



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service  
Food and Drug Administration  
1401 Rockville Pike  
Rockville, MD 20852-1448

**January 18, 2012 MEETING SUMMARY**

<b>Date and Time:</b>	January 18, 2012; 9:30 – 10:00 am
<b>Location:</b>	WOC2 – Room 2201
<b>Call-In Information:</b>	<b>Toll-Free Number:</b> -----(b)(4)-----
	<b>Passcode:</b> ---(b)(4)---
<b>STN #:</b>	125408/0
<b>Supplement Type:</b>	Original BLA submission
<b>Sponsor:</b>	Novartis Vaccines and Diagnostics Inc.
<b>Product:</b>	Optaflu, Influenza Vaccine (MDCK cells)

**CBER/FDA Invitees**

**COMMITTEE MEMBERS:**

<u>Name</u>	<u>Role</u>	<u>Division</u>	<u>Attended</u>
Timothy Nelle, Ph.D.	Chair	DVRPA/OVRR	yes
Melisse Baylor, M.D.	Clinical Reviewer	DVRPA/OVRR	yes
Nabil Al-Humadi, Ph.D.	Toxicology Reviewer	DVRPA/OVRR	yes
Tammy Massie, Ph.D.	Statistical Reviewer, Clinical	DB/VEB/OBE	yes
Damon Green, M.D.	Epidemiology Reviewer	DE/OBE	no
Lihan Yan, Ph.D.	Statistical Reviewer, Bioassay	DB/VEB/OBE	yes
Rajesh Gupta, Ph.D.	CMC Reviewer, Analytical Methods	DPQ/OCBQ	yes
Karen Campbell	Lot Release	DPQ/OCBQ	yes
Zhiping Ye, Ph.D.	Product Reviewer	DVP/OVRR	yes
Haruhiko Murata	Product Reviewer	DVP/OVRR	yes
Xianghong Jing	Product Reviewer	DVP/OVRR	yes
Pankaj Amin	Facility Reviewer	DMPQ/OCBQ	yes
Ellen Huang	Facility Reviewer	DMPQ/OCBQ	yes
Anthony Hawkins	Bioresearch Monitoring Reviewer	DIS/BMB/OCBQ	no
Maryann Gallagher	Labeling Reviewer	DCM/APLB/OCBQ	yes
LT David Schwab	Electronic Integrity Reviewer	DVRPA/OVRR	no
Brenda Baldwin, Ph.D.	Regulatory Project Manager	DVRPA/OVRR	yes
Timothy Fritz, Ph.D.	Regulatory Project Manager	DVRPA/OVRR	yes
Anissa Cheung, Ph.D.	Product Specialist, Inspection	DVP/OVRR	yes

**CBER/FDA Invitees:**

Elizabeth Sutkowski, Ph.D.	Branch Chief	DVRPA/OVRR	yes
Douglas Pratt, M.D.	Supervisory Medical Officer	DVRPA/OVRR	no
Martin Green, Ph.D.	Supervisory Toxicologist	DVRPA/OVRR	no
Rakesh Pandey, Ph.D.	Branch Chief	DVRPA/OVRR	yes
Amelia Horne, Ph.D.	Supervisory Mathematician	DB/VEB/OBE	no
Tsai-Lien Lin, Ph.D.	Lead Mathematician Statistician	DB/VEB/OBE	no

William McCormick, Ph.D.	Division Director	DPQ/OCBQ	no
Jerry Weir, Ph.D.	Division Director	DVP/OVRR	no
Chiang Syin, Ph.D.	Supervisory Chemist	DMPQ/OCBQ	no
Lori Austin-Hansbury	Senior Supervisory Regulator	DE/OBE	no
Lisa Stockbridge	Supervisory Consumer Safety Officer	DCM/APLB/OCBQ	no
Patricia Holobaugh	Supervisory Consumer Safety Officer	DIS/OCBQ	no
Keith Peden, Ph.D.	Supervisory Microbiologist	DVP/OVRR	yes
Prakash Rath, Ph.D.	Commissioner Fellow	OCS/OSAI	no
Catherine Poole	Biologist	DPQ/OCBQ	yes

### 1.0 Background and Purpose of Meeting

BLA STN #125408/0, Sequence #0 was submitted by Novartis Vaccines and Diagnostics GmbH on October 31, 2011 and received by CBER on November 1, 2011. Payment was not received until November 22, 2011 and thus the review clock was reset to begin November 22, 2011.

The proposed indication is for active immunization of persons 18 years of age and older for the prevention of influenza disease caused by influenza virus subtypes A and B contained in the vaccine.

The purpose of this meeting was to discuss any deficiencies that have been encountered and to update management on the review progress.

### 2.0 Outstanding Issues:

#### 2.1 Review Status Update

- Additional proprietary name review (PNR) for "Optaflu" is needed, sponsor has been asked to submit a new PNR request.
- Novartis has been asked to submit the results (as an amendment) from the suitability study regarding usage of egg-based reagents for SRID testing of the MDCK cell-produced Optaflu.
- Inspection of the --(b)(4)--- site will be waived. Waiver is in preparation and will be submitted soon. The Holly Springs, NC site is still in discussion. The Marburg, Germany site inspection is scheduled for the week of March 19, 2012
- BiMo inspection will not be performed since the pivotal efficacy trial site was already inspected during the Agriflu BLA efficacy trial supplement review (STN 125297/1).
- PeRC presentation is scheduled for June 27, 2012

### 3.0 Review Updates:

#### 3.1 Clinical

Melisse Baylor – Deficiencies in gender comparisons; and information on diary card verbal recall needs to be discussed with Novartis

#### 3.2 Statistical

**3.2.1 Clinical** Tammy Massie – no deficiencies  
**3.2.2 Bioassay** Lihan Yan – no deficiencies

### **3.3 Product**

**3.3.1 CMC – MDCK cell substrate** Haru Murata - no deficiencies  
identified yet from review of summary sections

**3.3.2 CMC – Flu vaccine** Zhiping Ye – no major review issues  
identified yet, but samples for confirmatory testing will  
need to be requested in the near future. Also, it appears that  
the sponsor did not provide the release specifications for  
the final bulk or final container.

**3.3.3 CMC – Analytical Methods** Rajesh Gupta – lot release protocol  
has not been found in BLA submission. Novartis will also  
need to submit the sample lots.

**3.4 Toxicology** Nabil Al-Humadi – raised a concern that BPL was listed as  
an impurity. After further discussion during the meeting, it  
was concluded that this was not a major concern since BPL  
is very labile and widely used in vaccine manufacturing.  
However, its presence in the final product should be below  
the limits of detection.

**3.5 Epidemiology** Damon Green – no issues identified

**3.6 Facilities** Pete Amin – no issues identified. Marburg inspection set for week  
of March 19<sup>th</sup>. Still thinking about whether to inspect Holly Springs since  
it will ultimately need an inspection once manufacturing is transferred to it  
from Marburg (post-licensure). If the decision is made to proceed with the  
inspection, it would most likely also occur in March.

## **4.0 Schedule**

### **4.1 Milestones (Updated, milestones in gray have been completed)**

Submitted: October 31, 2011

BLA Received: November 1, 2011; Fee Received November 22, 2011

Committee Assignment: November 15, 2011

First Committee Meeting: November 21, 2011

Filing Meeting: December 12, 2011

Filing Action: January 21, 2012 (sent January 12, 2012)

VRBPAC Determination: January 21, 2012

PeRC Determination: January 21, 2012

**Deficiencies Identified: February 4, 2012**

**First Draft Reviews Due: February 20, 2012 (March 21 for Stats and PhV)**

SWG Determination: April 20, 2012

Second Draft Reviews Due: May 15, 2012 (May 30 for Stats and PhV)

Final Reviews Due: July 14, 2012

Action Due: September 21, 2012

Action Package for Posting Due: September 21, 2012

**4.2 Meetings (meetings in gray have been completed)**

First Committee Meeting (via e-mail): November 16, 2011

Filing Meeting: December 12, 2011

Monthly Team Meetings:	January 18, 2012	February 29, 2012
	May 7, 2012	June 11, 2012
	July 9, 2012	August 6, 2012

Mid-Cycle Review Meeting: April 9, 2012

PeRC: June 27, 2012

VRBPAC Planning: No longer needed

Safety Working Group (SWG): TBD

Labeling Meetings: TBD

**4.3 Summary of Additional Action Items**

- **Prelicensure Facility Inspection (or waiver)** December 13, 2011
- **Schedule Facility Inspection (Marburg)** January 22, 2012
- **Determine Consistency/Launch Lots** February 20, 2012
- Facility Inspection Complete April 22, 2012
- BIMO Inspections Complete Not needed
- PMC to FDAAA SWG August 4, 2012
- Labeling Target September 3, 2012

**5.0 CONCLUSION**

1. Deficiency comments will need to be sent to the Chair and RPMs by noon Wednesday January 25, 2012 so that they may be incorporated into a deficiency letter to be sent to Novartis no later than February 4, 2012.
2. The Influenza seasonal strain change and pandemic licensing pathway VRBPAC is scheduled for February 28<sup>th</sup> and 29<sup>th</sup>. The committee was asked if they wanted the next monthly meeting scheduled for February 29<sup>th</sup> to be moved or to be performed via e-mail. The committee agreed to conduct the next meeting via e-mail.
3. Facilities reviewers will be able to provide either the waiver or the scheduled time for the Holly Springs, NC facility by January 27, 2012.