Dear Dana,

We are reviewing your Biologics License Application (BLA) dated March 24, 2014, for Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine and have determined that the following information pertaining to the validation reports listed below are necessary to take complete action:

- Validation report for SWI J003829, "ELISA Method for the Detection of Human Antibodies to Pertussis Toxin (PT) Antigen". C008666, Version 4.0. June, 2006.
- Validation report for SWI J003792, "ELISA Method for the Detection of Human Antibodies to Filamentous Haemagglutinin". C008396, Version 2.0. April, 2006.
- Validation report for SWI J003847, "ELISA Method for the Detection of Human Antibodies to Fimbrial Agglutinogens (2+3) Antigen". C008395, Version 2.0. April, 2006.
- Validation report for SWI J003848, "ELISA Method for the Detection of Human Antibodies to Pertactin (b) (4) Antigen". C008392, Version 2.0. April, 2006.

1. With regard to your experiment design to evaluate intermediate precision of the component Pertussis IgG ELISAs. According to your validation reports, (b) (4) . However, you presented substantially different values of degree of freedom (DF) in the intermediate precision results for the four component Pertussis ELISAs (PT, FIM, FHA, and Pertactin). Please clarify your statistical methods for intermediate precision analysis, particularly the calculation of DF and the cause for the differences in DF. Please also provide the SAS programs and the analysis datasets.

The following comments pertain to the Proposed Lot Release Protocol Templates submitted in the Original Application (titled batch-analyses-1-6):

2. For all of the Poliovirus lot release templates (titled batch-analyses-2-6) all headers should read

   cc: BL 125525/1726-B

   Lot No.:

   Licensed Name of Product: Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus

3. On page 2 of the Final Bulk template (titled batch-analyses-1), the cover page of lot release protocol, the Product License Number is not needed in the table, it will be in the header.

4. On page 2 of the Final Bulk template, please remove the reference to the Electronic Filename until CBER has approved the use of electronic protocols for this STN.

5. On page 13 of the Final Bulk template, please add (b) (4) test date.

6. On page 17 of the Final Bulk template, in the (b) (4) template, and other (b) (4) test results, on pages 11, 25, 31, 37, 43, 48 and 51 the units should be (b) (4) since the CBER (b) (4) standard [measured in (b) (4)] is no longer available.

7. On page 17, in the (b) (4) template, please add the specification.

8. Please note that the review of this BLA is ongoing and more changes may be requested as the review progresses.

Please promptly submit your written response to the following items so that we may continue evaluating your BLA . If you have any questions, please contact me.

Thanks,

juan

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