

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AJINOMOTO CO., INC.,

Petitioner,

v.

ABTIS CO., LTD.

Patent Owner.

CASE: IPR2025-00283

U.S. PATENT NO. 11,896,675

PATENT OWNER'S REPLY TO PETITIONER'S OPPOSITION TO
PATENT OWNER'S MOTION TO AMEND

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TABLE OF PATENT OWNER EXHIBITS

Exhibit No.	Description
2001	Statutory Disclaimer of U.S. Patent No. 11,896,675
2002	U.S. Patent App. No. 18/154,998
2003	U.S. Patent App. No. 16/980,503
2004	Declaration of Dr. Zhaohui Sunny Zhou
2005	<i>Curriculum Vitae</i> of Dr. Zhaohui Sunny Zhou
2006	Deposition Transcript of Dr. Lawrence Nathan Tumey
2007	Reserved
2008	Second Declaration of Dr. Zhaohui Sunny Zhou
2009	English Translation of Kirmse et al., “Destabilisierte 2-Norbornyl”
2010	Zeitschrift für Chemie, 1980, 20 (11), 416-417; English translation of title by the Chemical Abstract Service (CAS): Decomposition of iso-butylammonium N-alkylmonothiocarbamates in weakly acidic and neutral aqueous solutions

I. INTRODUCTION

Petitioner's Opposition does not satisfy its burden to prove, by a preponderance of the evidence, that proposed substitute claims 14-16 are unpatentable. Rather, Petitioner's Opposition abandons the flawed theories from the petition, and shifts to hindsight-driven reconstructions of alleged synthetic routes, and baseless 35 U.S.C. § 112 critiques that are inconsistent with Petitioner's prior art positions. As the Board reasoned in its Preliminary Guidance, Petitioner has not shown that claims 14-16 are unpatentable under any of its positions.

The proposed substitute claims are directed to concrete and structurally defined modified antibodies substituted at the lysine 248 residue with specific bioorthogonal groups attached by certain spacers. As noted in the Preliminary Guidance, Petitioner fails to show that the proposed substitute claims are not enabled, lack written description, are indefinite, or are anticipated or obvious over the prior art. Because Petitioner's challenges fail independently under §§112, 102, and 103, Patent Owner's Motion to Amend (Paper 23) should be granted.

II. THE PROPOSED SUBSTITUTE CLAIMS SATISFY 35 U.S.C. § 112

A. The '675 Patent Enables the Proposed Substitute Claims

Petitioner's enablement challenge asserts that the claims recite an antibody comprising "one or more modified heavy chain" while the specification allegedly only describes antibodies having two modified heavy chains. Enablement does not

require the specification to provide working examples for every numerical variant encompassed by the claims or to describe in detail every conceivable embodiment within the claim scope.

The proposed substitute claims are directed to structurally defined antibodies modified at the lysine residue at EU position 248 with the recited chemical functionalities. The '675 Patent's specification discloses the structural modification site, the chemistry used to modify that residue, and working examples demonstrating the modification. Ex. 2008, ¶¶ 3, 45-49. Petitioner does not contend that modification at lysine 248 cannot be routinely performed using the '675 Patent's methods; instead, it speculates that producing antibodies "having exactly/only one modified heavy chain or an antibody with three or more modified heavy chains" might require additional development effort. Petitioner's Opposition (Paper 25), at 4. Such abstract speculation ignores how antibody conjugation is practiced in the real world. Ex. 2008, ¶ 47. A person of ordinary skill in the art ("POSA") would recognize which antibodies have a heavy chain Fc domain that can be substituted with the claimed moieties.

Antibody substitution reactions produce molecules exhibiting a distribution of drug-to-antibody ratios ("DAR"), and a POSA would understand that the phrase "one or more modified heavy chain" encompasses antibodies within typical DAR distributions (i.e., fractional numbers) rather than requiring a distinct process for

producing antibodies bearing modified heavy chains in exact integers. Ex. 2008, ¶ 46. For example, preparations having an average DAR of approximately 1.8 (commonly referred to in practice as “DAR2”) may reflect typical reaction distributions in which some antibodies contain two modified heavy chains while others contain fewer. Ex. 2008, ¶ 46. Even Ajinomoto’s PepTalk Presentation (Ex. 1007) presents DAR values as non-integer measurements, i.e. DARs of 1.8 and 1.9 reflecting such distributions (*see, e.g.*, Ex. 1007 at 28), confirming that a POSA would understand antibody conjugation products to exist as mixtures rather than discrete whole number species. Ex. 2008, ¶ 46. Moreover, as the Preliminary Guidance notes, Dr. Tumey acknowledges that “a person of ordinary skill in the art would have understood that ‘modification reactions such as those described in EX2002, paras. [1272]-[1329] could produce a trastuzumab molecule with one modified heavy chain, two modified heavy chains, or zero modified heavy chains.’” Paper No. 27 at 9.

B. The ’675 Patent Provides Written Description Support for the Proposed Substitute Claims and Does Not Introduce New Matter

Petitioner’s written description challenge similarly fails. Petitioner asserts that the specification fails to describe a “modified antibody” comprising “one or more modified heavy chain” because those phrases do not appear verbatim in the specification. Pet. Opp’n, at 2-3. However, the claim terms “need not be used in

haec verba” in the specification to have written description support. *Blue Calypso, LLC v. Groupon, Inc.*, 815 F. 3d 1331, 1345 (Fed. Cir. 2016). Rather, to satisfy written description the specification “must clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed.” *Id.* at 1344. The ’675 Patent satisfies that requirement. The specification provides structural disclosure of the modified heavy-chain region, identifies the modification site at lysine 248, and describes the chemical moieties corresponding to the claimed modifications. *See* Patent Owner’s Motion to Amend, App’x A (listing proposed substitute claims 14-16); Ex. 2008, ¶¶ 45-47. Those structural disclosures demonstrate to a POSA that Patent Owner had possession of the full scope of the claim, including the claimed modified antibodies. Ex. 2008, ¶¶ 45-47.

C. The Proposed Substitute Claims are Not Indefinite

Petitioner’s indefiniteness argument ignores the structure of the claim and improperly isolates individual phrases rather than reading the claim language as a whole as required under *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 910 (2014) (“§112 [] require[s] that a patent’s claims, viewed in light of the specification and prosecution history, inform those skilled in the art about the scope of the invention with reasonable certainty.”). The Preliminary Guidance addressed this concisely, stating that “the preambles of the proposed substitute claims 14-16 each recite ‘[a] modified antibody comprising a bioorthogonal click chemistry functional

group,’ and the remaining limitations of the claims provide the location and the structure of the claimed bioorthogonal click chemistry functional groups by reciting modified heavy chains and modified lysine residues described in the specification.” Paper No. 27 at 10. Thus, when read as a whole, each proposed substitute claim could not, as Petitioner contends, be understood as describing a modified lysine structure containing a bio-orthogonal click chemistry group and a separate bio-orthogonal click chemistry functional group elsewhere. *See* Pet. Opp’n, 6; Ex. 2008, ¶¶ 48-49.

III. THE PROPOSED SUBSTITUTE CLAIMS ARE NOT ANTICIPATED

Petitioner’s anticipation theory depends entirely on its assertion that the proposed substitute claims allegedly lack written description support and enablement support in the earlier-filed applications and therefore are not entitled to their claimed priority dates. But, as explained thoroughly in Patent Owner’s Motion to Amend, the earlier-filed applications disclose every limitation of each of proposed substitute claims 14-16. Patent Owner MTA, 8-11. Because the proposed substitute claims are fully supported by the earlier-filed applications, they are entitled to their claimed priority dates, and the ’959 publication therefore does not qualify as prior art to those claims, and cannot anticipate them.

IV. THE PROPOSED SUBSTITUTE CLAIMS ARE NOT OBVIOUS

Petitioner's obviousness theory fails for two simple reasons: (1) no motivation—Petitioner does not identify any prior art that discloses, teaches, or suggests the structure of the claimed moieties; and (2) no reasonable expectation of success—Petitioner does not identify a prior art disclosure of how to make the claimed moieties that does not teach away from them because *Yamada* does not disclose how to make them, *Matsuda* teaches away from the ether oxygen (β)-heteroatom spacer, and Petitioner's new references are either not prior art or do not provide a scientifically feasible way to make the claimed moieties. Ex. 2008, ¶¶ 2-10.

A. Petitioner Provides No Motivation To Select The Structures of the Claimed Moieties

Petitioner does not provide a single source for all of the limitations of the proposed substitute claims, and continues to use *Yamada* as a chemical encyclopedia without it giving any particular direction or preference for a substitution. Even in attempting to use the PepTalk Poster, PepTalk Presentation, and *Matsuda* to piece together a reference for each component of a claimed moiety, Petitioner fails to show that a POSA would have been motivated to make any of the claimed structures.

Petitioner insists that a POSA would choose the claimed moieties from *Yamada*, even though *Yamada* discloses millions of possible compounds with no

preference or direction that would lead a POSA to the claimed moieties. Pet. Opp’n, 18-19. But *Yamada* is much more limited than Petitioner suggests. *Yamada* only describes its compounds within the framework of its disclosed reaction scheme, which defines how the intermediates are formed and how each modified antibody is produced. Ex. 2008, ¶¶ 31-33. *Yamada* discloses millions or billions of compounds in the variable structure of Formula (IV) L1-B-R’-T. That Formula (IV) is not a standalone class of compounds, but is the product of a specific reaction: the synthesis in Figure 2. Ex. 2008, ¶¶ 32-34. And the parties agree that the Figure 2 synthesis cannot produce the claimed compounds. Therefore, to the extent *Yamada* provides any structural direction, a POSA would understand that direction cannot include the claimed compounds. Ex. 2008, ¶¶ 8, 11-12, 33. Thus, *Yamada* points away from the claimed moieties. Ex. 2008, ¶¶ 12, 31-34.

Petitioner’s combination of *Yamada* and *Matsuda* also fails to disclose a modified antibody example with a norbornene group like claims 15 and 16, fails to show a modified antibody with (β) ether spacer like claims 14 and 16, and fails to show a modified antibody with no spacer like claim 15. Ex. 2008, ¶¶ 26-34. Because Petitioner cannot show the spacer in any of its cited prior art, it employs misleadingly incomplete statements about what the references actually disclose, stating that “[b]oth *Yamada* and *Matsuda* provide multiple examples of linkers with a heteroatom (including oxygen, specifically) underscoring the proven motivation and

feasibility of including a heteroatom in the linker.” Pet. Opp’n, 18. What is missing is that *Yamada* does not disclose an ether spacer in any example, and the only “oxygen, specifically” is a carbonyl oxygen, which is not the same. Ex. 2008, ¶¶ 29, 35. What is also missing is that *Matsuda* provides no instance of a (β)-heteroatom that worked—each did not progress. Ex. 2008, ¶¶ 29, 35. Likewise, neither of them provides an example with no spacer, as in claim 15. Ex. 2008, ¶¶ 29, 35. Therefore, there is nothing showing motivation or feasibility for the claimed spacers in *Yamada* or *Matsuda*. Ex. 2008, ¶¶ 29, 35-43.

Grounds 3 and 5 fare no better. They add the PepTalk Poster and PepTalk Presentation, respectively, to *Yamada* and *Matsuda*. But the PepTalk References do not disclose a modified antibody example with a norbornene group like claims 15 and 16, a modified antibody with a (β) ether spacer like claims 14 and 16, or a modified antibody with no spacer like claim 15. Ex. 2008, ¶ 35. Instead, Petitioner points to the shortest alkyl spacer in the PepTalk References, and states that a POSA would be motivated to incorporate oxygen into the linker, without any support in any reference for doing so. Pet. Opp’n, 21-23. For claim 15, Petitioner asserts that removing both carbons from the shortest linker is “one of the only ways” to “simplify” the spacer, without any support in any reference for why one would “simplify” the spacer, let alone to remove it altogether.

Finally, there are numerous amino acid sites for substitution on the Fc domain disclosed in the prior art, and Petitioner provides no reason to select lysine 248 from among them. Ex. 2008, ¶¶ 7, 28. The PepTalk References both mention lysine 248 as a previous technology, but then go on to suggest that other lysine sites are the target of Ajinomoto's next generation technology. Therefore, there is not a clear teaching toward lysine 248 in these references. Ex. 2008, ¶¶ 7, 28.

Obviousness requires more than showing that individual components could be found somewhere amongst the universe of prior art. It also requires more than showing that a POSA, after learning the invention, might be able to assemble them using experimentation. Those are all that Petitioner offers, and they fall short. Obviousness requires a demonstrated reason that a POSA would have combined the prior-art teachings in the specific manner claimed with a reasonable expectation of success. Because Petitioner does not (because it cannot) identify any concrete teaching, suggestion, or motivation to make the claimed compounds, its obviousness theory fails.

B. Petitioner Does Not Provide a Reasonable Expectation of Success in Making the Claimed Moieties

Petitioner assumes that a POSA would pursue the claimed moieties and attempts to show synthetic routes for them. Because *Yamada* failed to supply a synthesis that would make the claimed compounds, Petitioner and Dr. Tumey now

rely on *Matsuda* and numerous additional references that are not presented as parts of Grounds, some of which are not even prior art, to supply the missing chemistry. See Pet. Opp'n, 19; Ex. 2008, ¶ 23.

Matsuda itself reports that reactions involving ether-linked spacers did not progress while identifying other conjugations that progressed successfully: conjugations using analogs lacking the (β)-heteroatom (compounds 27-29). Ex. 1011, ¶¶ [1150]-[1152]; see also Patent Owner MTA, 21-23; Ex. 2008, ¶¶ 42-43. As such, a POSA reading *Matsuda* would understand that the ether-containing spacer required by proposed substitute claims 14 and 16 was disfavored relative to other alternative spacer designs disclosed in *Matsuda*. Ex. 2008, ¶¶ 42-43.

Nonetheless, Petitioner relies on *Matsuda* to justify pursuing precisely that approach, without identifying any teaching or suggestion that a POSA would have selected the ether-containing spacer or expected it to succeed under the reaction conditions required to generate the claimed moieties. Ex. 2008, ¶ 43. Thus, Petitioner's revised theory not only fails to identify any workable synthetic pathway or route that a POSA would have selected, but also depends on a reference that would have taught away from using that chemistry in the first place.

The additional references Dr. Tumey now cites do not show that a POSA would have had a reasonable expectation of success in making the claimed moieties. Many of them do not involve antibodies at all, let alone conditions conducive to

modifying them. Ex. 2008, ¶¶ 12, 19-24. Others are not prior art, and state that the results they report are significant or surprising discoveries, meaning a POSA would not have generally known those synthetic routes, and would not have reasonably expected to be able to make the claimed moieties using them. Ex. 2008, ¶¶ 23-24.

Most importantly, even if Petitioner and Dr. Tumey were to supply a feasible synthetic route to the claimed compounds that the art did not teach away from, that synthetic route alone would not provide the requisite motivation to pursue the claimed compounds. Ex. 2008, ¶¶ 13-24. Petitioner's combination of hindsight reconstruction disregarding a clear and teaching away confirms that Petitioner has failed to satisfy its burden of proving, by a preponderance of the evidence, that the proposed substitute claims would have been obvious.

C. Petitioner's Unexpected Properties Argument Fails

Patent Owner is not required to prove "unexpected properties" to rebut obviousness where, as here, the prior art neither discloses nor suggests the modified lysine structures recited in proposed substitute claims 14-16. *See Mylan Pharms. Inc. v. Merck Sharp & Dohme Corp.*, 50 F.4th 147, 156 (Fed. Cir. 2022) ("[T]here is no need to reach objective indicia of nonobviousness where the petitioner has not made a showing necessary to prevail on threshold obviousness issues.") (citing *Hamilton Beach Brands, Inc. v. f'real Foods, LLC*, 908 F.3d 1328, 1343 (Fed. Cir. 2018)); Ex. 2008, ¶¶ 47-48. None of the cited references identify the claimed

moieties or direct a POSA to select those particular bio-orthogonal click chemistry groups and linkers from the millions of possibilities. *See In re Petering*, 301 F.2d 676, 683 (Fed. Cir. 1962) (explaining that where “the compounds included in the[] claims are encompassed by [the prior art’s] broad generic class ... but so are many, many other compounds[,] [w]e do not think that [the prior art] would lead one of ordinary skill in this art to select and prepare the particular compounds defined in these claims.”); Ex. 2008, ¶ 48. Nevertheless, the cited art, particularly *Matsuda*, shows that the existence of claimed moieties is unexpected because it concluded that the compounds like those claimed could not be obtained by known processes. Ex. 2008, ¶ 48.

V. CONCLUSION

For the foregoing reasons, Petitioner has failed to demonstrate, by a preponderance of the evidence, that proposed substitute claims 14-16 are unpatentable under 35 U.S.C. §§ 112, 102, or 103. The earlier-filed applications provide full written-description and enablement support for the proposed substitute claims, the asserted ’959 publication does not qualify as prior art to those claims, and Petitioner’s obviousness theory relies on hindsight reconstruction rather than any articulated pathway that a person of ordinary skill in the art would have pursued with a reasonable expectation of success. Accordingly, the Board should grant Patent Owner’s Motion to Amend and find the proposed substitute claims patentable.

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CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that the foregoing Reply in Support of Patent Owner's Motion to Amend, exclusive of the exempted portions as provided in 37 C.F.R. § 42.24(a), contains no more than 12 pages and therefore complies with the limitations of 37 C.F.R. § 42.24(a).

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CERTIFICATE OF SERVICE

I hereby certify that on March 6, 2026, a true and correct copy of the foregoing was caused to be served by filing this document through the PTAB's P-TACTS Filing System as well as delivering a copy via electronic mail on the following counsel of record for Petitioner at the following address:

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