

**DEPARTMENT OF HEALTH & HUMAN SERVICES**  
FDA, Center for Biologics Evaluation and Research

**MEMORANDUM**

Date: June 19, 2015

From: Michael P. Schmitt, Ph. D.  
Chief, LRSP/DBPAP

Through: Jay Slater, M.D.  
Director, DBPAP/OVRR

Subject: CMC Review Memo for Diphtheria and Tetanus Toxoid manufacturing and testing for BLA 125563/0, PR5I ((b) (4) (DTaP-IPV-Hib-HepB)

Sponsor: MCM Vaccine Co.

To: File for BLA 125563/0

**SUBMISSIONS REVIEWED**

STN 125563/0; Original BLA

STN 125363/0.2; Stability data DP (Am. received 09/12/2014)

STN 125363/0.4; IR -clarification on role of MCM Vaccine Co. (Am. received 11/04/2014)

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## 1 Summary/Background

On August 12, 2014 Sanofi Pasteur submitted a Biologics License Application for Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, Inactivated Poliovirus, Hemophilus b Conjugate [Meningococcal Protein Conjugate] and Hepatitis B [Recombinant] Vaccine (DTaP-IPV-Hib-HepB). The applicant for the BLA is MCM Vaccine Co., which is a partnership between Sanofi Pasteur Inc, and Merck Sharp and Dohme. The manufactures of the drug substances used in the formulation of the final product are Sanofi Pasteur Inc, and Merck Sharp and Dohme. During development, the vaccine was referred to as PR5I, and the proposed proprietary name is (b) (4). For this review, the vaccine will be referred to as PR5I. PR5I is manufactured using existing (or slightly modified) bulk intermediates from US licensed vaccines produced by Sanofi Pasteur and Merck.

Clinical development of PR5I was conducted under IND 14496, which was submitted on 9/20/2010. PR5I is a hexavalent combination vaccine indicated for immunization of infants at 2, 4, and 6 months of age for protection against diphtheria, tetanus, pertussis, polio (types 1, 2, and 3), invasive *Hemophilus influenzae* type b and Hepatitis B. The vaccine is produced as a sterile liquid preservative-free suspension and is filled in single dose vials.

## 2 Review

### 2.1 Overview

This review covers Diphtheria Toxoid (DT) and Tetanus Toxoid (TT) drug substance manufacturing and testing, as well as formulation and testing of the drug product that impacts the DT and TT antigens. Areas covered by this review include all relevant information in Section 2 (CTD Summary) and Section 3 (Quality) that pertain to the manufacturing and testing of DT and TT. Updated Stability studies provided in amendment 2 are also reviewed.

In section 3 Quality; 3.2.S Drug Substance, the sponsor has provided a document titled “Note to Reviewers” for each of the drug substances contained in the DTaP-IPV component of the vaccine. In this document, the sponsor provides details on the differences in the CMC information between the drug substance in PR5I and the drug substance in Pentacel. Additionally, a similar document is included in section 3.2.P -Drug Product, which outlines the drug product differences between PR5I and Pentacel. The differences described in these documents will be the primary focus of this review, since the manufacturing and testing for the DT and TT antigens are virtually identical between PR5I and the currently licensed Pentacel vaccine. Most of the changes that are identified in these documents are minor and are not expected to have any impact on the potency, purity or safety of the DT and TT antigens present in the final PR5I drug product.

### 2.2 Diphtheria Toxoid Drug Substance

General Information (3.2.S.1) regarding structural, chemical and biological properties on the diphtheria toxin and diphtheria toxoid are the same as that provided in the Pentacel file.

*Manufacture of Diphtheria Toxoid Adsorbed*

(b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



[REDACTED]

[REDACTED]

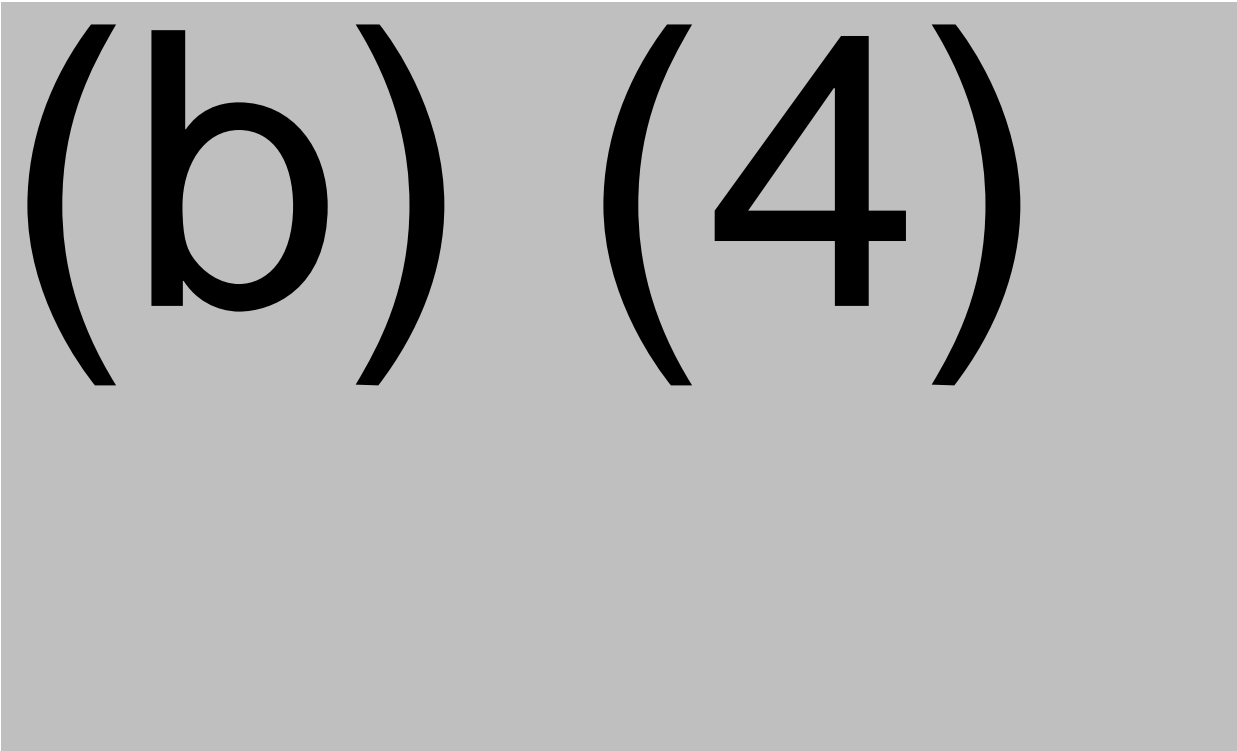
[REDACTED]



(b) (4)



(b) (4)





### **2.3 Tetanus Toxoid Drug Substance**

#### *Manufacture of Tetanus Toxoid Adsorbed*


Description of manufacturing process:

(b) (4)





(b) (4)



#### **4 Recommendation**

Based on information reviewed regarding the DT and TT antigens used in the production of the PR5I vaccine, I recommend approval of this BLA.