



**MID-CYCLE MEETING SUMMARY**

To:	The File
From:	Ramachandra S. Naik, Ph.D., RPM
Through:	Margaret Bash, M.D., M.P.H., Chair
Meeting Date:	November 7, 2014
STN #:	125546/0
Submission Type:	Original BLA
Applicant:	Novartis Vaccines and Diagnostics, Inc.
Product:	Bexsero, Meningococcal Group B Vaccine
Meeting Chair:	Margaret Bash
Meeting Recorders:	Edward Wolfgang, Kirk Prutzman and Ramachandra Naik

## CBER/FDA INVITEES

<b>Review Assignment</b>	<b>Committee Members</b>	<b>Present</b>	<b>Supervisors</b>	<b>Present</b>
Chair	Margaret Bash, MD, MPH	✓	Willie Vann, PhD	✓
Lead RPM	Edward Wolfgang, MSA	✓	Elizabeth Sutkowski, PhD	✓
Co-RPM	Kirk Prutzman, PhD	✓	Elizabeth Sutkowski, PhD	✓
Co-RPM	Ramachandra S. Naik, PhD	✓	Elizabeth Sutkowski, PhD	✓
Clinical	Anuja Rastogi, MD	✓	Jeff Roberts, MD	✓
Clinical, Consult reviewer	Douglas Pratt, MD		Wellington Sun, MD	✓
DBPAP Regulatory Coordinator	Tina Roecklein, MS	✓	Jay Slater, MD	✓
Bioassay (Clinical and product <sup>1</sup> )	Freyja Lynn, BS	✓	Jay Slater, MD	✓
Product test methodologies, CMC <sup>2</sup>	John Cipollo, PhD	✓	Willie Vann, PhD	✓
Product (CMC), Consult reviewer	Willie Vann, PhD	✓	Jay Slater, MD	✓
Coordination of lot release and Regulatory Coordinator – DBSQC	Karen Campbell, MS	✓	William McCormick, PhD	✓
Product test methodologies <sup>3</sup>	Anil Choudhary, PhD	✓	William McCormick, PhD	✓
Product test methodologies <sup>4</sup>	Noel Baichoo, PhD	✓	William McCormick, PhD	✓
Product test methodologies <sup>5</sup>	James Kenney, PhD		William McCormick, PhD	✓
Product test methodologies <sup>6</sup>	Hsiaoling Wang, PhD		Lokesh Bhattacharyya, PhD	
Product test methodologies <sup>7</sup>	Tao Pan, PhD	✓	Lokesh Bhattacharyya, Ph.D	
Coordination of lot release - DMPQ	Cheryl Hulme, MLT, ASCP		Joseph Quander III	
DMPQ RPM	Leigh Bernardino, RN, BSN	✓	James Crim, BS	
Statistical (Clinical-immunogenicity data)	Barbara Krasnicka, PhD	✓	Dale Horne, DrPH	✓
Statistical (Clinical-safety data)	Tammy Massie, PhD	✓	Dale Horne, DrPH	✓
Statistical (Serology assays)	Zhong Gao, PhD	✓	Dale Horne, DrPH	✓
Statistical (CMC, potency assays)	Tsai-Lien Lin, PhD	✓	Dale Horne, DrPH	✓
Non-Clinical Toxicology	Ching-Long (Joe) Sun, PhD	✓	David Green, PhD	
CMC, CCIT, Facilities reviewer and inspector	Donald Ertel, MT(ASCP), CQA(ASQ)	✓	Carolyn Renshaw, BS	✓
Epidemiology/Pharmacovigilance	Jane Baumblatt, MD	✓	Wei Hua, MD, PhD, MS, MHS	✓
Bioresearch Monitoring (BiMO)	Carla Jordan, BS, MT(ASCP), SBB	✓	Patricia Holobaugh, MS	✓
Advertising/Promotional Labeling	Michael Brony, PharmD		Lisa Stockbridge, PhD	✓
Labeling	Daphne Stewart		Laraine Henschal, MS	
Electronic Integrity	David Schwab, MSIS		Laraine Henschal, MS	

- 1 = Primary reviewer: Clinical serology and product potency assays (DP)  
2 = Primary reviewer: -----(b)(4)----- (DP), Purity -----(b)(4)----- (DS), Identity ----(b)(4)-- (DS), --(b)(4)-- (DS), --(b)(4)-- (DS), Extractables and Leachables  
3 = Primary reviewer: Identity (DP), --(b)(4)-- (DS)  
4 = Supporting reviewer: Purity by -----(b)(4)-----  
5 = Primary reviewer: Sterility and/or Bioburden (b)(4) DP), Endotoxin (b)(4) DP), other related pyrogenicity issues – RPT/MAT  
6 = Primary reviewer: -----(b)(4)-----; Appearance, pH, Deoxycholate and Sucrose (b)(4)  
7 = Primary reviewer: -----(b)(4)----- (DP); ---(b)(4)--- and pH (DP, -----(b)(4)-----

### Other Attendees:

Drusilla Burns	Laurie Norwood	Lihan Yan
Mark Schwartz	Oluchi Elekwachi (APLB)	Karen Farizo

## **1.0 BACKGROUND AND PURPOSE**

Following a pre-BLA meeting under IND (b)(4) (held on May 27, 2014), BLA STN 125546/0 was submitted by Novartis Vaccines and Diagnostics, Inc., as a rolling submission in three installments. The first rolling piece was received by CBER on June 16, 2014, and contained mainly summaries, nonclinical information and reports of the pivotal studies V72P10, V72P10E1, V72\_41, V72\_29 and V102\_03 and the two supportive studies V72P4 and V72P5. The second installment of the rolling BLA was received on July 10, 2014, and contained CMC information. The third and final rolling piece, which initiated the review clock, was received on July 24, 2014, and included the clinical overview, the Integrated Summaries of Safety and Efficacy, and datasets/programs for the clinical studies V72P13 and V72P16.

The BLA is intended to support the following indication and use: Active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B in individuals 10 through 25 years of age.

The purpose of this meeting is to discuss the progress of the review, identify and present any remaining issues, plan the remainder of the review including dates for further deliverables and interactions and obtain supervisory feedback, and agree upon the CBER comments/issues to be communicated in the Mid-Cycle Communication, etc.

## **2.0 MEETING AGENDA**

- Opening remarks from the Chair and Lead RPM
- Review of PDUFA V milestones and internal/projected target dates
- Status of IR comments sent to the sponsor and review of amendments received
- Reviewer updates on primary review status
- Other discussion items
- Action items

## **3.0 DISCUSSION**

### **3.1 Chair and Lead Regulator Project Manager updates**

Lead RPM informed the team of the review timetable and important deadlines.

The Chair reminded the review committee of the following deadlines regarding review memos:

- Draft review memo due to supervisor on November 21, 2014 (copy to Chair and Lead RPM)
- Signed reviews to Chair, on December 18, 2014
- Finalized review, signed by supervisor, uploaded to EDR, on December 24, 2014

The Chair also asked the review team to provide an update on whether they will have any additional comments/issues to be communicated with Novartis.

### **3.2. Reviewer updates on primary review assignments**

Each reviewer gave a very brief update on the status of their review of the BLA. No major issues were reported or discussed. Some reviewers (Product, Testing, Clinical and Statistical) stated that they are waiting for Novartis to respond to their IRs to complete their reviews. A limited number of reviewers [Bioassay (Product), Statistical (CMC, potency assays) and Testing]

indicated that they will have additional (follow-on) IRs to be sent to the firm very soon. All reviewers indicated that they were on track to finish their review by the prescribed deadlines.

#### **4.0 ACTION ITEMS**

- Prepare Mid-Cycle communication document for teleconference with Novartis.

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