FOOD AND DRUG ADMINISTRATION
CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

MEMORANDUM

DATE: February 28, 2007

TO: File, STN 125145/0
Sanofi Pasteur, Inc.
Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate) Reconstituted with Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed Combined with Poliovirus Vaccine Inactivated: PENTACEL™
Theresa Finn, Committee Chair

FROM: Willie F. Vann, Chief
Laboratory of Bacterial Polysaccharides, DBPAP/OVRR

SUBJECT: Review of CMC and Serology of Diphtheria and Tetanus Toxoids

THROUGH: Richard I. Walker, Director
DBPAP/OVRR

Summary

PENTACEL™ is the product combination of Haemophilus b Conjugate Vaccine (Tetanus Protein-Conjugate) reconstituted with Component Pertussis Vaccine Combined with Diphtheria and Tetanus Toxoids Adsorbed and Poliovirus Vaccine Inactivated (HCPDT-IPV). PENTACEL™ is intended to replace DAPTACEL®, IPOL™, and ActHIB™ given separately. HCPDT-IPV Vaccine is manufactured at Aventis Pasteur Limited (Canada) and Haemophilus b Conjugate Vaccine (Tetanus Protein-Conjugate) Vaccine referred to as PRP-T Vaccine is manufactured at Aventis Pasteur SA (France). PRP-T Vaccine (filled and freeze-dried) is received, at Aventis Pasteur Limited, where it is labeled and co-packaged with labeled HCPDT-IPV Vaccine.

During the clinical development of PENTACEL™, a similar acellular Component Pertussis vaccine, DAPTACEL® was licensed in the United States in May 2002. DAPTACEL® was introduced into the US market in 2002 for the active immunization of infants and toddlers at 2, 4, 6 and 17 to 20 months and has since been recommended by the Advisory Committee on Immunization Practices (ACIP). PENTACEL™ differs from DAPTACEL® only in that it has a higher content of the Component Pertussis PT and FHA antigens and contains Poliovirus antigens Types 1, 2 and 3. HCPDT-IPV Vaccine is

used to reconstitute PRP-T Vaccine at the time of use. The quantities of Diphtheria Toxoid, Tetanus Toxoid, PRN and FIM are the same.

CMC

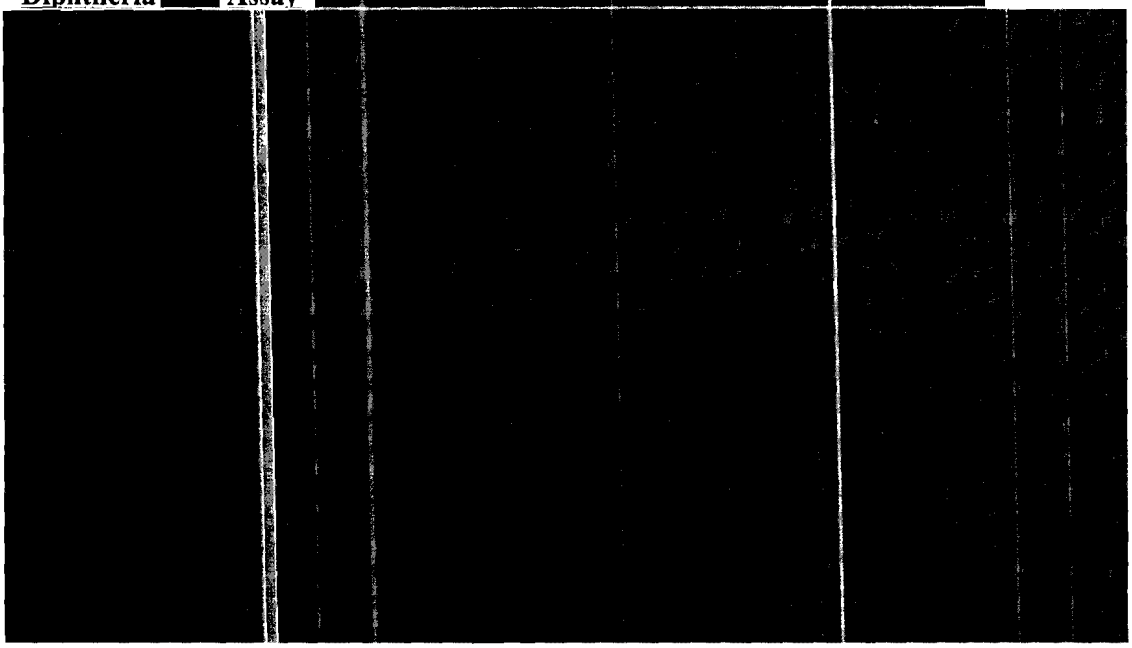
The diphtheria and tetanus toxoid components of PENTACEL™ are manufactured using a process identical to that used to manufacture the licensed products DAPTACEL® and Td adsorbed. All aspects of the manufacturing and testing methods for these components in PENTACEL™ are identical to those used for these two licensed products. Testing of the diphtheria and tetanus toxoids was conducted according to equivalent release and in-process test methodology currently used for release of the licensed products used in the U.S. market, including the use of reference standards.

SEROLOGY

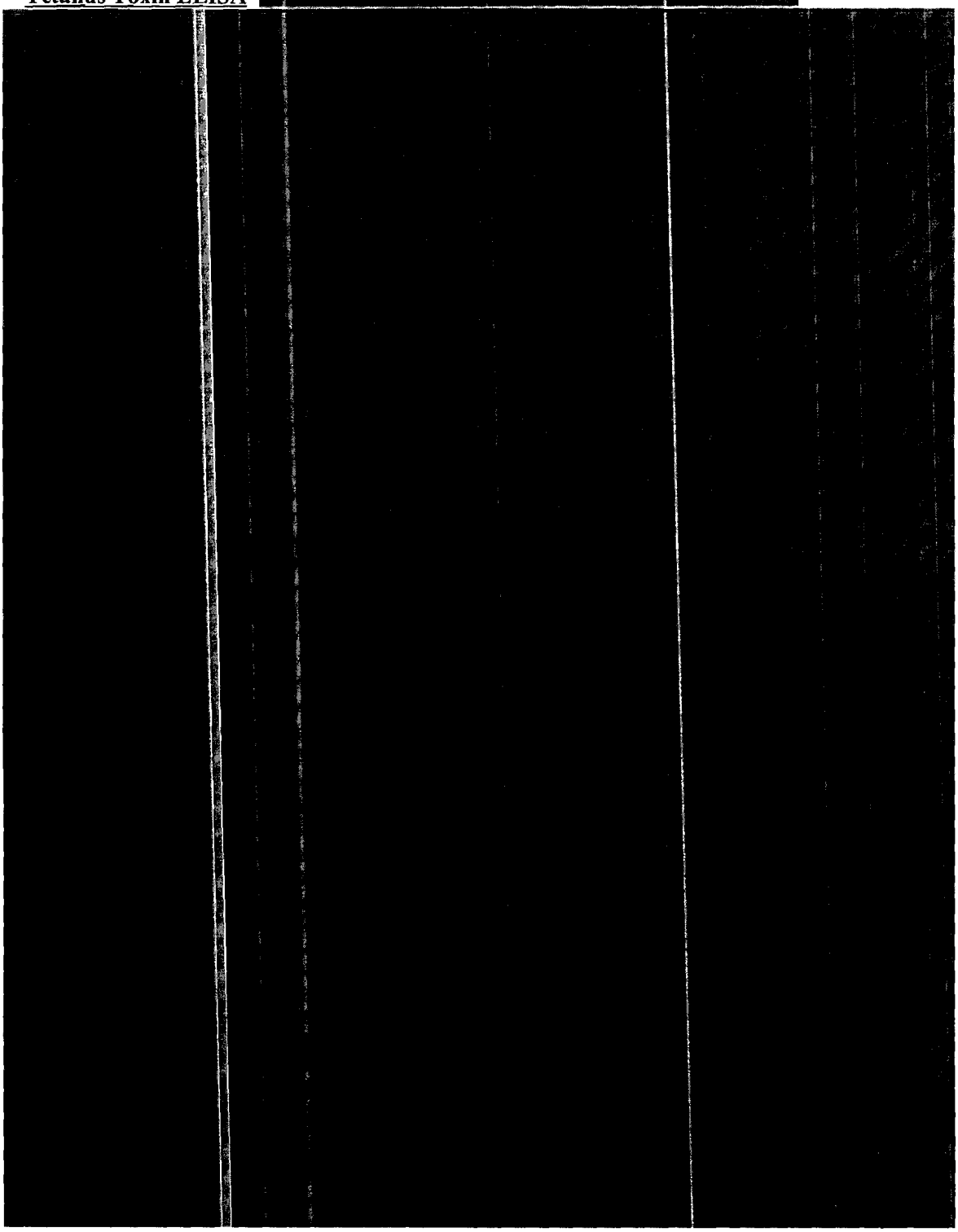
The serological assays used in the clinical evaluation of PENTACEL™, for diphtheria and tetanus antigens were the Diphtheria [redacted] and tetanus [redacted] ELISA. These assays were reviewed and approved earlier by CBER. In an IR letter dated October 20, 2000, CBER stated approval of Diphtheria [redacted] serology assays for pivotal trials.

In an IR letter dated October 25, 2001, CBER concurred on correlation of the Tetanus [redacted] ELISA and the [redacted] and approved the Tetanus [redacted] ELISA for testing of sera from pivotal clinical trials.

Diphtheria [redacted] Assay - [redacted]



Tetanus Toxin ELISA -



- Appropriate to measure the pre- and post-vaccination immune responses in clinical sera toward Tetanus antigen contained in PENTACEL™.

Recommendation:

There are no significant changes in the manufacture of the Diphtheria and Tetanus Toxoid components of PENTACEL™ and licensed vaccine DAPTACEL® thus the CMC section is acceptable for licensure of PENTACEL™. The transfer of the serological assays for these components from building [redacted] has been adequately validated and demonstrated as suitable for assay of human sera.