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Internal Memorandum

Date: February 26, 2007

From: Juan L. Arciniega, D.Sc. (HFM-443)

Subject: Review of BLA STN# 125145: "Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus used to reconstitute Haemophilus b Conjugate Vaccine Combined (Pentacel™)"

To: Theresa Finn, Ph.D. (HFM-481)
Committee Chairperson

Through: Drusilla L. Burns, Ph.D. (HFM-443)
Acting Chief, LMDQC

I have reviewed the response to our CR Letter (dated May 26, 2005), submitted on September 7, 2006. The responses of Aventis Pasteur (A-P) to my queries were all satisfactory, with the following exceptions:

Query 151:

You propose, in Section 4.14.5 of "HCPDT-IPV Specifications and Analytical Methods", to retain the [redacted] acceptance criterion for the minimal number of mice that should respond to PT and FHA in the potency test of the pertussis component of DTaP-IPV [redacted] According to your "Statistical Analysis of Responder Mice and Geometric Mean Unitage (GMU) for the Component Pertussis Mouse Immunogenicity Test for the HCPDT-IPV Vaccine (December 2004), Version Number 1.0," the proportion of responders to [redacted] of vaccine is consistently [redacted]

a. If the suitability of the [redacted] test dose is confirmed, please revise acceptance criteria for the number of responder mice to PT and FHA to accurately reflect the data.

b. If the test dose is revised, please provide data to support the proposed acceptance criteria for the number of responders to these antigens at the new test dose.

A-P acknowledge in their response to this query that the proportion of non responders to PT and FHA is higher for Pentacel™ [redacted] and that the vaccine will not have difficulties in meeting the [redacted] criterion for both antigens; however, they invoke my proposal to unify criteria for all products that share antigens manufactured by identical processes, to keep the same criterion for Pentacel™ [redacted] This justification is not adequate, because although PT and FHA manufacturing is common for all marketed combinations, concentration of these antigens in Pentacel™ is two and four times higher, respectively, than in DAPTACEL; acceptance of [redacted] may lead to a decrease in power to detect suboptimal lots.

In a submission dated December 22, 2006, A-P acknowledge a teleconference held on December 15 to discuss the issue. They have modified the criterion for responders to PT and FHA to be [redacted] This is acceptable.

Query 152:

DAPTACEL supplements 103666/5036, describing modifications to the [redacted] assays for all pertussis antigens and 103666/5041, describing modifications to the potency assay for the pertactin pertussis component, were approved on June 28, 2005. Please explain [redacted] approved for DAPTACEL testing, described in these supplements to the testing of the [redacted]

A-P have committed, in a document dated February 9, 2007, to submit [redacted]. This is acceptable.

In conclusion, I recommend the approval of STN# 125145.