

# Statistical Review - Rotarix

## Statistical Review

**Date:** February 28, 2008

**To:** Luba Vujcic

**From:** Lev A. Sirota

Vaccines Evaluation Branch

**Through:** A. Dale Horne

Branch Chief

**Subject:** BLA 125265/0.0 and BLA 125265/0.20 (GlaxoSmithKline Biologicals)

Human Rotavirus Vaccine Live, Oral

**c.c.** Chronological File

Laraine Henschel

A. Dale Horne

Henry Hsu

Steve Andersen

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## Executive Summary

I did not find statistical bioassay related issues that may preclude this submission from being approved by the agency.

## Background

I was asked to evaluate statistical reasoning and calculation supporting rotavirus potency test validation in BLA 125265/0.0. This review also covers supplemental BLA 125265/0.20. It contains the applicant's response to concerns CBER identified in the original BLA 125265/0.0. My comments are in italics.

Attachment 1 contains 2 pages of BLA 125265/0.20. Attachment 2 contains 7 pages of BLA 125265/0.0. Attachment 3 contains 2 pages of BLA 125265/0.20

## Results and Comments to CBER

In the **Validation of the Potency Test Protocol** section of BLA 125265/0.0 the applicant used the following definitions of Range, Limit of Detection (LOD), and Precision.

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*The definitions of the assay validation parameters are customary and appropriate with only the one following concern. The applicant used the ----- method, which is still in use although it is not recommended. CBER requested the applicant's justification for the usage of this method. The applicant provided justifications in the supplement BLA 125265/0.20. Attachment 2 to this memo contains the applicant's response. It contains complete and adequate justification for the usage of the ----- method in the current BLA.*

In the **Validation of the Potency Test Results** section of the BLA 125265/0.0 the applicant presented data on range of titration, precision, repeatability (intra-assay precision), and intermediate precision (inter-assay).

*The original BLA 125265/0.0 does not contain a substantial section on the inter-operator variability or sections addressing linearity and accuracy of the test. CBER requested the applicant to address these deficiencies. The applicant provided complete and satisfactory explanations in the supplemental BLA 125265/0.20. Attachment 3 to this memo contains analysis of total (operator and day) variability, demonstrating a low coefficient of variation. The applicant also explained their approach to linearity testing, which, I believe, is acceptable. The applicant justified the absence of the accuracy section in the following way. In the absence of an international reference, a comparative study to assess the accuracy against a reference value is not possible. The applicant's responses to CBER's question related to Validation of the Potency Test Results section are, therefore, complete, adequate, and satisfactory.*

*Data presented in the Validation of the Potency Test Results section of the BLA 125265/0.0 are satisfactory. I agree with the applicant's analysis. Sample sizes are customary and appropriate. I repeated selected calculations and did not find any errors. Attachment 2 to this review contains the applicant's data and explanations provided in the BLA 125265/0.0.*

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## **2 PAGE(S) DETERMINED TO BE NOT RELEASABLE**

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### **ATTACHMENT 2**

#### **4. VALIDATION OF ROTAVIRUS POTENCY TEST**

Potency of HRV vaccine is determined by virus titration which is conducted by end-point dilution. The potency test is applied at different stages of the HRV vaccine product and has been validated for HRV bulks as well as for HRV finished products.

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## **8 PAGE(S) DETERMINED TO BE NOT RELEASABLE**

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