

IPV Review Memo, January 11, 2010 - MenHibrix

- BLA/STN Number: BLA 125363/0
 - Sponsor: GlaxoSmithKline (GSK) Biologicals'
 - Products: MENHIBRIX (Meningococcal Groups C and Y and Haemophilus
b Tetanus Toxoid Conjugate Vaccine)
 - Purpose: Chemistry, Manufacturing, and Control

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Introduction

This Biologics License Application contains information to support the use of MenHibrix, which is a non infectious vaccine that contains *Neisseria meningitidis* serogroup C capsular polysaccharide (PSC), *Neisseria meningitidis* serogroup Y capsular polysaccharide (PSY), and *Haemophilus influenzae* type b capsular polysaccharide (polyribosyl-ribitol-phosphate, PRP), each covalently bound to tetanus toxoid. The vaccine formulation is a lyophilized product supplied in a (b)(4) monodose glass container, stoppered with rubber closures for lyophilization and closed with flipoff caps. The vaccine is to be reconstituted prior to intramuscular injection, with a liquid saline diluent supplied in ---b(4)----- containing (b)(4) of diluent. The reconstituted product contains 2.5 µg of PRP-TT, 5 µg PSC-TT and 5 µg PSY-TT per 0.5 mL dose volume.

The proposed vaccine is for active immunization of infants and toddlers 6 weeks through 15 months of age for the prevention of invasive diseases caused by *Neisseria meningitidis* serogroups C and Y and *Haemophilus influenzae* type b.

Poliovirus Vaccines used

The sponsor conducted some studies with Pediarix or Infanrix vaccines (contain the antigens D for poliovirus type 1, 2 and 3) in combination with MenHibrix, to evaluate their immunogenicity.

This review is limited to an evaluation of the sponsor's serological assays for measuring levels of anti-poliovirus 1, 2 and 3 antibodies in serum of vaccinees.

To examine the repeatability series of samples representing a range of Polio 1, 2 and 3 antibody levels were assayed (b)(4) in the same test run (table below).

To examine the Intermediate Precision (within laboratory variation) several series of assays were performed with samples representing a range of Polio 1, 2 and 3 antibody levels. The influence of the number of technicians performing the assay and the number of assays performed for the same sample were taken into account as to be representative of normal operational conditions.

The presented data were calculated for positive and negative samples, a negative titer of (b)(4) included in calculations as a value of -----(b)(4)----- . In this cell-based immunoassay, for each serum sample, the individual ratio between the maximum and minimum titers obtained for different assays/technicians were analyzed; then (table below) the value of the highest ratio (Max ratio) and the number of times the ratio was (b)(4) were recorded.

For type 1, type 2 and type 3, -----(b)(4)----- of the respective ratios were (b)(4).

Type 1

	Number of assays done for each sample	Sample assayed	Max. Ratio	# ration > 4
Repeatability Duplicate	(b)(4)	(b)(4)	(b)(4)	(b)(4)
Reproducibility --b(4)-----	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)
--b(4)-----	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)

Type 2

	Number of assays done for each sample	Sample assayed	Max. Ratio	# ration > 4
Repeatability Duplicate	(b)(4)	(b)(4)13	(b)(4)	(b)(4)
Reproducibility --b(4)----	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)
--b(4)-----	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)
	(b)(4)	(b)(4)	(b)(4)	(b)(4)

Type 3

Based on the Performance and Characteristics document provided in this submission; This -----(b)(4)----- test is adapted from World Organization Guidelines, and was shown to be reproducible and accurate when implemented in-house, Therefore, this assay is acceptable for use in support of the MenHibrix vaccine.

Questions to sponsor

None

Internal notes for discussion

1. -----(b)(4)----- test cut-off: (b)(4) for anti-polio type 1, 2 and 3
2. In clinical reports (section 5.3.5.1.3): 792014/001 (Hib-MenCY-TT-001) and 792014/002 (Hib-MenCY-TT-002), in paragraph of “criteria for evaluation”, in pages 8 and 4 respectively, the sponsor mentioned that (b)(4) was used for measurement of antibodies, if it is not a typo. The sponsor has to send to CBER the detailed description of the (b)(4)-- used for measurement of poliovirus antibodies.