DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

To: DATS: 580699

STN BLA 125525/0
Product: Diphtheria And Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine; DTaP-IPV

From: LCDR Donald Ertel, Regulatory Officer, OCBQ / DMPQ / MRB1

Through: Carolyn Renshaw, Branch Chief, OCBQ / DMPQ / MRB1

CC LCDR Juan Lacayo, RPM, OVRR/DVRPA/CMC1
LCDR Matthew Steele, Chair, OVRR/DVRPA/CMC1

Subject: DMPQ Final Review for Biologics License Application filed per 21 CFR 601.2 for active immunization against diphtheria, tetanus, pertussis and poliomyelitis in children 4 through 6 years of age.

Applicant: Sanofi Pasteur Limited (Sanofi) (License Number 1726)

Facility Toronto, CA Site; FEI # 3002888623

ADD: 24 Mar 2015

Conclusion and Recommendation

Since no changes to Facility, Equipment, Container Closure, or Process is occurring to the already approved Pentacel® product (125145/0), no evidence exists that the identity, strength, safety, quality and purity of the product produced and tested in the existing facilities would be adversely impacted by the new indication. I recommend approval of this submission.

Review Memo Format and Table of Contents▪

I have provided a summary of information provided in the submission that is under DMPQ purview as outlined in SOPP 8401.4: In general, my Review Assessment / Comments are provided at the end of review sections in a double lined box. Any information requests (IRs) related to review will be included in these boxes in bolded text. A summary of the firm's

response to that IR will immediately follow in italicized text. My assessment of the response will immediately follow in a double lined box.

The table of contents of this review is as follows (major sections numbered, subsections lettered):

1. Amendments related to Review

- 125525/0.1 received 14 Apr 2014 to Information Request on 02 Apr 2014 (in support of Inspection Waiver Memo).

2. Regulatory History

BLA STN# 125252/0 was submitted by Sanofi Pasteur Limited and received by CBER on 24 Mar 2014. I was assigned as CMC reviewer in 28 Mar 2014. The application was appropriately filed per 21 CFR 601.2

An Inspection Waiver was submitted and approved (16 Jun 2014) for this submission for the Toronto, CA Site; FEI # 3002888623.

I evaluated the submission per SOPP 8401.4: Review Responsibilities for the CMC Section of Biologic License Applications and Supplements. The following documents were reviewed:

- 1.12.14 – Environmental Analysis
- 3.2.P.3.1 - Manufacturer of Drug Product (DTaP-IPV)
- 3.2.S.2.1 - Manufacturer of Drug Substance_Component Acellular Pertussis Adsorbed
- 3.2.S.2.1 - Manufacturer of Drug Substance_Diphtheria Toxoid Adsorbed
- 3.2.S.2.1 - Manufacturer of Drug Substance_Poliovirus Vaccine Inactivated
- 3.2.S.2.1 - Manufacturer of Drug Substance_Tetanus Toxoid Adsorbed
- Section 1.4.4 – Cross Reference to Other Applications

3. Environmental Assessment

Sanofi requests a categorical exclusion under 21 CFR 25.31(c) from the preparation of an Environmental Assessment. With the action on the Biologics License Application for Diphtheria and Tetanus Toxoids, Acellular Pertussis Adsorbed, and Inactivated Poliovirus, there is no change to the product that would alter significantly the concentration or distribution of the substance, it metabolites, or degradation products in the environment. To the knowledge of Sanofi Pasteur Limited, no extraordinary circumstances exist.

Review Assessment / Comments: I am in agreement with the CE.

4. Background

The proposed indication is active immunization against diphtheria, tetanus, pertussis and poliomyelitis in children 4 through 6 years of age. The clinical development of this vaccine in the United States was performed under BB-IND 14668, initially submitted 25 Mar 2011.

Included with this submission are the relevant components of Module 1 (Administrative and Prescribing Information), Module 2 (CTD Summaries for Clinical Data), and Module 5 (Clinical Study Reports). In particular, Module 5 contains the immunogenicity and safety data to support the licensure of DTaP-IPV for administration as a 5th dose booster in US children 4 to 6 years of age as follows:

- Pivotal Study M5I02, Safety and Immunogenicity of DTaP-IPV (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliovirus Vaccine) Compared to DAPTACEL® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) + IPOL® (Poliovirus Vaccine Inactivated) as the 5th Dose in Children 4 to 6 Years of Age.
- Supportive Study Td508, Safety and Immunogenicity of ADACEL® (TdcP Vaccine) Compared with QUADRACEL® (HCPDT-mIPV Vaccine) as Fifth Dose in Children 4-6 Years of Age.
- Module 3 (Quality) (other than Section 3.2.P.5.4 which will contain the DTaP-IPV Lot Release Protocol) references the Pentacel BLA (STN BL 125145/0).

5. Overview

Manufacturing and testing of (b) (4) drug product occur exclusively at the Toronto site. Sanofi is reporting no change to Facilities, Equipment, Container Closure, or Process. According to Sanofi, the drug substances used to formulate DTaP-IPV vaccine are the same as those used in US-licensed Pentacel® vaccine. In addition, the drug product is formulated and filled in US-licensed facilities and the manufacturing process and release criteria for DTaP-IPV final fills are identical to those of the DTaP-IPV component of Pentacel. Sanofi reports no difference from production, formulation, or filling of this product to those of Pentacel® DTaP-IPV vaccine. It is important to note that Pentacel® is packaged as a kit containing the liquid DTaP-IPV vaccine in one vial and a lyophilized *Haemophilus influenzae* type b (Hib) vaccine in another vial, which are combined together /reconstituted just prior to administration. The product in this application (proposed tradename, Quadracel, initially approved by CBER in correspondence dated 07 Oct 2013) only contains the DTaP-IPV liquid vaccine.

Review Assessment/Comments: No additional evaluation is warranted since is referencing the already approved Facility, Equipment, Process, and container closure of Pentacel®.