

## **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: 21-August-2015 3:04 PM   Initiated by FDA? Yes

Telephone Number: N/A – E-mail communication

Communication Category(ies):

1. Other – Late-Cycle Memo

Author: Theodore Garnett

Telecon Summary:

Late-Cycle Memo

FDA Participants: Brenda Baldwin, Theodore Garnett and Kirk Prutzman

Non-FDA Participants: Mayuresh Gadre

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

See e-mail on the next page. Late-Cycle memo attached.



**125510/0: Late Cycle Memo**

|                                 |   |
|---------------------------------|---|
| <b>To:</b>                      | The File  |
| <b>Date:</b>                    | August 21, 2015   |
| <b>Re:</b>                      | Status of Review of STN 125510/0  |
| <b>Late Cycle Meeting Date:</b> | September 3, 2015   |
| <b>Late Cycle Meeting Time:</b> | 2:30 pm – 4:00 pm (Eastern)   |
| <b>Call-in Details:</b>         | local# (b) (4) ; toll-free# (b) (4) ; Meeting ID (b) (4)  |
| <b>STN #:</b>                   | 125510/0  |
| <b>Submission Type:</b>         | BLA (Original Application)  |
| <b>Product:</b>                 | Influenza Vaccine, Adjuvanted (Fluad)   |
| <b>Indication:</b>              | <b>Fluad</b> is indicated for use in persons 65 years of age and older for active immunization against influenza disease caused by influenza virus subtypes A and B contained in the vaccine. |
| <b>Applicant:</b>               | Novartis Vaccines and Diagnostics, Inc.   |
| <b>Meeting Chair:</b>           | Brenda Baldwin, Ph.D.   |

**1. Current status of pending issues that will require resolution prior to Action Date:**

**A. Nonclinical Studies**

Based on prior communications, CBER anticipates:

- a. Novartis to submit the reproductive and developmental reproductive toxicity study AB09779 to the BLA by August 28, 2015.

**B. Facilities**

Based on prior communications, CBER is expecting:

- a. An amendment to be submitted to the BLA regarding the change of the bulk, fill and finished drug products release site from (b) (4). CBER understands that all tests and manufacturing activities will remain the same.

**C. Sample Testing and Lot Release**

Based on prior communications, CBER expects:

- a. Novartis to send all samples for in-support testing to CBER by September 2, 2015. Please contact CBER prior to shipping the samples.

**D. Analytical Procedures and Validations**

- a. In amendment 16 (received on July 17, 2015) Novartis committed to update the following SOPs: SOP 278841 (Sodium Citrate (b) (4) – incorporation of an additional standard concentration); and SOP 102843 (Squalene ID and Content in Adjuvant (b) (4) incorporation of System Suitability criteria). These updated SOPs will need to be submitted to the BLA as soon as possible.
- b. To ensure that the SRID assay can accurately measure HA content in the presence of the adjuvant in the final drug product, Novartis has agreed in amendment 15 (received on July 13, 2015) to perform the study using the correct Drug Product matrix data and in amendment 18 (received August 18, 2015) to submit the report to the BLA by the end of September. CBER

requests that the repeated SRID study report be provided to the BLA no later than September 22, 2015.

## **2. Current assessment of the need for risk management actions:**

The following actions are recommended for post-licensure safety surveillance activities:

### **A. Routine passive surveillance:**

In order to support risk management strategies and to ensure compliance with regulatory reporting requirements, routine (standard) pharmacovigilance activities will need to be performed for Flud. We require that adverse experience reports be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). Some aspects of the routine pharmacovigilance activities include: 1) routine data collection on all adverse event reports and asymptomatic maladministration spontaneously reported or actively captured in post-marketing studies; 2) global literature review, timely reports (daily, PSURs, summary for licenses renewal); 3) production and distribution reports; 4) production of IND Safety Reports, signal detection, evaluation, and management; and 5) close monitoring of the following AEs: Bell's palsy, convulsion, demyelinating disorders, encephalitis, GBS, neuritis, vasculitis, vaccination failure, ITP, haemolytic anaemia, anaphylactic reactions, extensive limb swelling, death due to all causes, medication errors, and off-label use. These pharmacovigilance activities shall be conducted at different Novartis sites and countries where Flud is licensed.

### **B. Enhanced surveillance to provide reporting of all serious and non-serious autoimmune-mediated conditions as 15-day expedited reports to the Vaccine Adverse Event Reporting System (VAERS).**

### **C. Active surveillance:**

Novartis is proposing to conduct prospective active surveillance in both Canada and Italy, or different active surveillance approach(es) pending Novartis' response to CBER's IR dated August 7, 2015. We request that you work with CBER to develop pharmacovigilance activities tailored to the regulations and guidelines of the FDA.

## **3. Information requests sent and not received:**

- A. IR dated August 5, 2015, regarding the request to update latex statement language in the labels
- B. IR dated August 7, 2015, regarding the request for a description of the alternative plans for safety surveillance
- C. IR dated August 19, 2015, regarding the imbalance seen in the number of deaths associated with Flud versus the non-adjuvanted influenza vaccines, and MF59 container questions

## **4. New information requests to be communicated:**

No new information requests are pending as of August 21, 2015. However, additional information requests may be forthcoming as review continues.

## **5. Projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates:**

- |   |                    |
|---|--------------------|
| A. PerRC Meeting to discuss PSP:                | September 30, 2015 |
| B. First Labeling Comments to Applicant:        | October 26, 2015   |
| C. Identify any need for PMC/PMR (target date): | October 26, 2015   |

**6. Status Update**

We acknowledge your request for an exemption from the General Safety Test (GST) submitted November 25, 2014. However, the final rule for revocation of the GST became effective on August 3, 2015, therefore, you are not required to conduct the GST and it is not necessary to request an exemption.

**7. Novartis Agenda Items**

CBER asked Novartis to inform CBER by September 1, 2015, regarding items that Novartis would like to include in the agenda for the Late Cycle Meeting. This will ensure that CBER has the appropriate reviewers and supervisors in attendance at the meeting. A meeting agenda will be sent to Novartis on September 2, 2015. There will be an opportunity for discussion during the meeting if further topics for discussion arise.