



FOOD AND DRUG ADMINISTRATION
CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

MEMORANDUM

BLA REVIEW

DATE: June 15, 2015

FROM: Marian Major, Ph.D.

SUBJECT: STN# 125563
Subject: Review of anti-hepatitis B serology assay
Sponsor: Sanofi Pasteur
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)

TO: Katie Rivers, DVRPA
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THROUGH: Robin Levis DVP
Sara Gagnetten, DVP

Background

Sanofi Pasteur Ltd. and Merck Sharp & Dohme Corp. are jointly developing the hexavalent combination vaccine, (b) (4) for infants and toddlers against multiple infectious diseases. (b) (4) is manufactured using modified and/or existing bulk intermediates from licensed vaccines as follows:

PRP-OMPC Bulk Intermediate, from liquid PedvaxHIB (STN 103237) - Merck & Co., Inc.

HBsAg Bulk Intermediate from RECOMBIVAX HB (STN 101066) - Merck & Co., Inc.

Five component Acellular Pertussis Adsorbed and Diphtheria and Tetanus Toxoids Adsorbed intermediate as produced for Pentacel (STN 125145), DAPTACEL (STN 103666), and Quadracel (STM 125525) - Sanofi Pasteur Ltd.

Inactivated Poliovirus Types 1, 2 and 3 Bulk Intermediate as produced for IPOL (STN 103930), Pentacel and Quadracel – Sanofi Pasteur Ltd.

Each 0.5 mL dose of vaccine contains the following in a sterile, single-dose, liquid, and preservative-free formulation for intramuscular injection.

20 µg of pertussis toxoid (PT);
20 µg of filamentous haemagglutinin (FHA);
3 µg of pertactin (PRN);
5 µg of fimbriae Types 2 and 3 (FIM);

3 µg of polyribosylribitol phosphate polysaccharide coupled to the outer membrane complex of *Neisseria meningitidis* (PRP-OMPC);
10 µg of hepatitis B surface antigen (HBsAg);
15 Lf of diphtheria toxoid;
5 Lf of tetanus toxoid;
29, 7, and 26 –D antigen Units of Inactivated Poliovirus (IPV) Type 1 (Mahoney), Type 2 (MEF-1), and Type 3 (Saukett), respectively, by a D-antigen (b) (4) assay (equivalent to 40, 8, and 32 D-antigen units, respectively, by the (b) (4) assay); and
(b) (4) µg of aluminum.

The vaccine is administered as a 0.5-mL intramuscular injection in a 3-dose infant series given at 2, 4, and 6 months of age in the U.S. The vaccine must be stored at 2-8°C.

This review concerns the serology assay for anti-HBs antibodies. This assay was validated by Merck and testing for antibodies was carried out by Merck at (b) (4) Vaccines and Biologics Laboratory (the former Vaccine and Biologics Research Serology Testing Laboratory of Merck). Details of the validation and methodology are contained in the Recombivax IND (IND 1925).

On July 9, 2014 Merck submitted to CBER a letter of authorization for Sanofi Pasteur Limited, Canada, and MCM Vaccine Company, Swiftwater, PA, USA, to cross reference STN 101066 and BB-IND 1925, in support of the BLA for the combination vaccine Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, Inactivated Poliovirus, Haemophilus b Conjugate [Meningococcal Protein Conjugate] and Hepatitis B [Recombinant] Vaccine, ((b) (4) This authorized CBER to review information in the Recombivax BLA (STN#101066) and the Recombivax IND (BB-IND 1925) as part of the (b) (4) review.

This letter specifically referred to IND amendments to BB-IND 1925 which contained information relating to the serology assay used to test for anti-HBs antibodies. Validation documents for the assay have been reviewed under IND 1925 Am 478. The SOP for the assay and data to support stability of the assay have been reviewed under IND 1925 Am 526. Both of these reviews can be found in the EDR under IND 1925.

Following is a summary and review of the information submitted in BLA 125563 relating to the anti-HBs antibody serology testing.

Hep B (b) (4) Assay

Description of the Assay Method

(b) (4)



2 Pages Determined to be Not-Releaseable: (b)(4)

(b) (4)

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COMMENTS and RECOMMENDATION

The Hep B ^{(b) (4)} assay is acceptable for testing anti-HBs levels in human serum samples.