

From: Krissy.Carrington@sanofipasteur.com
To: [Rivers, Katie](#)
Cc: [Hoffman, Kelsy](#); [Chattopadhyay, Rana](#)
Subject: RE: Request for additional information - STN125563/0
Date: Friday, March 20, 2015 8:48:44 AM

Dear Katie

A quick note of acknowledgement of receipt for this request. Kind regards,
Krissy

From: Rivers, Katie [mailto:Katie.Rivers@fda.hhs.gov]
Sent: Friday, March 20, 2015 8:05 AM
To: Carrington, Krissy (sanofi pasteur)
Cc: Hoffman, Kelsy; Chattopadhyay, Rana
Subject: Request for additional information - STN125563/0

Dear Ms. Carrington,

We have the following request for additional information regarding STN125563/0.

Regarding tests performed on final bulks and final filled product:

1. For each release test performed on final bulk product lots and filled product lots, please provide a description of procedures for the retesting of samples (and replacement of results if applicable). Given this information should be included in the standard operating procedure (SOP) for each test, you may submit the SOPs for all tests if more convenient.
2. Please provide the calculated amount for each of the aluminum adjuvants contained in the vaccine (aluminum phosphate and amorphous aluminum hydroxyphosphate sulfate) and show how these amounts were calculated.
3. Regarding the vaccine residual components:
 - a. Please provide a brief description of the manufacturing step in which each of the following components is generated or used: yeast protein, bovine serum albumin, thiocyanate, formaldehyde, glutaraldehyde, neomycin, polymyxin B, streptomycin, and (b) (4)
 - b. For all components, except formaldehyde and (b) (4) which are tested for release of (b) (4), please provide the calculated amounts and show how these amounts were calculated.
 - c. Please provide information on any other residual components not included in the above list (comment #3a).
 - d. Please confirm that (b) (4) and polysorbate 80 (contained in Pentacel) are not used in any of the (b) (4) manufacturing processes.
4. You have not performed stability studies for the (b) (4) containers. Stability studies supporting this container closure system are required. Please provide a stability protocol for (b) (4) containers for our review.

Regarding tests for the hepatitis B surface antigen (HBsAg) component of (b) (4)

The following comments pertain to the (b) (4) tests for: a) HBsAg In Vitro Relative Potency (IVRP) assay performed on (b) (4) ; and b) (b) (4) HBsAg performed on (b) (4) and Identity of HBsAg performed on (b) (4) labeled filled product lots:

5. Please indicate who will be responsible for future qualification of reference standards (Sanofi Pasteur or Merck) for these assays.
6. If Merck will be performing the qualification of new reference standards please describe the procedures that will be performed in the Sanofi laboratories to verify the quality and suitability of the new reference standard before use in the IVRP assay and (b) (4) and Identity testing.
7. Please describe how all replacement reagents and components of the IVRP and (b) (4) Identity assays will be qualified when they reach expiry or are depleted.
8. Please provide the SOPs for the in-house In Vitro Relative Potency assay AP 56085.519 (Q_0511824) and the (b) (4) and Identity- Hepatitis B Vaccine assay AP 56085.517 (Q_0513647).
9. Please provide detailed validation of specificity testing for the IVRP assay (Section 3.2.P.5.3 Page 6 Validation Test Characteristics 2.1).
10. Please include a demonstration to confirm unequivocally that the other components present in the final product do not interfere with the performance of the HBsAg assays based upon the validation parameters of specificity, accuracy, linearity, precision, limit of quantitation, range and reproducibility.

Please let me know if you have any questions.

Thank you,
Katie

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