



## DEPARTMENT OF HEALTH & HUMAN SERVICES

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US Food & Drug Administration  
Center for Biologics Evaluation & Research  
Office of Vaccines Research and Review  
Division of Viral Products

### MEMORANDUM

**Date:** April 25, 2023

**Sponsor:** GlaxoSmithKline.

**From:** Ewan P. Plant, PhD CBER/OVRR/DVP

**To:** BLA 125775 / 0

**Through:** Zhiping Ye, CBER/OVRR/DVP  
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**CC:** Santosh Nanda, CBER/OVRR/DVRPA  
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Judy Beeler, CBER/OVRR/DVP  
Lynne Crim, CBER/OVRR/DVP

**Subject:** **Review of HI Assay and Validation:** The HI assay is used to evaluate the humoral immune response of an influenza virus vaccine used in RSVPreF3 OA co-administration studies.

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#### Summary of Recommendation:

The Hemagglutination Inhibition (HI) assay is used by the sponsor to assess the antibody response toward quadrivalent influenza vaccine co-administered with the RSV vaccine. Antibody response is used as a surrogate of protection for the influenza vaccine to assess effectiveness of the influenza and RSV vaccines to support vaccine coadministration.

The standard operating procedure for the HI assay is acceptable. The HI assay detects antibodies that bind influenza virus and is validated for the four types of influenza antigen included in quadrivalent influenza vaccines (H1N1, H3N2, and influenza B Victoria and Yamagata lineages).

There are minor issues with assay validation for the Yamagata lineage, but overall, the assay was found acceptable for detection and quantification of influenza antibody response.


#### Submission and Review:

Reviewer comments are in italics.

*The HI assay described in document TSOP.119.00510. (b) (4) revision G (effective 11/14/2019) belongs to (b) (4). This company performs assays for several sponsors and prior versions of the HI assay have been reviewed under MF (b) (4) (amendment 8), IND (b) (4) (amendment (b) (4)), IND (b) (4) (amendment (b) (4)) and BLA (b) (4) (supplement (b) (4)). The protocol was also reviewed under IND 18540 (amendment 116) when RVSPreF3 OA was being reviewed as an Investigational New Drug. The documents reviewed in this memorandum are in the [Flu-HI-007] section in the Summary of Clinical Assay Validation (in section 5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies).*


*The HI assay was used to assess the humoral response to influenza vaccination for a co-administration study using FLU-QIV with RSVPreF3 OA in study RSV OA=ADJ-007 described in 214488 (RSV OA=ADJ-007): A Phase 3, open-label, randomized, controlled, multi-country study to evaluate the immune response, safety and reactogenicity of RSVPreF3 OA investigational vaccine when co-administered with FLU-QIV vaccine in adults aged 60 years and above (in section 5.3.5.1 Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication) and in Integrated Analysis of Efficacy (in Section 5.3.5.3 Reports of Analyses of Data from more than one study).*

*The HI assay is performed in many laboratories throughout the world but there are small and sometimes significant variations in the methodology. Briefly, (b) (4)*



*The earliest versions of the assay used by (b) (4) defined the (b) (4)*

*(b) (4) the assay so that it conformed with CBERs interpretation of the (b) (4)*



*described in the HI assay review for BLA 125123/1946. These assay changes are acceptable.*

*The assay validation reports are provided for A/Hong Kong/2671/2019 (H3N2, effective 11/1/2021), A/Victoria/2570/2019 (H1N1, effective 11/2/2021), B/Washington/02/2019 (Victoria lineage, effective 11/1/2021), and B/Phuket/3073/2013 (Yamagata lineage, effective 11/1/2021). These are the strains that were recommended for inclusion during the 2021 southern hemisphere quadrivalent influenza vaccine formulation which was*


*recommended and used when the Phase 3 RSV OA=ADJ-007 clinical trial was conducted.*

*The validation reports provide data for (b) (4)*


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*The validation for the A/Hong Kong/2671/2019 antigen was performed in 2020 and again in 2021 (b) (4) Data from both validations are included in the report.*

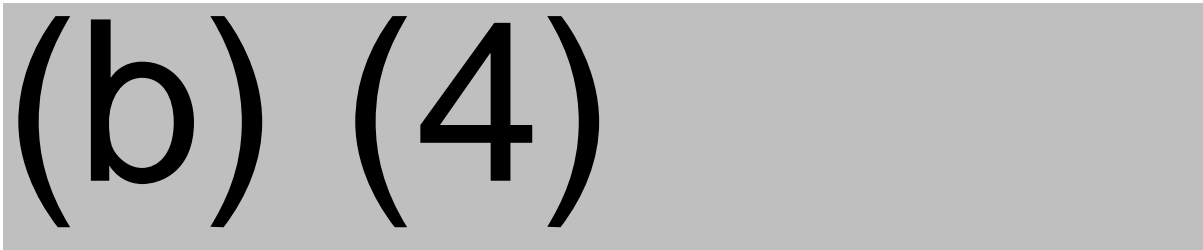
*(b) (4)*

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*A summary of the results from the (b) (4) validation reports is provided in the table below. Please note that a range of results is given to capture multiple measurements, for example: (b) (4)*

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**(b) (4)**

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(b) (4)

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**Reviewer's Conclusion:**

*The HI assay detects antibodies that bind influenza virus and is validated for the four types of influenza antigen included in quadrivalent influenza vaccines (H1N1, H3N2, and influenza B Victoria and Yamagata lineages). There are minor issues with assay validation for the Yamagata lineage, but the assay is acceptable for detection and quantification of influenza antibody response.*