

## 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: 31-March-2015 3:21 PM Initiated by FDA? Yes

Telephone Number: N/A – E-mail communication

Communication Category(ies):  
1. Information Request

Author: Theodore Garnett

Telecon Summary:  
Questions regarding bioburden and endotoxin testing

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:** Tuesday, March 31, 2015 3:21 PM  
**To:** 'GADRE, MAYURESH'  
**Subject:** FLUAD 65 - New Information Request

Dear Mayuresh,

Attached is a new information request from the CBER Review Team. Please acknowledge receipt of this request and provide a response at your earliest convenience so we may continue the timely review of your submission.

Thanks,  
Ted

**Theodore Garnett, Ph.D.**

LCDR, U.S. Public Health Service

Microbiologist (Regulatory)

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**CENTER FOR BIOLOGICS EVALUATION AND RESEARCH  
OFFICE OF VACCINES RESEARCH AND REVIEW  
DIVISION OF VACCINES AND RELATED PRODUCT APPLICATIONS**

**Date:** March 31, 2015

**Pages:** 3

**To:** Mayuresh Gadre  
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**From:** Division of Vaccines and Related Products Applications  
Office of Vaccines Research and Review  
Point of Contact: LCDR Theodore Garnett, Ph.D.  
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Silver Spring, MD 2993-0002  
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**STN#:** 125510/0

**Product:** Influenza Vaccine (IV), adjuvanted

**Subject:** CBER information request regarding bioburden and endotoxin testing

Our review of your original BLA submission is ongoing. We have the following request for additional information:

Bioburden testing for (b) (4)

1. CBER finds the statistical analysis of recovery of (b) (4) on (b) (4) in report no. R/0442/08/10 unacceptable. If Novartis still wants to use only (b) (4) media for bioburden testing of (b) (4), please repeat product suitability tests for (b) (4) using (b) (4), (b) (4).
2. Please provide method suitability report for (b) (4) bioburden testing performed at the (b) (4) facility after it is received from the (b) (4) facility.

Endotoxin testing for (b) (4)

3. According to Table 3.2.S.4.1-1 (b) (4), endotoxin specification for (b) (4) reference (b) (4). Since the US reference (b) (4) is not distributed anymore and Novartis' supplement requesting the removal of the requirement for each lot of influenza vaccine to be assayed for endotoxin in comparison to a reference preparation (i.e., currently designated as (b) (4) provided by the U.S. Food and Drug Administrations for the bacterial endotoxin release test was approved by CBER on 27 January, 2014, CBER requests an appropriate endotoxin specification in (b) (4) be set for (b) (4).
4. Endotoxin test specification should be specific for each product tested and reflective of that product's production process capability. A specification of (b) (4) for drug product (DP) seems very high when your process capability has shown (b) (4) for the lots submitted under 3.2.P.5.4 Batch Analysis. CBER requests product specific specification are set, which are reflective of their process capability and provides better quality oversight of the manufacturing process.
5. Please provide the Maximum Valid Dilution for endotoxin test performed for (b) (4) DP.
6. Please provide the positive control concentration used for (b) (4) the test samples during the endotoxin test qualifications for (b) (4) DP (b) (4) report number 294342-05).

Bioburden testing for (b) (4)

Bioburden test specification should be specific for each product tested and reflective of that product's production process capability. A specification of (b) (4) seems very high when your process capability has shown (b) (4) for the process validation lots submitted under 3.2.S.4.4 Batch Analysis. CBER requests product specific specification are set, which are reflective of their process capability and provides better quality oversight of the manufacturing process.

Please submit the requested information as an amendment to the BLA. 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 LCDR Theodore Garnett, Ph.D., at 301-796-2640.