and Petitioner's response to them) in greater detail in Section III(F)(1)(c) below.

a. Claim Limitations

We find, based on a preponderance of the evidence, that claim 1's limitations are taught, suggested, and obvious over WO '071 and the skilled artisan's knowledge.

Although WO '071's aim is producing ditaurinate from taurinate (or taurine), Petitioner and Dr. Lipton persuade us the skilled artisan would have understood more than that from WO '071's disclosure of an equilibrium reaction. *See, e.g.*, Ex. 1010, 2–3; Ex. 1003 ¶¶ 50, 56–63. Just as WO '071 suggests the equilibrium may be displaced toward further production of ditaurinate by removing ammonia, we find the skilled artisan would understand, applying fundamental principles of chemistry such as Le Châtelier's Principle and the Principle of Microscopic Reversibility, that the reaction may be modified and driven in an opposite direction to produce taurinate from ditaurinate. *See, e.g.*, Ex. 1003 ¶¶ 61, 86–90; Ex. 1019, 45–46; Ex. 1020, 81. As for a reason to produce taurinate/taurine, we address that further below, but note that the record is replete with evidence of taurine's known benefits, thus reflecting reasons for the skilled artisan to have formed taurine and improved on reactions capable of producing it. *See, e.g.*, Pet. 1–2; Ex. 1001, 1:15–22; Ex. 1012, 4; Ex. 1015, 6. We, thus, find that WO '071 in combination with the skilled artisan's knowledge discloses claim 1's preamble of "[a] process for the production of taurine from alkali ditaurinate."[15] Ex. 1001, 8:6–7.

[15] Petitioner has shown that the recitation in the preamble is satisfied regardless of whether that preamble is limiting.

Step (a) of claim 1 recites, in pertinent part, "adding an alkali hydroxide to a solution of alkali ditaurinate . . . to prepare a solution of dialkali ditaurinate." Ex. 1001, 8:9–12; Pet. 26–28. We find WO '071 teaches use of an alkaline (basic) media for the reaction including the addition of an alkali hydroxide, especially aqueous sodium hydroxide. Ex. 1010, 3, 6–7; Pet. 26–28. And evidence indicates the same basic reaction media would apply to catalyze the reaction, if conducted and driven in reverse. *See, e.g.*, Ex. 1003 ¶¶ 63, 70; Ex. 1010, 3; Ex. 1020, 81; *see also* Ex. 1003 ¶ 89 (testifying a POSA would have used a known ditaurinate byproduct, and process it further (through ammonolysis) by a reverse reaction suggested in WO '071). Evidence also shows it was well known before the '450 patent to add catalysts for ammonolysis, especially sodium hydroxide or sodium carbonate (strong bases), and to create a basic reaction medium necessary for ammonolysis. Ex. 1001, 1:54–2:3; Ex. 1012, 6; Ex. 1003 ¶¶ 43–44, 97[16]; Ex. 2001 ¶ 45. WO '071 does not expressly mention dialkali ditaurinate (e.g., disodium ditaurinate), but we find that adding sodium hydroxide to sodium ditaurinate, in a basic reaction medium, will convert at least some sodium ditaurinate to disodium ditaurinate. Ex. 1003 ¶¶ 70–72; Ex. 1067, 95:21–96:3 (testifying sodium hydroxide is a strong base); Ex. 2001 ¶¶ 33 (testifying that at a lower pH, such as between 5–8 after neutralization with an acid, monoalkali ditaurinate is

[16] As Dr. Lipton testifies, "ammonia is a moderate base, [and] it is important that a basic reaction environment is used . . . [because,] if the ammonolysis reaction environment is not basic, the ammonia will be consumed by the acidic reaction medium instead." Ex. 1003 ¶ 80 ("[T]he ammonolysis reactions described in prior art references all take place in basic environments."); Ex. 1067 (Maleczka Dep.), 64:20–65:20, 66:22–67:6 (testifying that ammonolysis proceeds in a basic environment).

predominantly present, but at higher pH, such as above 9, dialkali ditaurinate is the predominant form), 119 (calculating a pH range in WO '071 at between 8 to 14).[17] We, thus, find claim 1's step (a) is met.

Turning to claim 1's step (b), which relates to adding "excess ammonia" and "ammonolysis" to produce alkali taurinates, we find this step is met on this record as well. Ex. 1001, 8:13–16. Petitioner contends a "POSA would appreciate that the [WO '071] reaction can also be displaced on the reagent side, to generate taurinate . . . by adding excess ammonia into the reaction system." Pet. 29. We agree. And, for reasons explained above, we find it would have been obvious for the skilled artisan seeking to make taurinate to conduct and drive the reaction in the direction of that product through addition of excess ammonia. Ex. 1010, 3; Ex. 1019, 45–46; Ex. 1020, 81; Ex. 1003 ¶¶ 61, 86–90. Moreover, the record shows adding excess ammonia as part of ammonolysis is a well-known, routine step in the art. *See, e.g.*, Ex. 1012, 4–5; Ex. 1020, 102 ("use of a large excess of ammonia in alkylation of ammonia] synthesis favors monoalkylation"); Ex. 1001, 1:53–58 (describing prior art as conducting ammonolysis of isethionate in a molar ratio of 1:6.8); Ex. 1003 ¶ 42. Indeed, Patent Owner itself describes adding excess ammonia as "standard operating procedure." Ex. 1060 (Patent Owner's Second Amended Complaint) ¶ 128 (chart purporting to show claim 1's step (b) is met, asserting "addition of excess ammonia to perform ammonolysis is standard operating procedure").

[17] The claims neither recite nor require that any specific proportion of the ditaurinates or tritaurinates be in a fully deprotonated, dialkali- or trialkali-form upon addition of an alkali hydroxide.

For steps (c) and (d), Petitioner asserts that WO '071 discloses separating ammonia by distillation, and neutralizing the reaction mixture with an acid, which, according to Petitioner, "inevitably would form crystalline taurine, which can then easily be recovered through solid-liquid separation using known techniques in the art." Pet. 30–32. Here too, we agree. Claim 1's steps (c) and (d) relate to removing the excess ammonia, neutralizing alkali taurinates with an acid to form taurine, and recovering the taurine. Ex. 1001, 8:17–19. We find those steps are suggested in WO '071 or simply routine, prior art techniques the skilled artisan would predictably use for neutralizing and removing the desired reaction product—in this case, taurine—following ammonolysis. Pet. 31–32; Ex. 1010, 4 (disclosing removal of ammonia after the reaction, neutralization of the reaction mixture with sulfuric acid); Ex. 1012, 4 (same); Ex. 1001, 2:21–26 (describing prior art's use of "sulfuric acid to neutralize sodium taurinate to obtain solution of taurine," which taurine is then "easily obtained by filtration from a crystalline suspension"); Ex. 1003 ¶¶ 74–76.

b. Motivation and Reasonable Expectation of Success

We find a POSA would have been aware of taurine's many benefits. *See, e.g.*, Pet. 1–2; Ex. 1001, 1:15–22 (describing taurine, in background, as an "essential ingredient for human and animal nutrition"); Ex. 1012, 4 (taurine "plays a vital role in the development of the brain," and other organ systems); Ex. 1015, 6 ("Taurine has been applied extensively . . . as an important drug and food additive"); Ex. 1003 ¶ 89 ("[T]aurine is an important supplement that is very beneficial to a person's well-being"). Those recognized benefits would have provided reasons to make taurine, and improve on methods capable of doing so with the aim of producing higher yields. Combined with, at minimum, knowledge of WO '071's teachings of

an equilibrium reaction between taurinate and ditaurinate as explained, we find the skilled artisan would have been motivated to modify the reaction as proposed—conducting and driving it in a reverse direction to produce taurinate and ultimately taurine from ditaurinate. Ex. 1003 ¶¶ 88–90.

We further find the skilled artisan would have had a reasonable expectation of success in conducting and driving the reaction described in WO '071 in a desired direction to produce taurine from ditaurinate. *Id.* "[T]he expectation of success need only be reasonable, not absolute." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007) (holding that "obviousness cannot be avoided simply by a showing of some degree of unpredictability"). This reasonable expectation is buttressed, at least in part, by fundamental principles of chemistry related to a predictable manipulation and reversibility of such reactions as discussed above. Ex. 1003 ¶¶ 58–63, 86–87. WO '071 itself suggests the equilibrium may be displaced based on the reaction's ammonia content, consistent with Le Châtelier's Principle. Ex. 1010, 3; Ex. 1019, 45–46.[18] Moreover, while a desire for much higher taurine yields may well have motivated the skilled artisan to carry out the reactions in the manner proposed, the claims simply do not recite or require any specific yield of taurine actually be achieved, much less that the yield be 99% or higher—essentially quantitative. *Intelligent Bio-Systems Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016) (holding that "[t]he reasonable expectation of success requirement refers to the

[18] Insofar as Wu and Liu both also suggest removing taurine/taurinate and recycling ditaurinate from the mixture of byproducts and subjecting to another round of ammonolysis may improve taurine yields, we find those prior art references add to a POSA's reasonable expectation of success. *Supra* Section III(A)(2)–(3); Ex. 1012, 7; Ex. 1015, 6.

likelihood of success in combining references to meet the limitations of the *claimed invention*.") (emphasis added).[19]

c. Patent Owner's Arguments

Patent Owner's primary argument is that, contrary to WO '071's express disclosure, the reaction is *not* an equilibrium reaction and, thus, Petitioner's obviousness theory about driving the reaction in a reverse direction to arrive at the method of claim 1 must fail. *See, e.g.*, PO Resp. 1–4, 31–38. Patent Owner alleges there are inconsistencies in the art, and that tests run by Patent Owner undermine WO '071's teachings and Petitioner's equilibrium theory. *Id.*; *see also id.* at 16–22 (summarizing tests).

According to Patent Owner, Petitioner's challenge is "predicated on a single sentence in WO '071 . . . suggesting that converting taurinate to ditaurinate is an 'equilibrium reaction.' *But Petitioner and WO '071 are wrong*." PO Resp. 1 (Patent Owner's emphasis). Patent Owner argues, if WO '071's reaction was an equilibrium, "removing ammonia from the reaction would drive it to near completion—99% ditaurinate." *Id*. Also, Patent Owner contends, if the reaction was an equilibrium, the inventor of WO '071 logically would have driven the reaction to completion by removing ammonia and producing even higher yields of ditaurinate, rather than stopping at about 64%. *Id.* at 16–17 ("Why would the inventors [of WO '071] not have followed their own teaching and removed ammonia driving the process to completion—100% ditaurine the product they set out to generate?"). Moreover, Wu and Liu allegedly should not have "suffer[ed]

[19] Patent Owner does not argue here that the claims are nonobviousness on the basis of any particular objective indicia (such as any alleged unexpected taurine yield). *See* PO Resp., *generally*; Pet. Reply 19 ("PO does not allege that any secondary considerations exist.").

from the low yields exhibited" because "there would be nothing left to recycle." *Id.* at 16–17 ("Neither attained near quantitative yields"), 32–34.

Because "PO and Dr. Maleczka were unconvinced" by WO '071's teachings and Petitioner's theory, they opted to perform tests. PO Resp. 17. Patent Owner contends its tests prove WO '071 does not work as Petitioner said it would. *Id.* at 36–38; *see also id.* at 16–22 (summarizing tests). Patent Owner contends WO '071's reaction is unreliable and could not be driven to completion (consumption of ≥ 99% taurine); thus, Patent Owner argues the reaction cannot be an equilibrium, and a POSA would "dismiss Petitioner's theory" and consideration of WO '071. *Id.* at 22, 36 ("Dr. Maleczka's work showed that ammonolysis, did not go to completion as Petitioner's theory, and WO '071's teaching, both predict."), 38 ("[A] POSA would find [WO '071] unreliable and there is no reason that a POSA would rely on other teachings of WO '071"), 40 ("People interested in creating taurine would have no reason to look to WO '071 absent its discredited equilibrium theory.").

Patent Owner's tests are described in more detail in Dr. Maleczka's Second Declaration. Ex. 2007 ¶¶ 33–78. In general, the tests sought to assess whether the reaction of taurine to ditaurinate can be driven to completion (≥ 99% taurine consumption). *Id.* ¶¶ 26–27. The reactions were carried out in an autoclave, with steam and ammonia being periodically "bled" (vented) until the smell of ammonia could no longer be detected; samples of the reaction mixture were also periodically taken and assayed using HPLC to determine taurine content (i.e., percent of taurine remaining). *See, e.g.*, *id.* ¶¶ 34 (Experiment 1: using 125 g of taurine, 50 g of sodium hydroxide, and 750 mL of tap water mixed in an autoclave with a bleeding valve), 37.34 (describing analysis of HPLC peaks in a sample (taken about 6

hours after the autoclave was initially heated to 200°C; ammonia smell detected at sampling) as "corresponding to 31.5% taurine remaining" (about 68% of taurine consumed)), 37.28 and 37.36 (describing sample taken about 1.5 hours later (at which time an ammonia smell was not detected) with 23% taurine left (77% consumed)).[20] From this testing, Dr. Maleczka concludes "[t]he results overall suggest that somewhere around 80[%] taurine consumed, a steady state is reached and the addition or subtraction of ammonia will not drive the reaction in either direction." *Id.* ¶ 78.

For several reasons, Patent Owner's argument and evidence are unavailing, and we find it does not outweigh the evidence of obviousness.

As an initial matter, we observe that disclosures in prior art publications (like WO '071) are presumed to be enabled. *In re Antor Media Corp.*, 689 F.3d 1282, 1287–88 (Fed. Cir. 2012); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1355 (Fed. Cir. 2003). As explained above, WO '071 discloses, exemplifies, and claims a reaction in which taurinate forms ditaurinate and ammonia in a catalyzed, basic reaction media at, for example, 210°C. Ex. 1010, 3–4, 6–9. WO '071 also expressly discloses that the reaction is an "equilibrium reaction" and, thus, "may be displaced on the product side by the removal of the ammonia so formed." *Id.* at 3. This disclosure is consistent with well-known principles of chemistry identified above, as is Petitioner's argument that the skilled person

[20] The five experiments as generally described as follows: First Experiment ("proof of concept"); Second Experiment ("WO '071 Example 1"); Third Experiment ("example 1a of WO '071"); Fourth Experiment ("Proof of Concept: Closed System With Bleeding"); Fifth Experiment "modified proof of concept reaction (Fourth Experiment above) without bleeding"). Ex. 2007 ¶¶ 33, 46, 63, 67, 73 (emphases omitted).

would understand that the reaction is reversible and may be displaced in an opposite direction by addition of excess ammonia under similar reaction conditions. Pet. 25; Ex. 1003 ¶¶ 61–63, 87–89.

Furthermore, in an obviousness analysis, "a reference need not work to qualify as prior art; 'it qualifies as prior art, regardless, for whatever is disclosed therein.'" *Geo M. Martin Co. v. Alliance Mach. Sys. Int'l LLC*, 618 F.3d 1294, 1302–03 (Fed. Cir. 2018) (quoting *Amgen*, 314 F.3d at 1357). "Even if a reference discloses an inoperative device, it is prior art for all that it teaches." *Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1550–51 (Fed. Cir. 1989) (rejecting as a "misstatement of the law" the proposition that "a piece of prior art that doesn't work is not prior art" and "can't be relied on" to invalidate a patent).

Patent Owner, acknowledging these legal precedents, argues that "for all that it teaches" as in *Beckman* and its progeny "means 'for all that it teaches' correctly or operably." PO Sur-Reply 4–5 ("[P]rior art must teach a person of ordinary skill to make an apparatus that works for its intended purpose") (quoting *Geo M. Martin*, 618 F.3d at 1303). But we are unpersuaded on this record that the reaction described and suggested in WO '071 is inoperable as Patent Owner contends. Even considering Patent Owner's testing (about which we have other concerns, discussed below), it points to a consumption and conversion of taurine to ditaurinate and ammonia, and to an increase in the extent of taurine conversion with a removal of ammonia just as WO '071 suggests. Ex. 1010, 3. For example, in the second experiment—intended to resemble WO '071's Example 1 but ***with venting*** of ammonia—taurine consumption exceeded 80% or even 90%. Ex. 2007 ¶¶ 46, 53.71, 57; Ex. 1069 ¶¶ 17 (Dr. Lipton testifying that "[i]f the data from Dr. Maleczka's experiments is correct, Dr. Maleczka's

own experiments confirmed that WO 071's reaction is an equilibrium reaction"), 18 (testifying that "data show that he reached above 90% yield"); *see also* Pet. Reply 18–19 (noting that conversion with venting (in Experiment 4) was about 82%, and without venting (in Experiment 5) was about 64%). That is well above the stated taurine conversion range (1–70%) in WO '071 without a step of ammonia being bled off during the reaction. Ex. 1010, 3, 8–9.[21]

Insofar as Patent Owner's testing is alleged show that a reaction in which taurine is converted to ditaurine/ditaurinate does not go to full completion (~100% ditaurine), WO '071 does not indicate that it would. And neither did Petitioner or Dr. Lipton. Ex. 1069 ¶¶ 11–12 ("I did not claim that the yield of *ditaurine* can reach 99% in light of WO 071's disclosure and I would have no basis for saying that based on WO 071."); Pet. Reply 11 ("PO's selection of 100% ditaurine yield as the benchmark of whether WO 071's reaction is an equilibrium reaction is therefore

[21] Patent Owner's experiments test taurine content remaining in samples, not the content of resulting ditaurinate, although Dr. Maleczka opines that, if an equilibrium, a proportionate amount of ditaurinate would be created with taurinate consumed. Ex. 2007 ¶¶ 29–30; Ex. 1067, 286:4–7. In response to evidence that the experiments suggest Le Châtelier's Principle and equilibrium was at play because of the increased taurine consumption when ammonia was bled off (*see, e.g.*, Ex. 1069 ¶¶ 17–20), Patent Owner argues "one cannot equate taurine consumed with ditaurine produced." PO Sur-Reply 7. But that weakens Patent Owner's argument and testing when compared to data in WO '071, which does report ditaurinate content and yield after the reaction. *See, e.g.*, Ex. 1010, 6–8 (Examples (showing ditaurinate yield varying with taurine consumed)). While Patent Owner concludes it was unable to convert 100% of the taurine, it did not determine how much ditaurinate was produced and we do not agree that the ~100% ditaurinate benchmark it set was justified as explained elsewhere.

baseless."). Beyond that, the evidence here is in agreement that achieving essentially quantitative yields, is uncommon. Ex. 1069 ¶¶ 14–16 (testifying "it is very rare that a chemical reaction reaches 99% yield"); Ex. 1067 (Dr. Maleczka Dep.), 285:12–24 (testifying to an estimated 10% of reactions capable of the "upper nineties in percentage completion").

And, returning to enablement and whether the prior art enables the skilled artisan to make and use the *claimed invention*, we again observe that no particular yield of taurine is recited or required in the claims here. *See Beckman*, 892 F.2d at 1550 ("References relied upon to support a rejection for obviousness must provide an enabling disclosure . . . [that] place[s] the claimed invention in the possession of the public."); *Geo M. Martin*, 618 F.3d at 1294 (rejecting argument as to the alleged insufficiency and nonenablement of a prior art machine that was shown not to work at "production speed," because "the claims do not require a threshold throughput or commercial speed"). Hence, even accepting Patent Owner's testing, an inability of WO '071's reaction to go to ~100% completion does not demonstrate that the prior art fails to enable claim 1's subject matter.

Second, Patent Owner contends a POSA would not have credited WO '071's express teachings, and instead would have believed it necessary to first validate (or invalidate) the reaction through the testing presented here due to perceived questions in the art about the ability to drive the reaction to completion. PO Resp. 31–36 (noting, for example, that WO '071 suggests some compounds (beyond ditaurinate) may remain in the mixture, including "excess alkali hydroxide, perhaps water, perhaps free taurine"); Ex. 1010, 4. On balance, however, we find that Patent Owner's professed doubts about WO '071 (and Petitioner's theory) arise, not from WO '071 or other art, but from a different place. PO Resp. 31–36.

More specifically, Dr. Hu, the '450 patent's named inventor, designed the protocol in Patent Owner's present testing years ago (before the application for the '450 patent was filed) in an apparent, yet unsuccessful, effort to create 100% pure ditaurine from taurine and applying teachings in WO '071. For example, Dr. Hu testified:

> Q. So when you ran the experiment in this protocol [in April 2019] and you obtained the results, you knew that this reaction is not equilibrium reaction?
> A. This experiment is just repeating experiment of my 2013 experiment [related to WO '071]. When I did 2013 experiment, equilibrium reaction never come to my mind. When I saw your IPR theory, great theory, then I realized this theory is not supported by my experiment.

Ex. 1068 (Hu Dep.), 95:5–15, 96:9–16 (testifying to review of IPR Petition in Sept. 2018), 91:5–18 (testifying to running the present protocol/experiment by himself again in April 2019); PO Sur-Reply 8–9; *see also* Ex. 1068, 11:8–12:19, 15:12–16:23 (testifying to attempts in 2013 to make "hundred percent pure" ditaurine based on WO '071 but, because he was unable to get pure ditaurine, concluding it was a "failed procedure").[22] So, to the extent Patent Owner contends the ordinarily skilled person would disbelieve and dismiss WO '071's teachings based on an alleged inability to drive the WO '071 reaction to completion (~100% ditaurine), we find the contention arises primarily from Dr. Hu's own work, and results uniquely possessed by him, before the '450 patent was filed. What the inventor actually did or knew, however, is outside the scope of the obviousness

[22] *See* Ex. 1068, 16:7–23 ("Q. And you wanted to do that [make 100% pure ditaurine] using the procedures in the '071 patent? A. That's the only procedure I can find. . . . [Q] Does the '071 patent teach the making of pure ditaurine? A. No.").

inquiry. *Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985) ("One should not go about determining obviousness . . . by inquiring into what patentees (i.e., inventors) would have known or would likely have done, faced with the revelations of the references."). "What matters is the path that the person of ordinary skill in the art would have followed, as evidenced by the pertinent prior art." *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012); *Dystar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1361 (Fed. Cir. 2006) (prior art is "viewed through the eyes of an ordinary artisan").

Third, Patent Owner's argument that WO '071's reaction is not an equilibrium reaction is inconsistent with the '450 patent itself. As Petitioner highlights, the '450 patent discloses that "when sodium ditaurinate and sodium tritaurinate are reacted with aqueous ammonia under ammonolysis conditions, a mixture of similar compositions of sodium taurine, ditaurinate, and tritaurinate is formed in *an equilibrium state*." Ex. 1001, 2:44–48 (emphasis added); Pet. Reply 7–8. The '450 patent also explains that the equilibrium of the taurinates in the ammonolysis reaction is what makes the cyclic process possible. Ex. 1001, 2:44–49, 3:57–4:3 ("Clearly, an equilibrium state is reached among the three taurinates, irrespective of the starting materials.").

Patent Owner's response to this inconsistency is twofold: first, that an "equilibrium state" in the '450 patent refers to a "steady state reaction," not an equilibrium reaction; and, second, even if an "equilibrium state" implies

an equilibrium reaction, the '450 patent, like WO '071 (and Petitioner's theory), is wrong too. PO Resp. 23; PO Sur-Reply 16–17.[23]

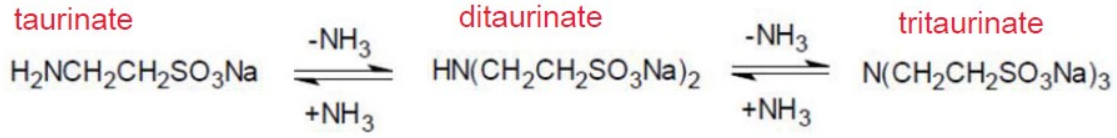
We find neither response persuasive. When tested on cross-examination, Dr. Maleczka had no credible answer to distinguish between an equilibrium reaction and an equilibrium state (or alleged "steady state reaction"). Ex. 1067, 266:6–16 (testifying that the purported distinction rested on "a little bit of . . . semantics . . . [b]ut basically, something that is at an equilibrium state, it would suggest that it's part of an equilibrium"). Ultimately, when asked, "to the extent the inventor of the '450 patent referred to equilibrium state, can you have an equilibrium state without an equilibrium reaction," Dr. Maleczka's answer was unequivocal: "No." *Id.* at 266:17–23; *see also id.* at 104:4–25; 266:24–267:17 (testifying that he only questioned WO '071's disclosure of an equilibrium, not the equilibrium disclosure in the '450 patent, despite the latter not including experimental data). Moreover, Dr. Lipton testified that, based on his 35-plus years as a chemist, the phrase "steady state reaction" was a "meaningless" or "made-up term." Ex. 1069 ¶¶ 45–47 ("I have never heard of the term 'steady state reaction' apart from its use in the phrase 'steady state *equilibrium*.") (emphasis added), 50 (citing Ex. 1019, 54).

As for Patent Owner's assertion that the '450 patent is, like the prior art, mistaken about the equilibrium reaction, we find that argument also unavailing. As Petitioner points out, the description of the reaction being an equilibrium does not end with the '450 patent. Pet. Reply 8. Rather, Patent

[23] In Sur-Reply, Patent Owner no longer refers to the '450 patent reaction as a "steady state reaction" and, instead, offers a new term—"competition reaction," which it contends is incompatible with an equilibrium. PO Sur-Reply 10–12. We address that terminology further below.

Owner has repeatedly filed documents, in both the U.S. Patent Office and abroad, describing the ammonolysis reaction as an equilibrium reaction. *Id.* (describing at least four other US patents, and at least two representations before the EPO); *see, e.g.*, Ex. 1075, 3:12–22 ("At higher molar ratio, the equilibrium is shifted to the formation of sodium taurinate at the costly expense of recovering excess ammonia. At lower molar ratio, the formation of sodium ditaurinate and sodium tritaurinate is excessive."); Ex. 1076 ¶¶ 18, 26, Claim 1 (describing formation of an "equilibrium mixture of sodium taurinate, sodium ditaurinate, and sodium tritaurinate"); Ex. 1069 ¶¶ 42–43 (identifying contradictory disclosures in other patent documents).

Patent Owner's inconsistent representations also continue in filings with the court.[24] Pet. Reply 9–10. For example, on November 6, 2018 (after the Petition was filed), Patent Owner represented that "[a]n *equilibrium state* is reached among the three taurinates as described by the following:"



Ex. 1059 ¶ 29 (annotated) (emphasis added); *see also id.* ¶ 33 (describing "equilibrium ammonolysis of the three taurinates"); Ex. 1060 ¶¶ 29, 33, 35, 144. The above equation depicts an apparent equilibrium conversion between the mono-, di- and tritaurinates with a respective consumption

[24] Ex. 1068, 96:9–18 (Dr. Hu testifying that he knew the reaction was not an equilibrium by at least September 2018); Ex. 1067, 273:2–15 (Dr. Maleczka testifying that he had expressed to Patent Owner's counsel his skepticism on the alleged equilibrium as of November 2018). According to Petitioner, this shows that Patent Owner continued to describe the reaction at issue as an equilibrium even after it knew that was allegedly incorrect. Pet. Reply 9–10.

(+NH_3) or production (-NH_3) of ammonia. We find these representations undercut Patent Owner's contention that the reaction in the '450 patent (and in WO '071) is not an equilibrium.

Patent Owner contends in Sur-Reply that, using Patent Owner's terminology, "competition reactions" among the taurinates means the reactions in the '450 patent and WO '071 "cannot be an equilibrium." PO Sur-Reply 10–12. We do not agree. Dr. Lipton's testimony is to the contrary. *See, e.g.*, Ex. 1069 ¶¶ 15–20, 43–44. And Patent Owner simply never questioned Dr. Lipton about whether a so-called "competition reaction" means there can be no equilibrium. Tr. 32:20–33:10.

Fourth, Petitioner has identified several issues with the design of Patent Owner's experiments and the reliability of the data arising from them. Petitioner urges us to disregard Patent Owner's testing because it relies on a protocol created by Dr. Hu, the '450 patent's inventor and Patent Owner's President, with no substantive input from Dr. Maleczka. Pet. Reply 4–7; *see, e.g.*, Ex. 1067, 292:3–18 (Dr. Maleczka testifying that the protocol "was provided to me by Vitaworks [(i.e., Patent Owner)]"); Ex. 1068, 86:8–22, 91:5–93:7; 94:21–95:24 (Dr. Hu testifying that he designed the protocol, and ran it himself alone before handing it over to counsel); *see also id.* at 89:19–23 (Dr. Hu testifying that he "did all the experiments" as Dr. Maleczka's "technician"), 105:3–9 (Dr. Hu testifying that he and counsel were present throughout while the experiments were conducted in Dr. Hu's lab); *see also* PO Sur-Reply 8–9 (asserting that Dr. Maleczka "oversaw and directed" the experiments run by Dr. Hu).

The evidence indicates that the protocol on which the present testing was based came from Dr. Hu, and that Dr. Maleczka's involvement in the design was minimal. Ex. 2007 ¶ 36; Ex. 1068, 107:22–108:10 (testifying

that Dr. Maleczka had no questions about the protocol and modified it only "to collect more data"). For that reason, we accord the testing evidence less weight than had it been designed and conducted by a disinterested third party. *See Moderna Therapeutics, Inc. v. Protiva Biotherapeutics, Inc.*, IPR2018-00680, Paper 46 at 40 (PTAB Sept. 10, 2019) (finding "the probative value of the testing is diminished by the involvement of Patent Owner's counsel, as well as the selection of Dr. Heyes [(Patent Owner's employee)], an interested party, to do the testing.").

Petitioner, supported by Dr. Lipton's testimony, also points out that the experiments rely on a "literal smell test" that is "inherently unscientific, subjective, and unreliable." Pet. Reply 11–12, 15; Ex. 1069 ¶¶ 22–25 (testifying that "no attempt to quantify, or even keep track of how much ammonia had been released" was made and, instead, Drs. Hu and Maleczka "relied on their sense of smell"). Dr. Maleczka opines that the "protocol is consistent with the type of protocol that a POSA would devise for this type of experiment" (Ex. 2007 ¶ 35), but no support is cited for the acceptability of using scent (of NH_3 or otherwise) in this way to test whether a reaction is an equilibrium, or has gone to completion. *See* 37 C.F.R. § 42.65(b) (requiring that, if a party "relies on a technical test or data from such a test," they must provide an affidavit, *inter alia*, explaining, "[h]ow the test is regarded in the relevant art").[25] In addition, Petitioner points out, the experiments did not account for any aqueous ammonia still in the reaction system, which cannot be smelled and would "prevent the realization of the

[25] Patent Owner responds that "[s]mell was only an indicator to determine" a point for sampling and analysis with a "highly sensitive method, HPLC." PO Sur-Reply 12. We will address Patent Owner's HPLC assay in turn.

99% or 100% ditaurine yield PO was looking for." Pet. Reply 11–12; Ex. 1069 ¶ 26 (explaining that "ammonia was still necessarily present in the reaction mixture and was not fully released").

Turning to Patent Owner's HPLC method and analysis, Petitioner, backed by the testimony of Dr. Foley, an analytical chemist with over 30-years' experience, contends that critical details and required precision are missing. Pet. Reply 14–18. More specifically, Petitioner contends Patent Owner fails to disclose key parameters, such as the type of HPLC column used (e.g., its dimensions or materials), which make it "impossible to repeat PO's experiments" or determine important variables like void time. *Id.* at 14–15; Ex. 1070 ¶¶ 21–23 ("Without understanding the specific type of column Dr. Maleczka used . . . , it would not be possible for anyone to repeat or verify the analysis"), 25–27 ("[B]ecause Dr. Maleczka did not disclose the column dimensions and the flow rate for his HPLC analysis, it is impossible for anyone to calculate the void time" and "[v]oid time is important because if sample components are eluting . . . at a time near the void time, then the resolution of those components will be poor if not impossible"), 31–33. Patent Owner responds that the information provided is sufficient for experiments "to be repeated and analyzed on *different* equipment using *different* parameters." PO Sur-Reply 15 (emphasis added). That, however, only underscores the problem noted by Petitioner; the lack of detail given means that Petitioner is unable to repeat or verify Patent Owner's results applying the *same* equipment and parameters.

Petitioner further contends Patent Owner's HPLC data are unreliable. Pet. Reply 16–17. For example, Dr. Foley testifies, there is no accounting for use of "Sanger's solution," which is capable of reacting with taurine in the samples, or sufficient explanation for observed (but unknown) peaks

appearing on the chromatograms. *See, e.g.*, Ex. 1070 ¶¶ 34–40 ("[T]he presence of this peak should have indicated . . . that there was an issue with the HPLC system, especially given how close this peak is to the purported taurine peak," and noting that, in "some cases, this peak is clearly overlapping with the purported taurine peak.") 43 ("This means the two peaks have eluted so closely together that their respective AUCs [areas under the curve] have joined . . . [and] [a]ny AUC data from these overlapping peaks would be unreliable."). And, Dr. Foley testifies that there is an unacceptable lack of precision, as evidenced by relative standard deviation ("RSD") with Patent Owner's data. *Id.* ¶¶ 51–76. For HPLC, Dr. Foley testifies that reliable quantitative analysis permits an RSD of "at most 2%." *Id.* ¶¶ 54–58 (citing Ex. 1082, 8). As Dr. Foley explains, however, Patent Owner's data consistently fails to meet that reliability threshold—with, for example, measurements of the same samples having a RSD over 40%. *Id.* ¶¶ 65–68 (calculating RSD for the Second Experiment and testifying "these data simply cannot be relied upon"); *see also id.* ¶¶ 59–60 (calculating an RSD of "78.61%," which is "appalling" and "simply not reliable and [is] unacceptable").

Patent Owner did not cross examine Dr. Foley. Instead, Patent Owner argues Dr. Foley "fails to account for Dr. Maleczka's use of an IS [internal standard]," and that "Dr. Foley's comparisons of the experimental runs with each other using Relative Standard Deviation (RSD) calculations is inappropriate, and scientifically wrong." PO Sur-Reply 15. Contrary to Patent Owner's argument, Dr. Foley recognized the preparation of an internal standard. *See, e.g.*, Ex. 1070 ¶ 59. On this record, we find unavailing Patent Owner's argument that Dr. Foley's essentially unrebutted

testimony—calling into doubt the reliability and accuracy of Patent Owner's data—is "inappropriate" or "scientifically wrong." PO Sur-Reply 15.

For the above reasons, we do not agree with Patent Owner's contentions that the ordinarily skilled person would dismiss WO '071's disclosure of an equilibrium reaction or Petitioner's theory based on it.

Patent Owner further contends that, regardless of equilibrium or reversibility of the WO '071 reaction, WO '071 does not disclose all the elements of claim 1. PO Resp. 40. More specifically, Patent Owner contends there is no disclosure of adding and removing excess ammonia, adding alkali hydroxide to alkali ditaurinate, or neutralization after ammonolysis and recovery of taurine. *Id.*

We do not agree. Satisfaction of the claim elements is explained above. Section III(F)(1)(a). Patent Owner's argument does not account for the obvious steps, applying routine and admitted prior art techniques, that would be undertaken by the skilled artisan driving the WO '071 reaction in reverse as explained: adding a highly basic catalyst (NaOH) to ditaurinate, and adding excess ammonia in ammonolysis to drive toward taurinate, and subsequently removing the ammonia, neutralizing (with an acid) to allow for recovery of the desired product—taurine. *KSR*, 550 U.S. at 421 (holding the skilled artisan is "a person of ordinary creativity, not an automaton."); *see also* Pet. 26–28, 31–32; Ex. 1003 ¶¶ 42, 43, 46, 74–76; Ex. 1001, 2:21–22; Ex. 1067 (Maleczka Dep.), 64:18–65:8 (undisputed that POSA would know ammonolysis reactions must proceed in a basic environment), 63:4–18 (undisputed that it was known to add excess ammonia in ammonolysis, and such will favor primary amines), 67:18–68:5 (undisputed it was known in the art to neutralize taurinate with acids to yield taurine).

In the Sur-Reply, Patent Owner contends (with its own depiction) that sodium hydroxide would be added to the left side of the reaction with taurine in WO '071, not to the side of the reaction with ditaurinate. PO Sur-Reply 17–18. What Patent Owner is showing, however, is the apparent deprotonation of the acid (taurine) to the salt form (taurinate), which salts combine to yield ditaurinate, ammonia, and water. *Id.* WO '071, however, teaches explicitly that addition of sodium hydroxide in the reaction mixture is advantageous even when starting with the salt (taurinate) and, as explained, we find WO '071 teaches an equilibrium, suggesting a forward and reverse reaction. Ex. 1010, 3. To that, Petitioner provided persuasive evidence that a POSA would regard the reaction conditions (catalyst, alkaline environment, etc.) as equally applicable to the reverse reaction (i.e., adding NaOH to ditaurinate and driving ammonolysis). *See, e.g.*, Ex. 1003 ¶¶ 43, 63, 70; Ex. 1020, 81.

For all the reasons explained above, we conclude, based on a preponderance of the evidence on this trial record, that the subject matter of claim 1 would have been obvious over WO '071 in view of the skilled artisan's knowledge.

2. Dependent Claims 3–7

Petitioner argues that WO '071 teaches or suggests the limitations that dependent claims 3–7 add to claim 1. Pet. 33–37, 42. For claim 4, which specifies that the catalysts include sodium hydroxide or sodium carbonate, Petitioner cites WO '071's teaching of the use of catalysts, especially alkali hydroxides (and sodium hydroxide, specifically) as advantageous. Pet. 34; Ex. 1010, 3; Ex. 1001, 1:63–2:3 (admitting that sodium hydroxide is a known catalyst to ammonolysis). According to Petitioner, the skilled artisan would recognize such catalysts operate as such whether the reaction is

driven forward or backward. Pet. 34; Ex. 1003 ¶¶ 79–80. On claim 5, Petitioner contends WO '071 discloses that sodium or potassium salts are formed, thus satisfying claim 5. Pet. 35; Ex. 1010, 3 (listing preferred alkali salts, "in particular sodium, ammonium or potassium salts"); Ex. 1003 ¶ 81. For claim 6, Petitioner points out that WO '071 discloses purification of the mixture by acid neutralization, listing sulfuric and hydrochloric acids. Pet. 35; Ex. 1010, 4; Ex. 1003 ¶ 82. Petitioner also notes that neutralization with acid following ammonolysis is an admitted and routine prior art step. Pet. 36 (citing Ex. 1001, 2:21–24). Thus, Petitioner contends, claim 6 is met. Pet. 35–37. On claim 7, which recites temperature and pressure ranges for the reaction, Petitioner contends the prior art's ranges for those parameters fall within the claimed range, thus satisfying claim 7. Pet. 36–37; Ex. 1010, 3–4 (identifying a preferred temperature range of 190–230°C and pressures between 0.9 to 40 bar); Ex. 1003 ¶¶ 55–57, 63, 70, 83, 84.

Patent Owner's arguments on claim 1 are discussed above, and Patent Owner did not provide additional argument during trial related to the dependent claims. PO Resp. 31, 42 ("Because the underlying obviousness argument as to claim 1 is deficient, claims 3-7 are patentable as well."). To the extent Patent Owner made separate arguments on the dependent claims before institution, but did not re-raise those arguments during trial, such preliminary arguments are waived. Paper 11, 7 ("Patent Owner is cautioned that any arguments for patentability not raised in the response [Patent Owner Response at Due Date 1] may be deemed waived.").

For the reasons recited in the Petition, with which we agree and apply here, we determine that Petitioner has shown by a preponderance of the evidence that claims 4–7 would have been obvious over WO '071 and the skilled artisan's knowledge. Pet. 33–37, 42; *see also* Ex. 1003 ¶¶ 79–84;

Ex. 1010, 3–4, 6–7 (Examples), claims 1, 3, 6, 7; Ex. 1020, 81. For example, on dependent claim 6, WO '071 clearly discloses use of acids (e.g., sulfuric acid) to neutralize the reaction mixture (Ex. 1010, 4), and use of acids in this way would have also been well known to a POSA in view of the admitted prior art. *See, e.g.*, Ex. 1001, 2:21–24; *see also* Ex. 1012, 4 (neutralization of taurinates with sulfuric acid); Ex. 1003 ¶ 83 (testifying "sulfuric acid is especially an obvious choice because it is readily available, low cost, and is a very effective strong acid").

On claim 3, we reach a different result. We pointed out at institution that Petitioner's analysis was wanting, and specifically that Petitioner had not, in the Petition, clearly connected its assertions about a use or recycling of ditaurinate from a prior ammonolysis to claim 3. Paper 10, 32–33 (explaining that Petitioner had not established a reasonable likelihood of success on claim 3, in particular, over WO '071). Because Petitioner failed to further address the Board's preliminary findings on claim 3 at any point during trial, we reiterate the Petition's deficiencies as to the analysis for that claim. *See id.* For those reasons, we conclude Petitioner has not established by a preponderance of the evidence that claim 3 would have been obvious over WO '071.[26]

G. Obviousness over Wu and WO '071

Petitioner contends that claims 1 and 3–7 are unpatentable as obvious over Wu (Ex. 1012) in further view of WO '071 (Ex. 1010). Pet. 42–52.

[26] As addressed below, however, we conclude that claim 3 would have been obvious based on Wu in view of WO '071 (Petitioner's Ground 3).

1. Claim 1

An overview of Wu is provided above. *See* Section III(A)(2). Petitioner cites, *inter alia*, Wu's teaching of an ammonolysis reaction, wherein sodium isethionate is reacted with ammonia in the presence of an alkaline catalyst to produce sodium taurinate and, in a side reaction, sodium ditaurinate as a byproduct. Pet. 43; Ex. 1012, 4. Petitioner further emphasizes Wu's teaching that, when residues "consisting primarily of (b) [(i.e., sodium ditaurinate produced in the above-noted side-reaction)] are fed again into the ammonolysis system, the total yield of the product [taurine] may very well increase." Pet. 43; Ex. 1003 ¶ 95; Ex. 2001 (Maleczka Decl.) ¶ 94 (testifying to Wu's side reaction, producing "sodium taurinate characterized as '(b)'" and remarking that "[t]he structure of (b) is the same as that disclosed in the '450 patent, also referred to as sodium ditaurinate").

We find, consistent with Petitioner's arguments, that the combination of Wu and WO '071 teaches or suggests claim 1's preamble of a process for producing taurine from alkali ditaurinate. This claim language is met, at minimum, by Wu's suggestion to separate taurine/taurinate from the initial reaction mixture and to subject residues of sodium ditaurinate to another round of ammonolysis to produce additional taurine. *See, e.g.*, Ex. 1012, 7; Ex. 1003 ¶¶ 95 (testifying "a POSA would appreciate [from Wu] that if sodium ditaurinate is fed back into the ammonolysis reaction, it can help increase the yield of taurine"), 98 ("Wu 2004 discloses subjecting sodium ditaurinate to an ammonolysis reaction in the presence of sodium carbonate to increase the production of sodium taurinate"); Ex. 2001 ¶ 73; Ex. 1067 (Maleczka Dep.), 243:20–244:2 (admitting that Wu discloses recycling ditaurinate back to the earlier ammonolysis process).

Turning to steps (a–d) of claim 1, Petitioner contends those steps are disclosed in the combination of Wu and WO '071. For step (a), Petitioner contends, *inter alia*, that Wu teaches that sodium carbonate (a strong base that forms sodium hydroxide in water) is a universal catalyst for an ammonolysis reaction. Pet. 44–45 ("a POSA would have known that because ammonia is a weak base, an ammonolysis reaction must proceed in a basic environment."); Ex. 1003 ¶¶ 43, 97; Ex. 1012, 4, 6. When residues of sodium ditaurinate are subjected to a further ammonolysis as suggested in Wu (Ex. 1012, 4), Petitioner contends that claim 1's step (a) would be met because "dialkali ditaurinate" would be "necessarily present" in solution based on conversion of at least some sodium ditaurinate to disodium ditaurinate in the presence of the strongly basic catalyst added to the system. Pet. 45; Ex. 1003 ¶¶ 71–72; Ex. 1012, 4–5 (teaching pH > 9 and up to 13); Ex. 1067, 245:20–246:4 (testifying that Wu reports pH values of 9 and 13 and agreeing those "indicate a basic environment"); Ex. 2001 ¶ 33 (Dr. Maleczka testifying that at pH 5–8, monoalkali ditaurinate is predominantly present, while at pH > 9 (i.e., in a basic environment), dialkali ditaurinate is the predominant form).[27]

We agree. We find that Wu suggests recycling sodium ditaurinate for further ammonolysis, that it was well known (from Wu and otherwise in the art) that catalysts are used and added in ammonolysis, and that the reaction environment must be rendered alkaline/basic for ammonolysis to proceed. *See, e.g.*, Ex. 1012, 6 (describing "sodium carbonate" as a "universal catalyst" for ammonolysis); Ex. 1003 ¶ 97 (testifying that sodium carbonate

[27] As noted previously, the claims do not recite that any particular proportion of the ditaurinates or tritaurinates be in the dialkali- or trialkali-form.

forms sodium hydroxide in an aqueous environment); *see also* Ex. 1001, 1:63–2:3 (describing prior art ammonolysis using, for example, sodium hydroxide as a catalyst); Ex. 1010, 3 (describing advantageous addition of sodium hydroxide); Ex. 1003 ¶¶ 43, 71–72, 80 (testifying "ammonolysis reactions described in prior art references all take place in basic environments").[28] Under those conditions, we are persuaded that at least some recycled sodium ditaurinate in solution will become fully deprotonated, disodium ditaurinate. Ex. 1003 ¶¶ 71–72; Ex. 2001 ¶ 33. Accordingly, we find claim 1's step (a) is met.

For step (b), Petitioner notes that Wu "does not explicitly disclose the mechanism through which ditaurinate produces taurine through ammonolysis." Pet. 46. Petitioner, however, contends that the skilled artisan would understand such a mechanism and reaction from WO '071—where the "equilibrium reaction" suggests ditaurinate reacts with ammonia in the presence of a reaction medium to produce a taurine salt. *Id.*; Ex. 1003 ¶¶ 66–67, 98–100. Accordingly, Petitioner contends Wu and WO '071 together suggest "adding an excess amount of ammonia to a solution of dialkali ditaurinate . . . and subjecting the solution to ammonolysis reaction to yield a mixture of alkali taurinates." Pet. 46; Ex. 1003 ¶¶ 98–99.

We again agree. We find that adding "excess ammonia" as in claim 1 is suggested by driving the disclosed equilibrium reaction of WO '071 in

[28] We separately observe that, consistent with Petitioner's arguments and evidence, Patent Owner asserted at the district court that ammonolysis will not proceed without forming a basic environment via addition of an alkali hydroxide. Ex. 1060, 34 ("without adding alkali hydroxide to the mixture of alkali ditaurinate and alkali tritaurinate to create a basic mixture, the reaction of ammonolysis cannot and will not proceed").

reverse in accordance with, for example, Le Châtelier's Principle as discussed above. *Supra* Section III(F); Ex. 1003 ¶¶ 58–63, 86–87; Ex. 1019, 45–46. Moreover, the evidence here indicates that adding excess molar amounts of ammonia incident to ammonolysis is a well-known and routine step. Ex. 1012, 4, 7; Ex. 1001, 53–58 (describing prior art as conducting ammonolysis with an excess molar ratio of ammonia); *see also* Ex. 1067 (Maleczka Dep.), 63:11–18 (not disputing Dr. Lipton's testimony (Ex. 1003 ¶ 42) that it was known that excess ammonia in ammonolysis favors the reaction producing the primary amine); Ex. 1060 ¶ 128 (Patent Owner asserting that "addition of excess ammonia to perform ammonolysis is standard operating procedure"). Insofar as Wu suggests another round of ammonolysis for the ditaurinate byproduct to increase taurine yield, we thus find that the skilled artisan would know that excess ammonia is needed for that subsequent ammonolysis. Ex. 1012, 7; Ex. 1003 ¶¶ 98–100.

For steps (c) and (d), Petitioner contends those steps are taught or suggested in Wu. Pet. 46–47. According to Petitioner, Wu teaches the remaining ammonia is expelled from the system following the reaction, and that the reaction mixture is neutralized with acid so that a taurine sample may be taken and analyzed. *Id.* at 47 (citing Ex. 1012, 4). Further Petitioner contends, neutralizing the reaction mixture of taurinates to form a crystalline taurine suspension following ammonolysis, and removing taurine through solid-liquid separation is a well-known technique—as admitted in the '450 patent, and as reflected in the art. Pet. 47 (citing Ex. 1001, 2:21–24); Ex. 1003 ¶ 96 (testifying as to Wu's reaction conditions, the removal of ammonia, and neutralization with sulfuric acid); Pet Reply 19–22 (contending the prior art, like the '450 patent, discloses more detailed

conditions for an initial ammonolysis, but not every subsequent round of ammonolysis that is suggested).[29]

We find steps (c) and (d) of claim 1 are met on this record. Removing excess ammonia follows obviously from step (b) where excess ammonia was added and is also consistent with known steps taken at the conclusion of the ammonolysis described in the prior art. *See, e.g.*, Ex. 1012, 4 ("After the reaction, the ammonia is expelled"); *see also* Ex. 1059 ¶ 129 (Patent Owner admitting that "[a]fter ammonolysis is performed, the excess ammonia must be removed"). Similarly, neutralizing the reaction mixture with an acid, especially sulfuric acid, to separate and recover taurine was a well-known technique in the art. Ex. 1012, 4 ("Concentrated sulfuric acid is used to adjust the pH value to 3.5 and a sample is taken"); Ex. 1003 ¶ 96 (testifying that a POSA would understand, with addition of the acid, sodium taurinate is protonated and neutralized to form a crystalline suspension of taurine); Ex. 1001, 2:21–24 (describing prior art as disclosing that crystalline taurine is "easily obtained" via solid-liquid separation); Pet. 46–47; *see also* Ex. 1015, 6 ("After neutralization reaction [with sulfuric acid], the mother liquor remains after separating the crude taurine and sodium sulfate.").

Petitioner contends the skilled artisan would have been motivated to combine the disclosures of Wu and WO '071 based on a desire to improve

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[29] From this, Petitioner contends that Patent Owner cannot assert that one level of disclosure for a subsequent round of ammonolysis is sufficient for the '450 patent, but that same level of disclosure is not sufficient in the prior art. Pet. Reply 22; *In re Epstein*, 32 F.3d 1559, 1568 (Fed. Cir. 1994) (holding "the Board's observation that appellant did not provide the type of detail in his specification that he now argues is necessary in prior art references supports the Board's finding that one skilled in the art would have known how to implement the features of the references").

taurine yields and to reduce waste, and that the skilled artisan would have had a reasonable expectation of success in carrying out the proposed recycling of ditaurinate to produce more taurine. Pet. 48–49. According to Petitioner, Wu teaches specifically recycling ditaurinate for another round of ammonolysis, and suggests that taurine yield will improve in doing so. *Id.*; Ex. 1012, 4. Petitioner contends a skilled artisan would also understand from WO '071 that a reaction between ditaurinate and ammonia can produce taurinate/taurine, helping to improve yield, and adding to the reasons for a skilled artisan to have considered the references together with a reasonable expectation of success in arriving at the claimed subject matter. Pet. 48–49; Ex. 1003 ¶¶ 63, 67, 99–102; Ex. 1010 2, 3.

We find the skilled artisan would have been motivated to consider and combine the teachings of Wu and WO '071. As discussed above, a POSA would have been aware of taurine's many benefits and sought to improve on methods capable of making it. *See, e.g.*, Pet. 1–2; Ex. 1012, 4 (taurine "plays a vital role in the development of the brain," and other organ systems). In that regard, Wu teaches that separating taurine and taurinate from the reaction mixture (following the EO process) and then feeding ditaurinate residues back into the system for another round of ammonolysis should improve total taurine yield. Ex. 1012, 7. Hence, the motivation for recycling ditaurinate to the ammonolysis stage as a means to produce more taurine comes directly and expressly from Wu. *Id.* And, as explained above, WO '071 provides further evidence about how such a reaction may, in fact, proceed; conducting and driving the reaction of ditaurinate and ammonia to produce taurinate. Ex. 1003 ¶¶ 88–90 (describing driving the WO '071 equilibrium reaction in reverse); *see supra* Section III(F)(1).

We further find the skilled artisan would have had a reasonable expectation of success in combining Wu and WO '071's teachings to arrive at the subject matter of claim 1. Here again, Wu's disclosure that, through recycling ditaurinate for additional ammonolysis, "total yield of the product [taurine] may very well increase" is persuasive on the question of what the ordinarily skilled person would have reasonably expected. Ex. 1012, 7. A lack of detail or data for Wu's clearly suggested "second" ammonolysis is a factor we have considered. But the lack of such detail for the second-run ammonolysis can reasonably be attributed to the relevant ammonolysis conditions being known, largely routine, or simply that a skilled artisan would employ substantially the same conditions described in Wu for the first ammonolysis. Ex. 1003 ¶¶ 96–97 (Dr. Lipton testifying a POSA would have understood the conditions should be maintained in successive cycles); *see supra* (discussing and citing evidence on the routine use of catalysts like NaOH, an alkaline reaction environment, addition of excess ammonia, acid neutralization following ammonolysis, etc.).[30] And, even if Wu is short on detail for its next round of ammonolysis, Petitioner has bolstered its challenge by citing WO '071's suggested reaction conditions, which Petitioner and Dr. Lipton assert would be recognized by the ordinarily

[30] The '450 patent also broadly discloses that the sodium ditaurinate byproduct converts to sodium taurinate under vague ammonolysis reaction conditions. *See, e.g.*, Ex. 1001, 2:44–48 ("when sodium ditaurinate and sodium tritaurinate are reacted with aqueous ammonia under ammonolysis reaction conditions, a mixture of sodium taurinate, ditaurinate," and other byproducts is formed), 3:56–62 ("When sodium ditaurinate and sodium tritaurinate are subjected to the ammonolysis reaction in aqueous ammonia under the *same conditions* at a temperature of 220° C. for 2 hours," sodium taurinate is obtained) (emphasis added).

skilled person as suitable for forming taurine through ammonolysis of ditaurinate. Pet. 41–42, 45–46; Ex. 1003 ¶¶ 42, 86–90, 99–100; *supra* Section III(F).

Patent Owner argues that the alleged obviousness of the claims over Wu in view of WO '071 must fail for the same reasons Patent Owner raised above on Petitioner's challenge to the claims over WO '071. PO Resp. 42–46; *see supra* Section III(F)(1)(c). According to Patent Owner, Petitioner's Wu-based obviousness challenge also turns "on the assumption that WO '071 discloses an equilibrium reaction—which is not the case." PO Resp. 42–43. And, Patent Owner contends, "Petitioner's reliance on WO '071 is much deeper than merely explaining a reaction mechanism" suggested in Wu. *Id.* at 43 ("[N]o aspect of Petitioner's argument for the unpatentability of the challenged claims . . . escapes the influence of WO '071 and its alleged teaching of an equilibrium reaction."), 47–49 (arguing no reason for a POSA to consider or combine, or derive any expectations from, WO '071 "without an equilibrium teaching"), 50 (arguing Petitioner cannot prevail because WO '071's "equilibrium teaching" is "wrong").

Even assuming Patent Owner's characterization of Petitioner's challenge over Wu in view of WO '071, and the extent of Petitioner's reliance on WO '071's disclosed equilibrium reaction, is correct, Patent Owner's argument is unavailing. We find Patent Owner's attack on WO '071's teachings unpersuasive for reasons discussed above. *Supra* Section III(F)(1)(c). Based on the same issues we cited with Patent Owner's testing argument and evidence above, we find that argument and evidence does not outweigh the evidence of obviousness over Wu in view of WO '071 on this record. *Id.*; PO Resp. 45–49 (arguing again that a POSA would have tested WO '071 in the way Patent Owner did and, thus, would have

concluded it does not describe an equilibrium reaction). In short, we do not agree on this record that WO '071's relevant teachings are inoperable and wrong, as Patent Owner has repeatedly argued.

Insofar as Patent Owner contends that WO '071 and Wu (and/or Liu[31]) are at odds with the notion of an equilibrium reaction and Petitioner's theory, we remain unpersuaded. Patent Owner contends WO '071 should have "take[n] their own advice" and driven the reaction to completion (~100% ditaurine) instead of settling for the lower yields. PO Resp. 44. But WO '071 never disclosed that essentially quantitative yield of ditaurine was possible (with or without removal of ammonia), nor did Petitioner say as much as discussed above. *Supra* Section III(F)(1)(c). To the contrary, as WO '071 suggests, some residual compounds may remain in the mixture (e.g., "taurinate," "perhaps free taurine" and "other components in small amounts [<5% by weight]"). Ex. 1010, 3. Moreover, it is not a requirement that the art provide working examples with experimental data for everything that is described or suggested within. *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992) ("It is well settled that a prior art reference is relevant for all that it teaches to those of ordinary skill in the art."); *Merck & Co. Inc. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989) (holding that all the prior art's disclosures must be considered in a § 103 inquiry).

As to Wu (or Liu), Patent Owner contends that, if all that was needed was excess ammonia, Wu's initial reaction should have produced ~100% taurine yield, but it did not. PO Resp. 44; PO Sur-Reply 10. Such initial

[31] While Petitioner is not expressly asserting a combination of Liu with both Wu and WO '071, Patent Owner contends that Wu and Liu are inconsistent Petitioner's equilibrium theory in general. *See, e.g.*, PO Resp. 44.

reaction (i.e., the EO process), and the components remaining in the mixture, may have raised questions about producing quantitative yields of taurine through a reaction of ditaurinate and ammonia as Patent Owner notes. On the other hand, the leftover mixture includes more than ditaurinate and ammonia, such as substantial sodium taurinate and sodium isethionate—compounds that contribute to forming ditaurinate and other byproducts in the mixture as both parties' declarants acknowledge. Ex. 1003 ¶¶ 46, 57–58; Ex. 2001 ¶¶ 44–45, 49, 55; *see* Ex. 1012, 4 (describing initial ammonolysis and side reaction; Ex. 1015 (identifying isethionate and various other compounds in the mixture); Ex. 1001, 1:63–2:3. And Wu suggests the leftover mixture is first purified further, with taurinate/taurine being separated out and residues primarily of sodium ditaurinate being recycled to the ammonolysis stage for a subsequent round to produce more taurine. Ex. 1012, 7. In that light, like the '450 patent, Wu does not suggest stopping with the initial mixture produced via the EO process.

Moreover, even if the yield reported in Wu from a single round of ammonolysis raised questions about an equilibrium and the extent to which ditaurinate may be fully converted to taurine in subsequent rounds, we are unpersuaded those questions would have prompted the ordinarily skilled person to engage in the testing Patent Owner has done here.[32] Rather than set out to determine whether it is possible to produce ~100% ditaurine from taurine (which, if not, is said to debunk WO '071's teachings), we find the skilled artisan more likely would have followed the path as laid out by Wu—

[32] As already explained, Patent Owner's testing mimics testing Dr. Hu performed before the invention was filed with the objective of making 100% pure ditaurine from taurine. *See* Section III(F)(1)(c).

recycle ditaurinate to the ammonolysis stage for production of more taurine. Pet. 47–49; Ex. 1012, 7; Ex. 1003 ¶¶ 94–95, 100–101. As explained above, WO '071 provides evidentiary support for the determination that the skilled artisan would, based on WO '071's disclosure of an equilibrium reaction, have reasonably understood and expected that it is possible to conduct and drive the reaction of ditaurinate and ammonia to produce additional taurinate, and ultimately taurine. Pet. 47–49; *see also* Ex. 1003 ¶¶ 56–63.

Patent Owner also contends that Wu undermines Petitioner's challenge because Wu discloses that the total ammonia "has a negative correlation to some extent." PO Resp. 44–45 (citing lower conversion rates of a starting material (sodium pyrosulfite) in examples with greater ammonia amounts); Ex. 1012, 6 (Table 5). As Petitioner and Dr. Lipton explain, however, substantial excess molar amounts of ammonia were still present in all instances. Ex. 1069 ¶ 68; Ex. 1067 (Maleczka Dep.), 251:9–16 (admitting excess molar amounts were used compared to sodium pyrosulfite in all examples).[33] Nothing in Wu, thus, suggests that excess molar amounts of ammonia should not be used in ammonolysis generally. Moreover, to the extent there is any negative correlation with ammonia amounts relative to sodium pyrosulfite conversion, we are unpersuaded on this record that means the same correlation would exist with the more particular reaction of excess ammonia and ditaurinate producing taurinate/taurine suggested based on the combination of Wu and WO '071.

[33] For example, ratios of about 6.9 moles (G) and 7.5 moles (B & C) to less than 1 mole of sodium pyrosulfite were used. Ex. 1067, 250:3–251:8 (explaining that the molecular weight of ammonia is 17 and, in examples, about 118g and 127g of ammonia used).

Patent Owner argues a "POSA would dismiss Wu [] as the starting point," based solely on Wu's allegedly poor yields. PO Sur-Reply 19–20. This argument is unavailing. None of the challenged claims requires any particular average yield of taurine be achieved. Also, Wu's reported average yield of 41% accounts for only the first-pass ammonolysis, not the second-pass that Wu encourages—and suggests is likely to improve taurine yields. Ex. 1012, 7. Even if Wu's average yields were lower than other methods in the prior art, we are unpersuaded that would negate the skilled artisan's motivation to improve them, as is evidenced by Wu itself. *Id.*; Pet. 48–49; Ex. 1003 ¶¶ 95–96, 99–102 (testifying on the motivation for, and reasonable expectation of, improved yields from Wu).

Patent Owner, for the first time in its Sur-Reply, refers to the ditaurinate in Wu's side reaction as "**di**sodium ditaurinate." PO Sur-Reply 19–21 (emphasis added). According to Patent Owner, Wu "discloses disodium ditaurinate as the product of a 'side' . . . reaction and does not say anything to suggest that this form of ditaurinate is preferable for recycling over the monosodium salt or anything else." *Id.* at 21.

We have concerns that Patent Owner's contention about the alleged "disodium ditaurinate" in Wu's side reaction comes too late in this trial proceeding. Tr. 10:8–11:22 (alleging that Patent Owner's contentions are untimely). Those contentions are plainly inconsistent with what Patent Owner and its declarant asserted previously about Wu's teachings. *See, e.g.*, PO Resp. 24 (describing Wu's residue (b) as "(i.e., sodium ditaurinate)"); Ex. 2001 (Maleczka Decl.) ¶¶ 70–73 (same). Patent Owner puts forth no explanation, much less persuasive justification, for why such contention was not previously raised. Office Patent Trial Practice Guide Update, referenced

at 83 Fed. Reg. 39,989 (Aug. 13, 2018), at 14 (discussing the limited scope for sur-replies (e.g., responding to arguments made in reply brief)).

But even considering the contention about Wu's compound (b) being disodium ditaurinate, it would not help Patent Owner. Quite the opposite, if compound "(b)" is disodium ditaurinate, then Wu's disclosure of feeding "residues consisting primarily of (b)" again into the ammonolysis system would provide an express reason in Wu itself to subject **di**sodium ditaurinate (i.e., a **di**alkali ditaurinate) to another round of ammonolysis, as explicitly recited in claim 1's step (b). And, as Patent Owner's declarant admits, "[i]f you're going [to] want to make . . . the di-anine ditaurinate, you do need to deprotonate both of those protons, yes," and "[t]he person [of ordinary skill] would know that to do that, it is necessary to add a base," further demonstrating that claim 1's step (a) would have been obvious. Ex. 1067, 101:18–102:3; *see also id.* at 100:3–101:4.[34]

For all the reasons explained above, we conclude, based on a preponderance of the evidence on this trial record, that the subject matter of claim 1 would have been obvious over Wu in view of WO '071.

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[34] As Dr. Maleczka's testimony also shows, after the acidification step (typical of the EO process), "a POSA would recognize that the ditaurinate could be in the form of a mixture of protonated ditaurine and monoalkali ditaurinate (*e.g.*, sodium ditaurinate) but it would not be in the form of dialkali ditaurinate (*e.g.*, disodium ditaurinate)." Ex. 2001 ¶ 80; Ex. 1012, 4 (describing neutralization of the reaction mixture in sulfuric acid). So, in that case, compound (b) in Wu's initial mixture would be neutralized with an acid but, upon subsequent addition of a base (e.g., sodium carbonate or sodium hydroxide) to create an alkaline reaction environment, ditaurine or sodium ditaurinate would be again deprotonated to dialkali ditaurinate for the suggested second-round ammonolysis. *See, e.g.*, Ex. 2001 ¶ 33 (testifying that at pH > 9 (i.e., in a basic environment), dialkali ditaurinate is the predominant form).

2. Claims 3–7

Petitioner argues that Wu in view of WO '071 teaches or suggests the limitations that dependent claims 3–7 add to claim 1. Pet. 49–53. For claim 3, reciting that the alkali ditaurinate, alkali tritaurinate, or their mixture are byproducts in the production of taurine by the ammonolysis reaction of, for example, alkali isethionate, Petitioner cites Wu's teaching that sodium ditaurinate is produced in a side reaction of the ammonolysis of sodium isethionate. Pet. 49–50; Ex. 1012, 4; Ex. 1003 ¶¶ 94–95. For claim 4, which specifies that the catalysts include, for example, sodium hydroxide or sodium carbonate, Petitioner cites Wu's teaching of the use of sodium carbonate. Pet. 50–51; Ex. 1012, 4, 6 (describing sodium carbonate as a "universal" catalyst in ammonolysis); Ex. 1003 ¶ 97. On claim 5, Petitioner contends that Wu discloses that sodium salts of the reaction species (e.g., sodium taurinate) are formed. Pet. 51; Ex. 1012, 4–6; Ex. 1003 ¶¶ 93, 94, 97, 104. For claim 6, Petitioner contends Wu discloses that, at the end of ammonolysis, concentrated sulfuric acid is used to neutralize the reaction mixture. Pet. 51–52; Ex. 1012, 4; *see also* Ex. 1001, 2:21–24 (admitting neutralization of taurinates with sulfuric acid known in the art); Ex. 1003 ¶¶ 96, 104. Finally, for claim 7, Petitioner contends Wu discloses reaction temperatures that range from 140–260°C, and pressures between 7–9 MPa (70 to 90 bar). Ex. 1012, 5; Ex. 1003 ¶ 104.

Patent Owner's arguments on claim 1 are discussed above, and Patent Owner did not provide additional argument during trial related to the dependent claims. PO Resp. 51 ("[B]ecause Petitioner's underlying obviousness argument as to claim 1 is deficient, claims 3–7 are patentable as well."). To the extent Patent Owner made separate arguments on the

dependent claims before institution, but did not re-raise those arguments during trial, such preliminary arguments are waived. Paper 11, 7.

For the reasons recited in the Petition, with which we agree and apply here, we determine that Petitioner has shown by a preponderance of the evidence that claims 3–7 would have been obvious over Wu in view of WO '071. Pet. 49–53; Ex. 1003 ¶¶ 104; Ex. 1012, 4–7. For example, on dependent claim 3, Wu teaches the production of sodium ditaurinate as part the ammonolysis of sodium isethionate (Ex. 1012, 4 (describing side reaction)), and then feeding the ditaurinate back to the ammonolysis system in a later step (Ex. 1012, 7)). We, thus, find Wu discloses claim 3's subject matter. Ex. 1003 ¶ 104. Wu also clearly discloses use of acids (e.g., sulfuric acid) to neutralize the reaction mixture, thus meeting claim 6's limitations. Ex. 1012, 4; Ex. 1003 ¶ 104; *see also* Ex. 1001, 2:21–24. Also, on claim 7, Wu teaches reaction temperatures from 140–260°C as well as pressures from 7–9 MPa (70 to 90 bar), thus overlapping and/or falling within ranges for the temperature and pressure parameters recited in claim 7. Ex. 1012, 5; Ex. 1003 ¶ 104.

H. Obviousness over Liu and WO '071

Petitioner also challenges claims 1 and 3–7 as obvious over Liu in view of WO '071. Pet. 53–63. As discussed above, we determine that Petitioner has shown by a preponderance of the evidence that those same claims are unpatentable over Wu in view of WO '071. Therefore, we do not reach the further challenge based on Liu in view of WO '071. *Beloit Corp. v. Valmet Oy*, 742 F.2d 1421, 1423 (Fed. Cir. 1984) (holding that once a dispositive issue is decided, there is no need to decide other potentially dispositive issues); *see, e.g.*, *Formlabs Inc. v. Envisiontec, Inc.*, IPR2017-01258, Paper 41 at 17 (PTAB Oct. 5, 2018).

IV. CONCLUSION[35]

Based on the information presented, we conclude Petitioner has shown by a preponderance of the evidence on this record that claims 1 and 3–7 of the '450 patent are unpatentable for obviousness.

Claim(s)	35 U.S.C. §	Reference(s) / Basis	Claims Shown Unpatentable	Claims Not Shown Unpatentable
1, 3–7	102	WO '071		1, 3–7
1, 3–7	103	WO '071	1, 4–7	3
1, 3–7	103	Wu, WO '071	1, 3–7	
1, 3–7	103[36]	Liu, WO '071		
Overall Outcome			1, 3–7	

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 1 and 3–7 of U.S. Patent No. 9,428,450 are held unpatentable; and

[35] Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding*. *See* 84 Fed. Reg. 16654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. *See* 37 C.F.R. § 42.8(a)(3), (b)(2).

[36] As explained above, we do not reach this asserted ground because claims all challenged claims are determined to be unpatentable over Wu in view of WO '071.

FURTHER ORDERED that because this is a final written decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.

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