



DEPARTMENT OF HEALTH & HUMAN SERVICES

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

January 18, 2012 MEETING SUMMARY

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| Date and Time: | January 18, 2012; 9:30 – 10:00 am |
| Location: | WOC2 – Room 2201 |
| Call-In Information: | Toll-Free Number: -----(b)(4)----- |
| | Passcode: ---(b)(4)--- |
| 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>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:

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|----------------------------|---------------------------------|------------|-----|
| 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 |

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|--------------------------|-------------------------------------|---------------|-----|
| 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 19th. 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

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|------------------------|------------------|-------------------|
| 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 28th and 29th. The committee was asked if they wanted the next monthly meeting scheduled for February 29th 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.