

# Bioresearch Monitoring Final Review Memo, November 20, 2014 - BEXSERO

MEMORANDUM  
DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Food and Drug Administration  
Center for Biologics Evaluation and Research

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DATE November 20, 2014

FROM

Carla Jordan, Bioresearch Monitoring  
Division of Inspections and Surveillance  
Office of Compliance and Biologics Quality

THROUGH

Patricia Holobaugh, Bioresearch Monitoring Branch Chief  
Gilliam B. Conley, Director, OCBQ, Division of Inspections and Surveillance

TO

Margaret Bash, Chair, BLA Committee  
Edward Wolfgang, Regulatory Project Manager  
Kirk Prutzman, Regulatory Project Manager  
Ramachandra Naik, Regulatory Project Manager

SUBJECT

Bioresearch Monitoring Final Review Memo

STN: 125546/0

Product: Bexsero, Meningococcal Group B Vaccine

Sponsor: Novartis Vaccines and Diagnostics S.r.l.

## **SUMMARY STATEMENT**

CBER Bioresearch Monitoring (BIMO) issued six high-priority foreign inspections for three pivotal trials in support of this Biologics Licensing Application (BLA). The inspections of one study, V72P10, contributed to the Agency requesting that the Sponsor revise its reactogenicity rates. The inspections for two other pivotal studies, V72\_29 and V72\_41, did not reveal significant problems that impacted the data submitted in this marketing application.

## **BACKGROUND**

The BIMO member of the review committee proposed clinical sites to be inspected for each of three studies identified as the pivotal studies for this application. The clinical sites inspected for each study were selected based on the number of subjects who enrolled, previous inspectional history, number and types of adverse events, number and types of protocol deviations, and geographic location. The review committee concurred with the proposed sites.

The inspections were conducted in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators. The inspections also focused on specific questions concerning the study protocol and the comparison of data submitted in the BLA to source documents. The investigations of each study are described in more detail below. (KEY: NAI-no action indicated, VAI-voluntary action indicated)

### **STUDY V72P10**

*A Phase 2b/3, Multi-Center, Observer-Blind, Controlled Study of the Safety, Tolerability, and Immunogenicity of Novartis Meningococcal B Recombinant Vaccine Administered to Healthy Adolescents Aged 11-17 Years According to Different Vaccination Schedules*  
Three of the ten sites were selected for inspection. These three sites represented 30% of the subjects enrolled in this study. The two investigators who ran these three sites were responsible for 80% of the enrolled subjects at multiple sites across Santiago, Chile.

<b>Site Number</b>	<b>Study Site</b>	<b># Subjects</b>	<b>FDA Form 483</b>	<b>Final Classification</b>
11	Complejo Educacional Eduardo Cuevas Valdes, Santiago de Chile	182	No	NAI
14	Colegio Parroquial Santa Rosa de Lo Barnechea, Santiago de Chile	132	Yes	VAI
41	Colegio Antonio Hermida Fabres, Santiago de Chile	181	No	NAI

### **STUDY V72\_29**

*A Phase 3 Observer blind Randomized, Multicenter, Controlled study to evaluate the effect of Novartis Vaccine's Meningococcal B recombinant and MenACWY Conjugate vaccines on Pharyngeal Carriage of N. meningitides in Young Adults*  
One of the 10 sites was selected for inspection. This site represented 27% of the subjects enrolled in this study.

<b>Site Number</b>	<b>Study Site</b>	<b># Subjects</b>	<b>FDA Form 483</b>	<b>Final Classification</b>
01	National Institute for Health Research Sheffield, South Yorkshire, United	822	Yes	VAI

Site Number	Study Site	# Subjects	FDA Form 483	Final Classification
	Kingdom			

### STUDY V72\_41

*A Phase 3, Randomized, Comparative, Multicenter Observer-Blind, Study Evaluating the Safety and Immunogenicity of Novartis rMenB+OMV NZ Vaccine Formulated with OMV Manufactured at Two Different Sites, in Healthy Adolescents Aged 11-17 Years*  
Two of 12 sites were selected for inspection. These two sites represented 41% of the subjects enrolled in this study.

Site Number	Study Site	# Subjects	FDA Form 483	Final Classification
51	Medicor Research, Inc. Sudbury, Ontario, Canada	90	No	NAI
52	TASC Research Services Surrey, British Columbia, Canada	51	No	NAI

### FINANCIAL DISCLOSURE

The Clinical Investigator Compliance Program directs the FDA investigator to ask the clinical investigator if and when he/she disclosed information about his/her financial interests to the sponsor and also the interests of any sub-investigators, spouse(s) and dependent children, and if and when the information was updated. The information submitted to the BLA was verified for the personnel at each of the inspected clinical sites.

### SPONSOR ISSUES

None noted.

### NOTEWORTHY INSPECTIONAL FINDINGS

During the inspections for V72P10, it was revealed that some clinical safety data that appeared to be missing was documented elsewhere because it was not in the format required for the diary cards that were issued to the subjects. It was also noted that some subjects withdrew due to adverse events; however the reasons for any withdrawals were documented only in the source documents. These inspection findings contributed to the Agency requesting that the Sponsor revise its reactogenicity rates.

### BIMO ADMINISTRATIVE FOLLOW-UP

BIMO issued letters to four of the five clinical investigators. Sites 11 and 14 were both administered by the same clinical investigator. There was no contact information available for the clinical investigator at TASC Research Services because the facility is out of business.

Please contact me at (240) 402-8975 if you have any questions about this memo or any aspect of bioresearch monitoring.

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Carla V. Jordan  
Consumer Safety Officer