

RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125510/0 Office: OVRR

Product:
Influenza Vaccine, Adjuvanted

Applicant:
Novartis Vaccines and Diagnostics, Inc.

Telecon Date/Time: 22-May-2015 12:40 PM Initiated by FDA? Yes

Telephone Number: N/A – E-mail communication

Communication Category(ies):
1. Information Request

Author: Theodore Garnett

Telecon Summary:
CBER comments regarding the container closure system and the GST exemption request

FDA Participants: Theodore Garnett

Non-FDA Participants: Mayuresh Gadre

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

From: Garnett, Theodore
Sent: Friday, May 22, 2015 12:40 PM
To: 'GADRE, MAYURESH'
Subject: STN 125510/0 (FLUAD 65): Request for information
Importance: High

Dear Mayuresh,

Please find attached a new request for information from CBER. Feel free to contact me if you have any questions or concerns.

Best regards,

Ted

Theodore Garnett, Ph.D.

LCDR, U.S. Public Health Service

Microbiologist (Regulatory)

U.S. Food and Drug Administration

CBER|OVRR|DVRPA|CMC3

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U.S. Public Health Service Rapid Deployment Force PHS-2 ("*Second to None*") Admin/Finance
Section, Home Support Branch Director

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993-0002

DATE: May 22, 2015

TO: Mayuresh Gadre, M.S.

FROM: LCDR Theodore Garnett, Ph.D.
CBER/OVRR/DVRPA

SUBJECT: BLA 125510/0

PRODUCT: FLUAD 65

SPONSOR: Novartis Vaccines and Diagnostics

We are reviewing your biologics license application (BLA) dated November 25, 2014 for Influenza Vaccine, Adjuvanted and have determined that the following additional information is necessary. Please promptly submit your written response to the following items so that we may continue evaluating your BLA:

1. 3.2.P.2 Container Closure System (FLUAD, syringes):
 - a. The 3.2.P.2 Container Closure System states that the pre-filled syringes with FLUAD are closed with a grey (b) (4) . At the same time, Attachment 1 contains a summary of the report generated by Chiron (06/10/2005) that summarizes study of leachables using FLUAD-filled syringes that used plunger stoppers manufactured by (b) (4) . Please clarify the comparability of the stoppers from the two sources and the validity of the leachables testing. If you are unable to show the comparability of the stoppers and the validity of the test, please provide the protocol and report results of the study of leachables performed in syringes with the (b) (4) plunger stopper.
 - b. The summary report provided in Attachment 1 in 3.2.P.2 does not contain a description of the conditions or duration of the leachables study. Please provide this information. Please also indicate if you analyzed for more compounds than just (b) (4) .
 - c. Please clarify if an extractables study was performed using the (b) (4) 1 ml syringe, (b) (4) plunger stopper and (b) (4) tip cap that will be used for the final product presentation of FLUAD.
2. GST exemption requests will be considered on a case-by-case basis. To be consistent with regard to data requested to support an exemption from the General Safety Test, we have

determined that the following information must be submitted in order that an exemption to the GST can be considered:

- a. Explanation of why the GST is unnecessary or cannot be performed due to the mode of administration, method of preparation, or the special nature of the product.
 - b. Results from GST performed on lots of the product for which an exemption from the GST according to 21 CFR 610.11(g) (2) is requested (including lots shown to fail GST testing) adequate to demonstrate a record of compliance and to demonstrate that the product has been consistently free of extraneous toxicity. If the GST is not performed according to 21 CFR 610.11(g), the testing protocol will need to be provided and determined to be adequate.
 - c. A statement indicating the following: “All materials used in the manufacturing process of the drug substance and the final product meet pre-defined standards as documented in the in-process control and release testing in place for each product. Technicians are trained in the various manufacturing stages and all training is documented. All equipment, utilities, and facilities involved in the manufacturing process are qualified and validated as appropriate. Rigorous change control procedures for the manufacturing process are followed. Environmental monitoring is routinely performed and during specific critical activities. Validated cleaning procedures exist for all equipment that comes into contact with the product.”
3. Please revise the Package Insert according to the adjusted HAI immunogenicity data in the pivotal clinical trial V70_27 and submit to the BLA.

Please submit the requested information as an amendment to the BLA as soon as possible. We recommend that you restate each item and follow it with your response. Use of this format helps organize the relevant information and provides a self-contained document that facilitates future reference.

If you have any questions, please contact the Regulatory Project Manager, LCDR Theodore Garnett, Ph.D., at (301) 796-2640.