



DATE: August 15, 2019

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THROUGH: Dennis Cato, Branch Chief, Bioresearch Monitoring Branch

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TO: Bharat Khurana, DVM, PhD, MBA, Chair  
Sixun Yang, MD, Clinical Reviewer  
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Josephine Resnick, PhD, RPM

SUBJECT: Amended Bioresearch Monitoring Final Review Memo  
SPONSOR: Bavarian Nordic A/S  
PRODUCT: Smallpox (Modified Vaccinia Ankara) Vaccine, Live, Non-Replicating  
BLA: STN 125678/0

#### FINAL SUMMARY STATEMENT

Bioresearch Monitoring (BIMO) inspections were conducted at five clinical study sites that participated in the conduct of either Study POX-MVA-006 or Study POX-MVA-013. The inspections did not reveal substantive issues that impact the data submitted in this original Biologics License Application (BLA).

#### BACKGROUND

Five BIMO clinical investigator inspection assignments were issued for two protocols in support of this original BLA.

Protocol POX-MVA-006, “*A Randomized, Open-Label Phase III Non-Inferiority Trial to Compare Indicators of Efficacy for MVA-BN Smallpox Vaccine to ACAM2000® in 18-42 Year Old Healthy Vaccinia-Naïve Subjects*,” enrolled 440 study subjects who were eligible for the study. The clinical study was conducted at two study sites in South Korea. Both study sites were overseen by one clinical investigator. The inspection represented 100% of the enrolled study subjects.

Protocol POX-MVA-013, “*A Randomized, Double-Blind, Placebo-Controlled Phase III Trial to Evaluate Immunogenicity and Safety of Three Consecutive Production Lots of IMVAMUNE® (MVA-BN®) Smallpox Vaccine in Healthy, Vaccinia-Naïve Subjects*,” was a multicenter study conducted at a total of 34 clinical study sites in the United States. A total of 4005 subjects was randomized to receive at least one dose of the investigational vaccine. The four (4) domestic sites selected for inspection represented approximately 19% (771) of the subjects. The clinical sites selected for Protocol POX-MVA-013 were based on subject enrollment, previous inspectional history, adverse events, protocol deviations and other info submitted in the BLA.

The inspections were conducted in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators, and the inspection assignment included specific questions concerning the clinical study. Information submitted in the BLA was compared to source documents at each selected study site.

### BIMO INSPECTIONS

- INSPECTIONAL FINDINGS:**

No significant inspectional findings that impact the submitted data were identified.

The table below summarizes the site information and the outcome of the BIMO inspections:

Protocol	Site ID	Inspected Study Site Name and Location	Final Classification
POX-MVA-006	N/A	USAMRIID Fort Detrick, Maryland	NAI
POX-MVA-013	111	Lynn Health Science Institute Oklahoma City, Oklahoma	NAI
	125	Alabama Vaccine Research Clinic South Birmingham, Alabama	NAI
	134	Rapid Medical Research, Inc. Cleveland, Ohio	NAI
	137	Clinical Research Associates of Tidewater, Norfolk, Virginia	NAI

LEGEND: NAI = NO ACTION INDICATED

- SPONSOR/MONITORING ISSUES:**

No sponsor or monitoring issues were identified during the clinical study site inspections.

- 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/or 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 each of the inspected clinical sites.

### ADMINISTRATIVE FOLLOW-UP

Information letters were issued to the clinical investigators at all inspected study sites. Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at 240-402-8038.

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Haecin Chun  
Consumer Safety Officer

## **Distribution**

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EDR BLA 125678/0

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### History:

Draft: Chun: 7/24/19

Review: Cato: 8/6/2019

Amended: Chun: 8/15/2019 [Removed "Issued 483" column from the table describing the outcome of the BIMO inspections]