

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

VALNEVA AUSTRIA GMBH,
Petitioner,

v.

TAKEDA VACCINES, INC.,
Patent Owner.

Case IPR2025-00776
U.S. Patent 11,730,802

**PETITIONER'S REPLY TO PATENT OWNER'S SUPPLEMENTAL
PRELIMINARY RESPONSE**

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Regulations

37 C.F.R. §42.51(b)(1)(iii)	1, 4
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PETITIONER’S LIST OF EXHIBITS

Previously Filed:

Exhibit No.	Description
1001	U.S. Patent 11,730,802 (“the ‘802 patent”)
1002	Declaration of Farshad Guirakhoo, Ph.D.
1003	Selected file history of the ‘802 patent
1004	Thomas PCT/US2017/035046 (WO2017/210215)
1005	Barbero Calzado PCT/EP2016/082662 (WO2017/109223)
1006	Murata et al, Plaque purification as a method to mitigate the risk of adventitious-agent contamination in influenza vaccine virus seeds, Vaccine, 2011 Apr 12;29(17):3155-61
1007	Faucette et al., Immunization of pregnant women: Future of early infant protection, Human Vaccines & Immunotherapeutics 11:11, 2549-2555; November 2015
1008	PCT/US2018/059233 (published as WO2019/090238)
1009	Provisional application No. 62/592,995
1010	Provisional application No. 62/581,500
1011	Version 8 of Clinical Trial NCT02952833
1012	Liu, et al., Clinical and Vaccine Immunology, Vol. 19, No. 1 (January 2012) pp. 73-78
1013	Declaration of Robert Paarlberg
1014	U.S. NAT’L LIBRARY OF MED., NAT’L INST. OF HEALTH, Press Release: National Institutes of Health Launches “ClinicalTrials.gov” (February 29, 2000), https://www.nlm.nih.gov/archive/20040831/news/press_releases/clntr_lpr00.html

Exhibit No.	Description
1015	U.S. NAT'L LIBRARY OF MED., NAT'L INST. OF HEALTH, ClinicalTrials.gov, Clinical Trial Reporting Requirements, https://clinicaltrials.gov/policy/reporting-requirements#InternationalCommittee (last accessed March 4, 2025)
1016	U.S. National Institutes of Health, ClinicalTrials.gov, About ClinicalTrials.gov, https://web.archive.org/web/20081013222556/www.clinicaltrials.gov/ct2/info/about (Oct. 13, 2008)
1017	U.S. NAT'L LIBRARY OF MED., NAT'L INST. OF HEALTH, ClinicalTrials.gov, History, Policies, and Laws, https://clinicaltrials.gov/ct2/about-site/trends-charts (last accessed March 4, 2025)
1018	U.S. NAT'L LIBRARY OF MED., NAT'L INST. OF HEALTH, https://clinicaltrials.gov (last accessed March 4, 2025)
1019	ClinicalTrials.gov, Protocol Data Element Definitions, https://web.archive.org/web/20090411233717/http://prsinfo.clinicaltrials.gov/definitions.html (April 11, 2009)
1020	Registering Clinical Trials with ClinicalTrials.gov, https://web.archive.org/web/20090410230211/http://prsinfo.clinicaltrials.gov/registering.pdf (April 10, 2009)
1021	ClinicalTrials.gov, Disclaimer, https://clinicaltrials.gov/about-site/disclaimer (last accessed March 4, 2025)
1022	FAQ: ClinicalTrials.gov - Submission and Review of Information, https://web.archive.org/web/20090511070156/http://nlm.nih.gov/services/ctmaintain.html (May 11, 2009)
1023	ClinicalTrials.gov, How to Edit Your Study Record, http://clinicaltrials.gov/submit-studies/prs-help/how-edit-record (last accessed March 4, 2025)
1024	ClinicalTrials.gov, Background, https://web.archive.org/web/20170315024655/http://www.clinicaltrials.gov/ct2/about-site/background (March 15, 2017)

Exhibit No.	Description
1025	Study Details A Phase 1, First-in-human, Double-blinded, Randomized, Placebo-controlled Trial of a Zika Virus Purified Inactivated Vaccine (ZPIV) With Alum Adjuvant in Healthy Flavivirus-naive and Flavivirus-Primed Subjects, https://clinicaltrials.gov/study/NCT02963909?term=NCT02963909&rank=1
1026	ClinicalTrials.gov Glossary Terms ClinicalTrials.gov, https://clinicaltrials.gov/study-basics/glossary
1027	Record History NCT02963909 ClinicalTrials.gov, https://clinicaltrials.gov/study/NCT02963909?term=NCT02963909&rank=1&tab=history
1028	Study Details ZIKA Vaccine in Naive Subjects ClinicalTrials.gov, https://clinicaltrials.gov/study/NCT02952833?term=NCT02952833&rank=1
1029	Record History NCT02952833 ClinicalTrials.gov, https://clinicaltrials.gov/study/NCT02952833?term=NCT02952833&rank=1&tab=history
1030	Record History ver. 1-8: 2016-11-01 NCT02952833 ClinicalTrials.gov, https://clinicaltrials.gov/study/NCT02952833?term=NCT02952833&rank=1&tab=history&a=1&b=8#version-content-panel
1031	Record History ver. 8-10: 2017-06-29 NCT02952833 ClinicalTrials.gov, https://clinicaltrials.gov/study/NCT02952833?term=NCT02952833&rank=1&tab=history&a=8&b=10#version-content-panel
1032	Record History ver. 18: 2018-12-06 NCT02952833 ClinicalTrials.gov, https://clinicaltrials.gov/study/NCT02952833?term=NCT02952833&rank=1&a=18&tab=history#version-content-panel

Exhibit No.	Description
1033	Study Details Zika Virus Purified Inactivated Vaccine (ZPIV) Accelerated Vaccination Schedule Study ClinicalTrials.gov, https://clinicaltrials.gov/study/NCT02937233?term=NCT02937233&rank=1
1034	Record History NCT02937233 ClinicalTrials.gov, https://clinicaltrials.gov/study/NCT02937233?term=NCT02937233&rank=1&tab=history
1035	Declaration of Dan H. Barouch, M.D., Ph.D. in IPR2023-00354, dated December 15, 2022
1036	Schuller et al., Comparison of a single, high-dose vaccination regimen to the standard regimen for the investigational Japanese encephalitis vaccine, IC51: A randomized, observer-blind, controlled Phase 3 study, Intercell AG, Campus Vienna Biocenter 2, 1030 Wien, Austria
1037	Barouch et al., Prospects for a Zika Virus Vaccine, Immunity 46, February 21, 2017 ^a 2017 Elsevier Inc.

Petitioner files this response to Takeda's Supplemental Patent Owner Preliminary Response as authorized by the Board. Takeda, Takeda's counsel and Dr. Barouch (collectively "Takeda") relied upon Schuller in a recent, prior IPR proceeding. Schuller teaches that a single 12 µg dose of a JEV vaccine achieved a seroconversion rate greater than 60% at 28 days post administration. In the present IPR, Takeda repeatedly asserted that "[i]n fact ... before November 3, 2017, inactivated flavivirus vaccines known in the art did not provide greater than a 60% seroconversion rate in a population of human subjects after a single dose." Paper 6, p. 42; *See also Id.*, pp. 9, 46; EX2001, ¶¶44-45, 115, 117-118; Paper 7, pp. 12, 16, 44-45; EX2026, ¶¶53, 55, 109, 111. This frequently repeated misrepresentation of fact is both undeniably false and used by Takeda to support its argument that a POSA would not have been motivated by prior art to arrive at the subject matter of claim 11, which includes achieving a seroconversion rate of at least 60% after a single dose or prime administration.

Takeda is now arguing patentability in direct contradiction to its earlier understanding of Schuller. Takeda would not be addressing Schuller if Petitioner had not raised this issue. Accordingly, Takeda violated its duty under 37 C.F.R. §42.51(b)(1)(iii) to disclose prior art information that is inconsistent with its material positions advanced in support of patentability.

Takeda also asserts that Dr. Guirakhoo failed to identify support for his

position that vaccine dose is a result-effective variable known in the prior art. Dr. Guirakhoo cited to Thomas's express teachings on varying dose and relied upon his knowledge and experience in the field. Nothing in Takeda's Preliminary or Supplemental Patent Owner Response supports discretionary denial of the Petition.

I. TAKEDA'S MISREPRESENTATIONS ARE DIRECTLY MATERIAL TO THE SCOPE OF CLAIM 11

Claim 11 is directed to a method of vaccinating against Zika virus infection in a human subject. A vaccine or immunogenic composition is administered one or more times. A seroconversion rate of at least 60% is achieved by a single dose or prime administration after 14 and/or 28 days.

Contrary to Takeda's misdirection (*see, e.g.*, Paper 9, p. 1 citing Paper 7, pp. 12-18, 44-46; EX2026, ¶¶53-55, 108-112), claim 11 is not limited to a single dose vaccination method. Claim 11 plainly allows at least one additional dose in the vaccination method, i.e. "administered one or more times." At the very least, claim 11 purports to be a vaccination method by administering "a single dose or prime administration" achieving a seroconversion rate of at least 60% in a human population. Accordingly, a 60% seroconversion rate is sufficient for human vaccination against Zika virus infection. Takeda's entire patentability argument seems premised on the notion that higher seroconversion rates are needed for vaccination and were not achieved by single dose administration in the prior art. *Id.* But, that notion is entirely inconsistent with the scope of claim 11's plain meaning.

Obviousness requires assessing the scope and content of the prior art and comparing the prior art to the claimed subject matter, both of which are issues of fact. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Randall Mfg. v. Rea*, 733 F.3d 1355, 1362 (Fed. Cir. 2013). Takeda attempted to limit the true state of the scope and content of the prior art with respect to claim 11 by asserting “[i]n fact, as discussed above in §II.C., before November 3, 2017, inactivated flavivirus vaccines known in the art did not provide greater than a 60% seroconversion rate in a population of human subjects after a single dose.” Takeda repeated these assertions many times. *See*, Paper 8, 12-13, 17, 46, *citing* Paper 7, pp. 13, 15, 27, 42, 45, and 53; EX2001, ¶¶44-45, 115, 117-118; EX2026, ¶¶53, 55, 109, 111. Takeda now admits that Schuller clearly teaches that a single dose vaccine achieved a seroconversion rate of at least 60% in humans after 28 days. Paper 9, pp. 4 (“Schuller reported a *point estimate* SCR of 65.8% at Day 28 for the 1×12µg dose group...”). That teaching of Schuller, along with Takeda’s prior position regarding Schuller in IPR2023-00354 (*see* Paper 8, p. 15 *citing* IPR2023-00354, Paper 2, p. 24 and Ex. 1002, ¶172) directly contradicts Takeda’s argument that “inactivated flavivirus vaccines investigated in human subjects before November 3, 2017 required more than one dose to achieve a seroconversion rate of at least 60% in the vaccinated human population. EX2001 [Barouch Declaration], ¶¶44-45” (Paper 6, p. 13) and its argument that “[i]n fact, as discussed above in §II.C., before November 3, 2017,

inactivated flavivirus vaccines known in the art did not provide greater than a 60% seroconversion rate in a population of human subjects after a single dose.” *Id.*, p. 42. Takeda’s failure to identify Schuller as contradictory prior art violates its duty of candor under 37 C.F.R. §42.51(b)(1)(iii).

Furthermore, Takeda’s arguments regarding motivation to combine and reasonable expectation of success with respect to claim 11 rest on the false position that the prior art did not teach achieving a 60% seroconversion rate after a single dose administration. This is clearly not true in view of Schuller and also for the reasons set forth in the Petition and Dr. Guirakhoo’s Declaration. Takeda has presented no issue on the merits supporting discretionary denial.

II. PETITIONER HAS PROVIDED SUBSTANTIAL EVIDENCE THAT VACCINE DOSE IS A RESULT EFFECTIVE VARIABLE

Claim 11 requires a single dose administration within about 1-40 µg achieving a seroconversion rate of at least 60% and clearly allows additional administrations in a method of vaccinating humans against Zika virus infection. Dr. Barouch expressly stated that Dr. Guirakhoo’s opinion on dose amount being a result effective variable “runs contrary to what was known about inactivated flavivirus vaccines known in the art before November 3, 2017...” Ex. 2001, p. 52-53.

Contrary to Takeda’s arguments, Dr. Guirakhoo properly demonstrated through citation to supporting evidence and provision of technical reasoning that POSA would have understood based on Thomas that both dose and adjuvant affect

seroconversion, thereby making each a result-effective variable *See e.g.*, Ex. 1002, ¶169-178, *citing* Ex. 1004, 4:15-28, 7:11, 7:30-8:2, 18:17-20, 42:4-23, Table at 42:19; *See also* Paper 8, pp. 42-44. That is all the law requires. *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9, at *15 (PTAB Aug. 24, 2022). Dr. Guirakhoo’s opinions stand on their own without Schuller. However, Schuller (*e.g.*, Ex. 1036, Table 2) contradicts and shows the lack credibility in Takeda’s arguments while further “support[ing] Dr. Guirakhoo’s opinions based on the teachings of Thomas as well as his education, knowledge, and experience that vaccine dose is result effective in terms of seroconversion and would have motivated one of skill to administer a single dose and to increase single dosage amount to increase seroconversion rates.” Paper 8, p. 44-45.

III. CONCLUSION

Even when given the opportunity to provide an explanation for its mischaracterization of the state of the art and withholding of evidence contrary to the positions it has asserted, Takeda fails to do so. While Schuller clearly contradicts Takeda’s positions, Valneva’s demonstration of reasonably likelihood of success stands on its own. Takeda has not shown that there is any basis for discretionary denial especially given the strength of the evidence in the Petition showing the obviousness of the claims that Takeda has not already statutorily disclaimed and as set forth in Grounds II and VII-XI.

Dated: August 13, 2025

By: /Robert F. Altherr, Jr./

Robert F. Altherr, Jr.
Reg. No. 31,810
Banner & Witcoff, Ltd.
1100 13th Street, NW
Suite 1200
Washington, DC 20005
(202) 824-3000
raltherr@bannerwitcoff.com

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), I hereby certify that I caused a true and correct copy of this **PETITIONER'S REPLY TO PATENT OWNER'S SUPPLEMENTAL PRELIMINARY RESPONSE** in connection with IPR2025-00776 to be served via e-mail on August 13, 2025, in its entirety on the following counsel of record for Patent Owner:

EELLISON-PTAB@STERNKESSLER.COM
OPARTINGTON-PTAB@STERNEKESSLER.COM
CGALLO-PTAB@STERNEKESSLER.COM
PTAB@STERNEKESSLER.COM

Dated: August 13, 2025

By: /Curtis King/

Curtis King