Memorandum

Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Compliance and Biologics Quality
Division of Manufacturing and Product Quality

Date: 20 February 2007

To: **File:** STN 125145/0/10 Diphtheria & Tetanus Toxoids & Acellular Pertussis (5-component) Vaccine Adsorbed & Inactivated Poliovirus Vaccine combined with Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)

Sanofi Pasteur Limited (License No. 1726)

From: Nancy Waites, Facility Reviewer, MRB1/DMPQ/OCBQ/HFM-675

REVIEWED
By Nancy Waites at 2:48 pm, Feb 20, 2007

Subject: Review of Biologics License Application Amendment submitted electronically by Sanofi Pasteur Limited, received 24 Feb 2006.

Through: Carolyn Renshaw, Acting Branch Chief /MRB1/DMPQ/OCBQ/HFM-675

APPROVED
By Deborah Trout at 1:22 pm, Feb 26, 2007

Cc: Edward Wolfgang, RPM, OVRR/DVRPA/BVB/HFM-475

Conclusion: I recommend approval of this submission if all other review disciplines do not have any concerns.

Review Narrative and Comments

This amendment contains responses to a CR letter, dated 16 November 2005 for STN [redacted] The information on shipping for the product in STN 103935 also applies to the product in STN 125145. The items listed are from the CR letter (in bold) and Sanofi's responses follow.

1. This supplement contains information on activities performed by Aventis Pasteur Ltd., Canada after receipt of the PRP-T from Aventis Pasteur SA, France: labeling and co-packaging of the PRP-T and DTaP-IPV components, lot numbering system and assignment of expiration dating for Pentacel™ and validation of the Pentacel™ shipping process from Aventis Pasteur Ltd. (Canada) to Aventis Pasteur Inc. (US). Please confirm that this information was provided for reference purposes only as indicated during the October 14 2005, teleconference and confirm that these procedures have been submitted for review under the Pentacel™ BLA (STN 125145/0).

Sanofi stated that they confirm the PAS information has been submitted to the ActHIB® license for reference purposes only and that they will submit this administrative supplement to the PENTACEL™ BLA as an amendment.

This response is acceptable and I have confirmed that the information was also submitted to the PENTACEL eBLA (STN 125145/0). It was submitted as STN 125145/0/10.

2. Page 14, Section 2.1, Validation of the Shipping Process from Aventis Pasteur SA (France) to Aventis Pasteur Limited (Canada) - You state in this section that you have implemented a new validation protocol (094693) in order to qualify a new packaging system for shipment of PRP-T from France to Canada. Please address the following with regard to your shipping validation studies:

> **a. Please provide the protocol for validation study 094693 and supporting data, if available. If the study has not been performed, please indicate when the study will be initiated and completed.**

Sanofi submitted document number 101 634 titled "Validation of Product Shipments [redacted] for the US and Canada". This is the English translation of Protocol 094 693.

I reviewed the protocol and the data from the first phase and thought it was acceptable. The first phase validated the ability of a new shipping packing configuration [redacted] to maintain the internal temperature of the package to within the target range of [redacted] while maintaining the structural integrity of the packaging while in transit. The package was shipped from France to Canada.
The validation study involved [redacted] consecutive shipments and monitoring of [redacted] per shipment. Two temperature probes were placed in the shipping container, one at the top near the cold packs and one at the bottom of the shipping container. The monitors recorded the data every [redacted] The longest time period the vials were in transit was 53 hours 30 minutes and the temperature remained within specifications throughout the time period.

> **b. Please provide the protocol and data from the shipping validation study performed in support of your current procedure for shipping PRP-T vials from France to Canada.**

Sanofi stated that as of Q4 2005, the current procedure for shipping PRP-T vials from France to Canada is the procedure they validated per Protocol 094 693.

This response is acceptable

c. Please clarify which shipping procedure you will use to ship PRP- T vials from France to Canada.

Sanofi stated they will use the [redacted] shipping procedure that was validated in Protocol 094 693 to ship PRP-T vials from France to Canada.

This response is acceptable.

3. This supplement is a companion supplement for Pentacel™ BLA. Please acknowledge that this supplement cannot be approved until the companion application, currently under review is also ready for approval.

Sanofi concurred that this supplement could not be approved until the PENTACEL BLA was ready for approval.

This response is acceptable.