

**AUGUST / INTERNAL LATE-CYCLE MEETING SUMMARY**

To: The File
From: Kirk Prutzman, Ph.D., RPM
Through: Brenda Baldwin, Ph.D., Chair
Date: August 24, 2015
STN #: 125510/0
Submission Type: Original BLA
Applicant: Novartis Vaccines and Diagnostics, Inc. (NVD)
Product: Influenza Vaccine, Adjuvanted (Fluad)
Meeting Chair: Brenda Baldwin, Ph.D.

1.0 CBER/FDA INVITEES

<u>Review Assignments</u>	<u>Committee Members</u>	<u>Attendance</u>	<u>Supervisors</u>	<u>Attendance</u>
Chair	Brenda Baldwin, PhD	✓	Elizabeth Sutkowski	
RPM	Theodore Garnett, PhD	✓	Elizabeth Sutkowski	
RPM	Kirk Prutzman, PhD	✓	Elizabeth Sutkowski	
RPM	Pin Zhang, Ph.D.	✓	Elizabeth Sutkowski	
Clinical	Sarah Browne, MD	✓	Jeff Roberts	✓
Toxicology	Nabil Al-Humadi, PhD	✓	David Green	
Assays Stats	Zhong Gao, PhD	✓	Dale Horne	✓
Clinical Stats	Gideon Solomon, PhD	✓	Dale Horne	✓
CMC - Antigens	Hang Xie, PhD	✓	Zhiping Ye	✓
CMC - Adjuvant	Marina Zaitseva, PhD	✓	Hana Golding	✓
DS and DP release assays	Manju Joshi, PhD	✓	William McCormick	✓
DS and DP release assays	Lokesh Bhattacharyya, PhD		William McCormick	✓
DS and DP release assays	Alfred Del Grosso, PhD		Lokesh Bhattacharyya	
DS and DP release assays	Simleen Kaur, PhD	✓	James Kenney	
LRP and Testing Plan Development	Josephine Resnick, PhD		William McCormick	✓
Lot Release Protocol	Jacqueline Glen	✓	Joseph Quander III	
CMC, CCIT, Facilities reviewer and inspector	Peter Amin	✓	Marion Michaelis	
BIMO	Anthony Hawkins	✓	Patricia Holobaugh	
Advertising/Promotional Labeling	Sonny Saini	✓	Lisa Stockbridge	
Pharmacovigilance	Maria Said, M.D.	✓	Wei Hua	
OBE Regulatory Coordinator	Lori Austin-Hansberry, MSA, BSN		Steve Anderson	
Labeling	Daphne Stewart		Laraine Henchal	
Electronic Integrity	David Schwab, MSIS		Laraine Henchal	

Other Attendees:

Karen Campbell Laurie Norwood
 Karen Farizo Wellington Sun
 Anissa Cheung Tsai-Lien Lin

2.0 PURPOSE

1. to prepare for the September 3, 2015, Late-Cycle Communication Meeting with Novartis,
2. discuss the progress of the review,
3. identify and present substantive issues and plans to address substantive issues,
4. plan the remainder of the review including dates for further deliverables and interactions,
5. obtain supervisory feedback

3.0 BACKGROUND

US development of Influenza Vaccine, Adjuvanted (FLUAD) was conducted under IND 14368, with an initial submission to CBER on May 14, 2010. The BLA was submitted on November 25, 2014 for licensure under the Accelerated Approval pathway.

The BLA is intended to support the following indication and use: active immunization of persons 65 years of age and older against influenza disease caused by influenza virus subtypes A and B contained in the vaccine.

4.0 MEETING AGENDA

4.1 Opening remarks from the RPM

The RPM discussed the upcoming deadlines for the Late Cycle Communication meeting with Novartis scheduled for September 3, 2015. A PeRC meeting for Fluad was scheduled on September 30, 2015, and the PeRC documents needed to be finalized and sent to the committee by September 16, 2015. The RPM also updated management that there have been 2 labeling meetings and that the entire Package Insert label had been reviewed.

4.2 Status update (including any major concerns that have been identified so far) from each member of the review committee

4.2.1 Chair

The Chair discussed the items contained in the Late-Cycle Memo sent to NVD on August 21, 2015.

4.2.2 Clinical

The Clinical reviewer indicated that her review was ongoing. She was waiting for NVD to respond to an IR.

4.2.3 Clinical Stats

The Clinical Stats reviewer indicated that his review was ongoing and that there were no major issues identified that would preclude approval.

4.2.4 Assay Stats

The Assay Stats reviewer indicated that his draft review was complete and with his supervisor. There were no major issues identified that would preclude approval.

4.2.5 CMC Antigen

The CMC Antigen reviewer discussed she was almost finished reviewing the 3 manufacturing supplements submitted to the Agriflu BLA that affects the manufacturing of the Fluad Antigen. If these supplements are acceptable, there will be no major issues identified that would preclude approval.

4.2.6 CMC Adjuvant

The CMC Adjuvant reviewer indicated that her draft review was complete and with her supervisor. There were no major issues identified that would preclude approval.

4.2.7 Toxicology

The Toxicology reviewer discussed that he expected his review of STN 125510/0.19 to be completed in approximately 5 weeks.

4.2.8 Facilities

The Facilities reviewer indicated that his draft review was complete and with his supervisor. There were no major issues identified that would preclude approval.

4.2.9 BiMO

The BiMO reviewer indicated that all of the inspections were complete and no major issues were identified. Information letters were already issued to each of the inspected clinical investigators.

4.2.10 DS and DP Release Assays

4.2.10.1 DP/DS Coordinator

The DP/DS Coordinator indicated that they are reviewing the revised LRP submitted in 125510/0.18. They are still waiting for NVD to submit samples for in support testing.

4.2.10.2 Potency Testing

The Potency reviewer indicated that she is waiting for NVD to respond to her IR. Her draft review was mostly completed.

4.2.10.3 Chemistry Testing

No issues to report.

4.2.10.4 Endotoxin/Bioburden

The Endotoxin/Bioburden reviewer indicated that her review was complete and uploaded into the EDR. There were no issues identified that would preclude approval.

4.2.11 Lot Release Protocol

The Lot Release Protocol reviewer discussed that there were no major issues identified that would preclude approval.

4.2.12 Pharmacovigilance

The Pharmacovigilance reviewer indicated that the previous reviewers draft review was complete and with her supervisor. No safety signals were identified to warrant a safety PMR. However, the Pharmacovigilance reviewer was waiting for Novartis to submit their plans for

active surveillance studies in Italy and Canada, given low enrolment in the previous season. This information will be necessary to determine the need for a PMC.

4.2.13 APLB

The APLB reviewer indicated that his review was complete and uploaded into the EDR. There were no issues identified that would preclude approval.

Meeting Ended.