



DEPARTMENT OF HEALTH & HUMAN SERVICES

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

February 29, 2012 MEETING Summary

Date and Time:	February 29, 2012
Location:	E-mail
STN #:	125408/0
Supplement Type:	Original BLA submission
Sponsor:	Novartis Vaccines and Diagnostics Inc.
Product:	Optaflu, Influenza Vaccine (MDCK cells)

CBER/FDA Invitees

COMMITTEE MEMBERS:

<u>Name</u>	<u>Role</u>	<u>Division</u>	<u>Responded</u>
Timothy Nelle, Ph.D.	Chair	DVRPA/OVRR	yes
Melisse Baylor, M.D.	Clinical Reviewer	DVRPA/OVRR	no
Nabil Al-Humadi, Ph.D.	Toxicology Reviewer	DVRPA/OVRR	yes
Tammy Massie, Ph.D.	Statistical Reviewer, Clinical	DB/VEB/OBE	no
Alan Ou, M.D., MPH	Epidemiology Reviewer	DE/OBE	yes
Lihan Yan, Ph.D.	Statistical Reviewer, Bioassay	DB/VEB/OBE	yes
Rajesh Gupta, Ph.D.	CMC Reviewer, Analytical Methods	DPQ/OCBQ	no
Karen Campbell	Lot Release	DPQ/OCBQ	yes
Zhiping Ye, Ph.D.	Product Reviewer	DVP/OVRR	no
Haruhiko Murata	Product Reviewer	DVP/OVRR	no
Xianghong Jing	Product Reviewer	DVP/OVRR	no
Pankaj Amin	Facility Reviewer	DMPQ/OCBQ	yes
Ellen Huang	Facility Reviewer	DMPQ/OCBQ	yes
Anthony Hawkins	Bioresearch Monitoring Reviewer	DIS/BMB/OCBQ	yes
Maryann Gallagher	Labeling Reviewer	DCM/APLB/OCBQ	no
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	no

CBER/FDA Invitees:

Elizabeth Sutkowski, Ph.D.	Branch Chief	DVRPA/OVRR	no
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	no
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	no
Prakash Rath, Ph.D.	Commissioner Fellow	OCS/OSAI	no
Catherine Poole	Biologist	DPQ/OCBQ	no

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 is to convey any issues and to update management and others on the review team the progress that has been made.

2.0 Outstanding Issues:

2.1 CBER Requests for Information:

- Additional proprietary name review (PNR) for “Optaflu” requested on 12-15-11, sponsor has not submitted a response.
- Novartis was asked to submit on 12-23-11 the results from the suitability study regarding usage of egg-based reagents for SRID testing of the MDCK cell-produced Optaflu, sponsor has not submitted a response.
- Requested facilities information for ---(b)(4)--- and Holly Springs, NC sites on 1-19-12, response received 2-13-12 (Amendment 2).
- Requested samples for in-support testing on 1-30-12, sponsor stated that samples are ready to ship but seeks additional guidance in March 7, 2012, scheduled telecon.
- Requested additional information on the GCP violation (at 1 of the 2 sites) in the Optaflu lot consistency trial on 1-26-12. Novartis stated that sensitivity analysis would be submitted by mid-February, sponsor also has not submitted.
- OCBQ requested information on the columns used in the manufacturing process on 2-15-12, response received 2-28-12 (Amendment 3).
- Novartis stated that they would submit the lot release protocol template by February 29th (draft was submitted by e-mail on 2-29-12 to DPQ)

3.0 Review Updates: Drafts received by Rajesh Gupta (2-17-12), Karen Campbell (2-17-12), Xianghong Jing (2-14-12), Anthony Hawkins (2-17-12), Haruhiko Murata (2-16-12), Nabil Al-Humadi (2-16-12), Lihan Yan (2-1-12). Still need

draft review from Melisse Baylor. Tammy Massie and Alan Ou draft reviews due 3-21-12.

3.1 Clinical Melisse Baylor – no comment

3.2 Statistical

3.2.1 Clinical Tammy Massie – no comment

3.2.2 Bioassay Lihan Yan – possible concerns with HI assay validation.
Discussion ongoing.

3.3 Product

3.3.1 CMC – MDCK cell substrate Haru Murata – no comment

3.3.2 CMC – Flu vaccine Xianghong Jing, Zhiping Ye – no
comment

3.3.3 CMC – Analytical Methods Rajesh Gupta – no comment

3.4 Toxicology Nabil Al-Humadi – review completed – a few questions
need to be conveyed to the sponsor

3.5 Epidemiology Alan Ou – no comment

3.6 Facilities Pankaj Amin, Ellen Huang – inspection set for week of March 19th
for Marburg; inspection for Holly Springs set for week of April 16th

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, Holly Springs) 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. A teleconference is scheduled for March 7, 2012 so that Novartis may discuss with DPQ:
 - Novartis status on SRD Tests – CBER reagents qualification and validation
 - Timing for qualification of egg based reagents and standards for cell based vaccine
 - Comments and approval of protocol for validation of SRD Method for ----(b)(4)----- (attached word document-“Verification Protocol for the Determination of Hemagglutinin Content by SRD (USA), for Testing FCC Optaflu Trivalent Vaccine. SOP Protocol Number: 288924)
 - Samples of OPTAFLU to be submitted to CBER for testing
 - They do not have formulated trivalent bulk however they have 1 ml Pre Filled Syringe. They can either submit 20 syringes of each trivalent formulated bulk or dispense a quantity of 20 ml from the syringes and submit to CBER.
 - For the A/Victoria strain they do not have adequate samples from 2 PV lots. They intend to submit 2 lots that were manufactured for cleaning validation studies.
 - The manufactured lots expire from Feb-April 2012 i.e. are close to expiration. Is CBER ok with this?