



DATE: November 5, 2018

TO: File: STN # 125563/0.35

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PRODUCT: Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine
Adsorbed, Inactivated Poliovirus, Haemophilus B Conjugate
[Meningococcal Protein Conjugate] and Hepatitis B [Recombinant]
Vaccine, PR5I
(b) (4) (Vaxellis)

SUBJECT: Replacement of the (b) (4)

APPLICANT: MCM Vaccine Company

1. General Information

- **Submission Tracking Number (STN):** 125563/0
- **Submission received by CBER:** Original submission received 13 August 2014, response to Complete Response letter received 29 June 2018, amendment to replace (b) (4) received 28 June 2018.
- **Review completed:** October 24, 2018
- **Material Reviewed:** 125563/0.35
- **Related Master File, INDs and BLAs:** IND 14496/0.105, -0.113, and -0.127

2. Executive Summary

MCM proposes to replace the *in vivo* (b) (4) test with the *in vitro* (b) (4) Assay. The (b) (4) is performed to detect (b) (4) in the adjuvanted Acellular Pertussis combination vaccines possibly remaining after (b) (4) Product release testing stage and for stability monitoring.

I have extensively reviewed the (b) (4) assay under BB-IND 14496 (amendments 0.105, 0.113, & 0.127) and find that the assay has been appropriately validated to

support the intended purpose of the assay. The (b) (4) assay results together support that the (b) (4) levels in the PR5I formulation meets specification and shows no evidence of (b) (4). The results also demonstrate that the (b) (4) assay is a more robust test than the (b) (4) test for product release and stability monitoring of the PR5I formulation. The proposed acceptance criteria for the (b) (4) assay, (b) (4) for release of (b) (4), for stability monitoring of the Final Drug Product are acceptable and supported by data from assay validation, manufacturing history, and clinical experience.

3. Background

(b) (4)



(b) (4)



3 Pages Determined to be Not-Releasable: (b)(4)

(b) (4)

The proposed (b) (4) for stability monitoring of the Final Drug Product are acceptable and supported by data from assay validation, manufacturing history, and clinical experience.

5. Recommendation

The data support replacement of the (b) (4) assay for detection of (b) (4) in the adjuvanted Acellular Pertussis combination vaccines possibly remaining after (b) (4) Product release testing stage and for stability monitoring of Final Product. The proposed acceptance criteria (b) (4) for release of (b) (4) for stability monitoring of the Final Drug Product are acceptable and approximate the levels used in the (b) (4)