



Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

Memorandum

DATE: OCTOBER 27, 2015

FROM: Diana Kouivskaia, CMC reviewer, DVP

TO: The file STN **125563/0.0**

THROUGH: Steven Rubin, DVP

COPY: Robin Levis, DVP
Sara Gagneten, DVP
Kelsy Hoffmann, RPM
Katie Rivers, RPM

STN: **125563/0.26**

SPONSOR: MCM Vaccine Company

PRODUCT: Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, Inactivated Poliovirus, Haemophilus b Conjugate [Meningococcal Protein Conjugate] and Hepatitis B [Recombinant] Vaccine ((b) (4)) also referred to as PR5I

SUBJECT: Review of response to the Information Request of October 16, 2015 regarding D-antigen (b) (4) assay performed on PR5I vaccine (b) (4)

Summary and recommendation:

This memo reviews Amendment STN 125563/0.26, which was submitted in response to the CBER information request (IR) of October 16, 2015. The IR was in regard to validity criteria applied to the D-Antigen (b) (4) assay used to determine D-Antigen content in the (b) (4) product of PR5I vaccine. The company's response is acceptable.

CMC of Vero IPV (vIPV) component of the PR5I vaccine (BLA STN 125563/0 and Amendments) is reviewed in the memo of October 20, 2015. With the resolution of this IR, there are no outstanding requests regarding vIPV component of the vaccine. I recommend approval of the BLA.

Background:

(b) (4) D-Antigen (b) (4) assay is used at the (b) (4) Product stage to assess D-Antigen content in the PR5I vaccine and is a Lot release test for Vero IPV component of the vaccine. One sample in triplicate is tested in the (b) (4). No validity criteria were provided for the triplicate values obtained for each sample. The requests to provide sample validity criterion were communicated to the sponsor in Information Requests of April 10, 2015 (Question 4g), and June 19, 2015 (Question 1). In the responses to the Information Requests the sponsor provided the following validity criteria applied to the (b) (4) D-Antigen (b) (4) used to determine D-Antigen content in the PR5I vaccine (b) (4) product (STN 125563/0.9):

1. Value of the reference standard for (b) (4) fall between control limits (b) (4);
2. Calculated results of validity control falls within established range (validity control lot (b) (4))

The D-antigen (b) (4) was validated to test a single sample in triplicate and all validation parameters were found to be within the acceptance criteria. The sponsor stated that no validity criteria are imposed on the triplicate values observed for each sample. When testing for D-antigen content in Vero IPV containing products, assessment of the sample result is done based on (b) (4) data from (b) (4) (STN 125563/0.15).

Information Request of October 16, 2015:

Although you indicate that the (b) (4) was validated to provide a reliable result based on testing of the single sample in triplicate without imposing rules for inter-replicate values, we recommend that you establish such a criterion to provide additional assurance of assay performance and precision of the reported result. We acknowledge that additional data will be required to establish the requested criterion. Please commit to providing this information as soon as possible.

The response was submitted in Amendment STN 125563/0.26 on October 26, 2015.

The sponsor stated that the (b) (4) method is a validated method used across several SP sites globally, with the same procedure for all sites; assessment of the test and sample validity is performed consistently for all vIPV containing products.

There is no validity criterion for intra-replicate precision at the (b) (4) stage of the procedure. Specific criterion for inter-replicate values will not be established at this time.

However, a validity criterion is applied at the (b) (4) D-Antigen unit (b) (4) values generated from (b) (4) where the reported result must be calculated using a minimum of (b) (4) values that have a percent coefficient of variation that is (b) (4)

Comment:

In the response to the IR of October 16, 2015, the sponsor provided a validity criterion that is applied to the (b) (4) D-antigen concentration values (D-antigen units per ml) generated from (b) (4). This response is acceptable.