

From: Kristen.Mayer@sanofi.com [mailto:Kristen.Mayer@sanofi.com]
Sent: Monday, October 15, 2018 2:15 PM
To: Hoffman, Kelsy <Kelsy.Hoffman@fda.hhs.gov>
Subject: RE: BLA 125563 Information Request regarding potency testing and acceptance criteria for the IPV Component of PR5I

Hi Kelsy,

I acknowledge receipt and we will target a response by 22Oct.

Best regards.
Kristen

From: Hoffman, Kelsy [mailto:Kelsy.Hoffman@fda.hhs.gov]
Sent: Monday, October 15, 2018 1:56 PM
To: Mayer, Kristen /US <Kristen.Mayer@sanofi.com>
Subject: [EXTERNAL] RE: BLA 125563 Information Request regarding potency testing and acceptance criteria for the IPV Component of PR5I
Importance: High

Ms. Mayer,

I would like to ask that you please respond to this IR by October 22, 2018.

Kelsy F. Hoffman, Ph.D.
LCDR, USPHS
Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
U.S. Food and Drug Administration
Tel: 301-796-2640
Kelsy.Hoffman@fda.hhs.gov



THIS MESSAGE IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify the sender immediately by e-mail or phone.

From: Hoffman, Kelsy
Sent: Monday, October 15, 2018 1:14 PM
To: 'Kristen.Mayer@sanofi.com' <Kristen.Mayer@sanofi.com>

Subject: BLA 125563 Information Request regarding potency testing and acceptance criteria for the IPV Component of PR5I

Dear Ms. Mayer,

With regard to BLA 125563, we have the following request for additional information:

Comments Pertaining to Amendment 0.33 (Sequence 33 submitted on April 23, 2018)

1. With regard to the reference standard used in the rat immunogenicity test:
 - a. Based on the information provided on your investigation into the OOS result for IPV Type 2 in the rat-based stability testing of DTaP-IPV-Hib vaccine, it appears that the potency of reference lot (b) (4) is decreasing over time, resulting in the likelihood of overestimating the relative potency of vaccine lots when tested in rats. Please comment.
 - b. Please provide stability data for D-antigen content of the reference lot (b) (4)
2. With regard to the reference standards used in the D-antigen (b) (4)
 - Please provide stability data for the reference lot (b) (4) stored at the Toronto site and used to determine IPV potency in the PR5I (b) (4) product.
 - Please identify the location where lot (b) (4) was qualified (Toronto or MLE).

Comments Pertaining to Amendment 0.39 (Sequence 38 submitted on August 31, 2018)

The following comments pertain to document Q_0268418 "Design Specification for D-antigen (b) (4) Calculation Program for Polio":

3. On page 57, (b) (4). However, on page 63, (b) (4) do not appear to be (b) (4). Please comment.
4. Please confirm whether the following shown on page 64:

(b) (4)

Should instead be:

(b) (4)

(b) (4)

5. Please confirm whether the reference standard concentration corresponding to (b) (4) response shown on page 65:

(b) (4)

Should instead be:

(b) (4)

Please comment or revise the SOP as indicated in items 1 to 3 and resubmit the revised SOP to the BLA.

Comments Pertaining to Amendment 0.44 (Sequence 43 submitted on October 5, 2018)

6. We have reviewed your responses to question 1 regarding establishment of IPV potency acceptance criteria for PR5I release and stability. While we concur with your explanation for why application of correction factors obtained with vIPV is not appropriate, we do not concur that the currently proposed acceptance criteria for the minimum potency at release (b) (4) D-antigen units for poliovirus types 1, 2, and 3, respectively) provides assurance that "PR5I is as immunogenic as the currently licensed component vaccine control(s) (i.e., PENTACEL™ and RECOMBIVAX HB™ in the US, and INFANRIX™ hexa in Europe)" as stated in the BLA. One approach to setting acceptance limits for PR5I could be to make them proportionally equivalent to those for Pentacel as shown in Tables 1 and 2.

Table 1 - Pentacel and PR5I minimum D-antigen specifications (per 0.5 mL dose) for release of (b) (4)

(b) (4)

Table 2 - Pentacel and PR5I minimum D-antigen specifications (per 0.5 mL dose) for stability of final containers

(b) (4)

(b) (4)

(b) (4)

Although potency criteria should preferably be based on clinical experience with PR5I, we need to formulate an approach that is logical to assure that the potency of PR5I is equivalent to the potency of Pentacel. Therefore, we request that you revise the proposed potency lower limits for PR5I release and stability for the IPV Types 1, 2, and 3 components to reflect those of IPV in Pentacel as follows:

- (b) (4)
- For stability monitoring of PR5I Filled Containers:
(b) (4)

Please revise all affected CMC sections of the BLA and update the blank LRP.

Please let me know if you have any questions.

Thank you,

Kelsy F. Hoffman, Ph.D.
LCDR, USPHS
Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
U.S. Food and Drug Administration
Tel: 301-796-2640
Kelsy.Hoffman@fda.hhs.gov



THIS MESSAGE IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify the sender immediately by e-mail or phone.