

From: Dana.Harrison@sanofipasteur.com
To: [Hoffman, Kelsy](mailto:Hoffman_Kelsy)
Cc: [Chattopadhyay, Rana](mailto:Chattopadhyay_Rana); Krissy.Carrington@sanofipasteur.com; [Rivers, Katie](mailto:Rivers_Katie); Dana.Harrison@sanofipasteur.com
Subject: RE: BLA 125563/0 (b) (4) Information Request
Date: Friday, April 17, 2015 4:31:50 PM

Dear Kelsy,

I acknowledge receipt of this additional information request.

Kind Regards,
Dana

From: Hoffman, Kelsy [mailto:Kelsy.Hoffman@fda.hhs.gov]
Sent: Friday, April 17, 2015 3:29 PM
To: Harrison, Dana (sanofi pasteur)
Cc: Chattopadhyay, Rana; Carrington, Krissy (sanofi pasteur); Rivers, Katie
Subject: BLA 125563/0 (b) (4) Information Request

Ms. Harrison,

We remain concerned about the apparent increased frequency of mouse deaths in the (b) (4) for PR5I final drug product relative to DTaP-IPV. The cause for the increased number of mouse deaths in the (b) (4) should be further investigated to allow for a more complete characterization of the vaccine and to further ensure its safety. We note in your recent response (received April 9, 2015; Amendment 6) to CBER's Information request dated February 23, 2015 that you have initiated studies in an attempt to determine the cause for the increased number of deaths in the (b) (4). We believe the results of this investigation, as well as the additional information requested below, may be helpful in determining the root cause of the apparent increased frequency of mouse deaths in the (b) (4) for PR5I final drug product. Hence, we have the following comments regarding your proposed specification for the (b) (4) test for PR5I:

1. Preliminary data that you have provided from these investigations suggest that the matrix alone (Mock PR5I) may result in a slight increase in mouse deaths in the (b) (4) tests relative to the negative control.
 - a. In addition to the studies you described, please provide data on Mock PR5I matrix that has not been (b) (4)
 - b. Please provide the protocols used for these studies.
 - c. While we understand that these studies are ongoing and may be limited in scope and power, we recommend that the conclusions from these studies be supported by adequate statistical analyses showing significant differences. If that is not possible, please submit power calculations indicating the number of mice necessary to achieve reasonable power and discuss the feasibility of such experiments.
2. In the recent (b) (4) stability data that you provided, we note that additional OOS results were obtained on (b) (4) lots of (b) (4) (Amendment 6, Table 1). You indicated that these OOS results are currently under investigation.
 - a. Please provide the results from those OOS tests.
 - b. Please provide complete results of your investigations into the cause of the increase

in mouse deaths in these (b) (4) tests.

Please provide a timeline indicating when we can expect to receive each of the items requested above.

Thanks,

Kelsy F. Hoffman, Ph.D.
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