



August 5, 2025

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Dear Dr. Iyengar:

This letter describes the results of a United States Food and Drug Administration (FDA) inspection that concluded on May 24, 2024. During the inspection, the FDA investigator met with you and your staff to review the conduct and oversight of a clinical study titled *A Phase 3, randomized, placebo-controlled, observer blind, multi-country study to demonstrate the efficacy of a single dose and annual revaccination doses of GSK's RSVPreF3 OA investigational vaccine in adults aged 60 years and above (Protocol 21294, RSV OA=ADJ-006)* (hereinafter, the protocol). The FDA conducted this inspection under the Bioresearch Monitoring Program that includes inspections designed to review the conduct of research involving investigational products.

At the conclusion of the inspection, a Form FDA 483, Inspectional Observations was issued and discussed with you and your staff. We reviewed the Establishment Inspection Report, the Form FDA 483, and your response letter dated June 13, 2024, to the Form FDA 483 (Response Letter). Your violations include, but are not limited to the following:

1. Failure to immediately report to the sponsor any serious adverse event (SAE), whether or not considered drug related, including those listed in the protocol or investigator brochure, and failure to record nonserious adverse events (AEs) and report them to the sponsor according to the timetable for reporting specified in the protocol. **[21 CFR 312.64(b)]**

The protocol (sections 8.3.1, 8.3.3, 10.3.8, and 10.3.10) requires the investigator to record all relevant information regarding an AE, SAE, or AE of special interest (AESI) in the electronic case report form (eCRF) and to report SAEs and new relevant information for an SAE to the sponsor within 24 hours using the electronic Expedited Adverse Events Report in the eCRF. According to Section 10.1 of the Study Procedures Manual, which is a supplement to the protocol, participant information, including safety information, must be recorded into the eCRF, within five (5) calendar days of being available.

- a. In October 2022, subject (b) (6) experienced the following AEs: hypomagnesemia, hypophosphatemia, worsening of hypertension, prolonged QTc interval and constipation. The site was aware of the AEs on January 12, 2023 according to (b) (6) initials on the medical history documentation. However, these AEs were not

recorded in the eCRF until April 29, 2024, falling outside of the protocol's five (5) calendar day recording requirement.

- b. On May 16, 2022, the site was aware that subject _____ cause of death was bronchopneumonia and immobility related to recent surgery, and aspiration associated with poor swallow based on hard-copy adverse event records. However, this cause of death was not reported and entered in the electronic Expedited Adverse Events Report until April 12, 2023, falling outside of the protocol's 24-hour SAE reporting requirement.

We acknowledge that your Response Letter did not address these findings because they were not included on the Form FDA 483 you received.

2. Failure to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation [21 CFR 312.62(b)].

- a. On March 28, 2024, (b) (6), a clinical research coordinator (CRC), noticed that multiple initials and signatures on the Swab Processing and Shipping log forms appeared falsified and were not her own. (b) (6) reported the discovery and an investigation was initiated on April 11, 2024. Compliance Manager KM conducted an investigation and reviewed study documentation including signature and delegation logs, employee training, study procedures, Swab Processing and Shipping Logs and study visit records. In total, 55 Swab Processing logs dated July 2022 through January 2023 were reviewed, and 18 of 55 logs contained questionable signatures. Of the 18 logs with questionable signatures, 12 logs contained signatures from dates when (b) (6) was not on site. For example, on November 30, 2022 and December 2, 2022 there were four (4) logs signed with (b) (6) initials however she was on leave and not at the site on those days.

The investigation report incorrectly stated that 11 signatures were not written by the person to whom they belong, but by another person, but there were in fact 12 false signatures found during the investigation. The investigation report also concluded that this signatory practice had no impact on efficacy trial data nor on patient safety, and that the suspected CRC worked alone. Per the investigation report, the individual alleged to be involved was dismissed in February 2023 but that individual was not named in the investigation report.

Through interviews conducted during the inspection and Delegation Log reviews, the Office of Inspections and Investigations (OI) investigator indirectly learned that employee (b) (6) was the alleged suspected person responsible. Multiple employees would not directly confirm (b) (6) identity. Dr. Iyengar confirmed that (b) (6) was suspended in February 2023 and dismissed March 23, 2023 due to misconduct but Dr. Iyengar would not provide further details. KM stated that the person who conducted the falsifications is no longer at the site but could not elaborate due to legal reasons. It appears that a thorough investigation was not conducted for the following reasons:

- The site only reviewed 55 of 259 Swab Processing Logs as part of the investigation. The scope of document review in the investigation was not

expanded beyond Swab Processing Logs and did not include additional study records dated prior to July 2022 or after January 2023 even though [REDACTED] was delegated responsibilities from June 26, 2021 through their dismissal in February 2023.

- It is unclear how the site determined the identity of the suspected person responsible and concluded that they were no longer employed at the site. The suspected person responsible was not named in the investigation summary, nor were they interviewed. The summary also lists the suspected person as a CRC, however, Site Signature Logs list [REDACTED] as a research nurse/technician.
- It is unclear why [REDACTED] was dismissed and if [REDACTED] prior misconduct was adequately investigated since the signature falsifications were discovered a year after [REDACTED] left the site.

In addition to the inaccurate case histories identified during the inspection, your incomplete investigation to adequately identify the full extent of signature falsifications and potential other misconduct raises concern relating to the integrity of the subject data collected at your site and associated documentation.

We acknowledge that your Response Letter did not address this finding because it was not included on the Form FDA 483 you received.

- b. Multiple shipping logs were reviewed and signed prior to completion with some logs containing errors. During monitoring visits, clinical research associate (CRA) [REDACTED] reviewed and signed at least 15 Swab Processing and Shipping logs prior to log completion by site staff. For example, the shipping logs for February 24, 2022 and July 25, 2022 were signed as reviewed on February 23, 2022. [REDACTED] also reviewed and signed shipping logs that were missing freezer transfer initials and contained incorrect visit names. For example, the shipping log for May 10, 2022 contained two (2) incorrect visit names and was certified as complete on August 11, 2022 but was reviewed on July 22, 2022. Also, the shipping log for July 1, 2022 was missing both freezer transfer initials but was signed as reviewed on July 27, 2022.

We acknowledge that your Response Letter did not address these findings because it was not included on the Form FDA 483 you received.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical investigation. It is your responsibility to fully comply with the law. You should address any deficiencies and ensure that any ongoing or future studies comply with the Federal Food, Drug and Cosmetic (FD&C Act), PHS Act, and applicable FDA regulations.

We request a written response to this letter within fifteen (15) working days from your receipt of this letter, outlining the specific steps you have taken or plan to take to address any violations and prevent their recurrence. Include any documentation necessary to show that the matters have been addressed. If you cannot address these matters within fifteen (15) working days, please explain the reason for your delay and the timeframe for completion. If you believe that you have complied with the FD&C Act, PHS Act and applicable regulations, include your reasoning and any supporting information for our consideration. FDA has several

references available at

<http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm> for more information on human subject protection and the conduct of clinical research.

Send your electronic response to CBERBIMONotification@fda.hhs.gov and cc FDAInternationalBIMO@fda.hhs.gov. If you have any questions regarding this letter, you may contact Kanaeko Sharp at Kanaeko.Sharp@fda.hhs.gov

Sincerely,

MELISSA J. MENDOZA -S

Digitally signed by MELISSA J. MENDOZA

Date: 2025.08.05 12:19:40 -0400

Melissa J. Mendoza, JD
Director, Office of Compliance and Biologics Quality
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cc:

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