



**DATE:** September 27, 2018

**TO:** File: STN # 125563/0.31, 0.33 and 0.40

**FROM:** Freyja Williams, BS, Pertussis potency testing  
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**THROUGH:** Jay Slater, MD  
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**PRODUCT:** Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine  
Adsorbed, Inactivated Poliovirus, Haemophilus B Conjugate  
[Meningococcal Protein Conjugate] and Hepatitis B [Recombinant]  
Vaccine, PR5I  
(b) (4)

**SUBJECT:** Updates to the pertussis potency testing affecting PR5I

**APPLICANT:** MCM

## 1. General Information

**Submission Tracking Number (STN):** 125563/0

**Submission received by CBER:** Original submission received 13 August 2014, amendments 0.31, 0.33, and 0.40 received 5 April 2018, 23 April 2018, and 25 September 2018 respectively

**Review completed:** September 11, 2018

**Material Reviewed:** 125563/0.31, 0.33 and 0.40

**Related Master File, INDs and BLAs:** IND # 14496, and STN #103666/5387 +3, 103666/5157 +1

## 2. Executive Summary

Prior to submission of the applicant's response to the complete response letter, MCM submitted amendments describing updates to pertussis antigen testing that apply to Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, Inactivated Poliovirus, Haemophilus B Conjugate [Meningococcal Protein Conjugate] and Hepatitis B [Recombinant] Vaccine, PR5I. These changes were reviewed and approved under the appropriate BLAs for each pertussis containing vaccine licensed in the United States. The changes submitted have been appropriately applied to PR5I and documented.

### 3. Background

Under IND 14496, Amendment 104, dated 25 May 2017, MCM requested permission to submit Quality Amendments to STN BL 125563 prior to providing a response to the Complete Response Letter issued by CBER on 2 November 2015. In an email correspondence dated 01 August 2017, CBER agreed that MCM could submit Quality Amendments to the file. Three submissions, amendments 0.31, 0.33 and 0.40, were submitted to the file that included information related to the testing of the pertussis components of PR5I. These amendments as they apply to the pertussis components are reviewed in this memo.

### 4. Review

#### 4.1. STN 125563/0.31 submitted 5 April 2018

This amendment, as it pertained to pertussis component testing, provided cross references and information on the change of reference standard lot and positive control used in the ELISA for the quantitation of pertussis toxin. The materials were replaced due to expiration of existing lots. In-house PTx Reference Standard lot (b) (4) was replaced with lot (b) (4). In-house PTx Positive Control lot (b) (4) was replaced with lot (b) (4). The applicant provided a Basis for Submission Statement and updated Module 3.2.S.5. The cross referenced BLAs were STN #103666/5387 +3. Review of the replacement materials can be found in Anita Verma's memo to that file dated 2 August 2016. The replacement materials were found to be acceptable and the BLAs approved 24 August 2016. The review and approval also can be applied to this BLA as the pertussis toxoid drug substance and testing in PR51 is the same as that in the other licensed pertussis containing products. No additional information is needed.

#### 4.2. STN 125563/0.33 submitted 23 April 2018

This amendment, as it pertained to pertussis component testing, provided information on a replacement reference standard ((b) (4)) lot used in the *in vitro* portion of the acellular pertussis mouse immunogenicity assay. The amendment states that a comparability protocol (SOP Q\_0235230) was approved for use in the replacement of the reference standard on 13 July 2007 under STN # 103666/5155 and 125111/109, 8 May 2008 under 103666/5157 and 125111/116, and 18 December under 125145/20. The reference standard lot approved for use for the licensed pertussis containing vaccine was (b) (4). However, the comparability protocol for the preparation and qualification of an in-house secondary reference standard for component pertussis mouse immunogenicity assays submitted to 103666/5157 +1 and approved was SOP A004335. An information request letter was sent to the applicant 18 September 2018 as follows:

In amendment 0.33 to your application STN # 125563 you cite approval of a comparability protocol (SOP Q\_0235230) under STN # 1033666/5157 as support for the implementation of the new lot of reference standard used in the *in vitro* portion

of the acellular pertussis mouse immunogenicity assay. However the approved SOP appears to be SOP A004335. Please provide the SOP number of the appropriate approved comparability protocol used to evaluate reference standard lot (b) (4) describe any changes to the protocol since approval, and clarify any discrepancies.

In response the applicant confirmed that the different SOP numbers were due to migration of documents to a new database and reassignment of document numbers. SOP A004335 and Q\_0235230 are the same document. The document was provided and cites both numbers. The response is adequate. The approval of the comparability protocol and the use of the new reference standard is applicable to PR5I. No additional information is needed.

## **5. Recommendation**

The information provided in amendments 0.31, 0.33 and 0.40 updated the BLA with relevant changes to the pertussis potency testing approved under STNs for other pertussis containing products. The updates are applicable and appropriate to the testing of PR5I. No additional information regarding the pertussis potency is required for approval of PR5I. The performance of the pertussis potency test is adequate for approval.