



Our STN:125678/0

**LATE-CYCLE  
MEETING MEMORANDUM**  
August 19, 2019

Bavarian Nordic A/S  
Attention: Dr. Renee Boerner  
3025 Carrington Mill Boulevard,  
Morrisville, NC 27650

Dear Dr. Boerner,

Attached is a copy of the memorandum summarizing your July 23, 2019, Late-Cycle teleconference with CBER. This memorandum constitutes the official record of the teleconference. If your understanding of the teleconference outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER in writing as soon as possible.

Please include a reference to STN125678/0 in future submissions related to JYNNEOS.

If you have any questions, please contact Sudhakar Agnihothram, Ph.D. and Josephine Resnick, Ph.D., at 301-796-2640.

Sincerely,

Loris D.  
Mcvittie-S

Digitally signed by Loris D. Mcvittie -S  
DN: c=US, o=U.S. Government, ou=HHS  
ou=FDA, ou=People  
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cn=Loris D. Mcvittie -S  
Date: 2019.08.19 15:30:27 -0400

Loris McVittie, Ph.D.  
Deputy Director (Regulatory)  
Division of Vaccines and Related Products  
Applications  
Office of Vaccines Research and Review  
Center for Biologics Evaluation and Research

### **Late-Cycle Meeting Summary**

**Meeting Date and Time:** July 23, 2019, 10:30 AM - 12:00 PM

**Application Number:** BLA STN 125678/0

**Product Name:** Smallpox (Modified Vaccinia Ankara) Vaccine, Live, Non-replicating

**Proposed Indications:** For prevention of smallpox or monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection

**Applicant Name:** Bavarian Nordic A/S

**Meeting Chair:** Bharat Khurana, DVM, Ph.D, MBA

**Meeting Recordors:** Sudhakar Agnihothram, Ph.D.  
Josephine Resnick, Ph.D.

### **FDA ATTENDEES**

Bharat Khurana, DVM, Ph.D, MBA	OVRP/DVRPA
Sudhakar Agnihothram, Ph.D.	OVRP/DVRPA
Josephine Resnick, Ph.D.	OVRP/DVRPA
Sixun Yang, MD, Ph.D.	OVRP/DVRPA
Sheral Patel, MD	OVRP/DVRPA
Alexandra Yonts, MD	OVRP/DVRPA
Meghan Ferris, MD	OVRP/DVRPA
Afolabi Meseda, Ph.D.	OVRP/DVP
Nabil Al-Humadi, Ph.D.	OVRP/DVRPA
Alonzo Garcia, Ph.D.	OVRP/DVP
Pankaj Amin	OCBQ/DMPQ
Oluchi Elekwachi, PharmD, MPH	OCBQ/APLB
Haecin Chun, MS	OCBQ/BIMO
Salil Ghosh, Ph.D.	OCBQ/DBSQC
Most Nahid Parvin, Ph.D.	OCBQ/DBSQC
Anissa Cheung	OVRP/DVP
Ruoxuan Xiang, Ph.D.	OBE/DB
Lei Huang, Ph.D.	OBE/DB
Kerry Welsh, MD, Ph.D.	OBE/DE
Timothy Fritz, Ph.D.	OVRP/DVRPA
Tsai-Lien, Lin, Ph.D.	OVRP/DVRPA
Keith Peden, Ph.D.	OVRP/DVP
Manette Niu, MD	OB/DE
Loris McVittie, Ph.D.	OVRP/DVRPA
Doran Fink, MD, Ph.D.	OVRP/DVRPA
Carmen Collazo, Ph.D.	OVRP/DVRPA
Sarah Browne, MD	OVRP/DVRPA
Carrie Mampilly	OCBQ/DBSQC
Jerry Weir, Ph.D.	OVRP/DVP
Marion Gruber, Ph.D.	OVRP IOD

David Rouse, Ph.D.  
Craig Zindermann, Ph.D.  
Joseph Kulinski Ph.D.  
John Trefry, Ph.D.

CBER OD  
OBE/DE  
OVRD/DVRPA  
OVRD/DVRPA

### **APPLICANT ATTENDEES**

Heinz Weidenthaler	VP, Clinical Strategy Infectious Diseases
Cindy Handelsman	VP, Clinical Operations
Jane MacLennan	Clinical Program Lead, Manager Clinical Operations
Sanja Vidojkovic	Pharmacovigilance Officer
Teresa Perschy	Senior Clinical Project Leader, Clinical Operations
(b) (4), (b) (6)	
Liddy Chen	VP, Biometrics and Head of Biostatistics
(b) (4), (b) (6)	
Erika Menius	Senior Manager, Biostatistics
Niels Wulff	Manager, Bioanalysis
Darja Schmidt	Senior Manager, Quality Control
Thomas Meyer	Manager Scientific Quality Control, Clinical Development
Ariane Volkmann	Senior Director, Early Development
Kathrin Endt	Senior Scientist, Early Development
Barbara Petzold	Senior Director, Regulatory Affairs
Renee Boerner	Senior Director, Regulatory Affairs
Andrea Knappe	Senior Manager, Regulatory Affairs
Britt Christensen	Senior VP, Quality

### **BACKGROUND**

BLA STN 125678/0 was submitted on October 25, 2018 by Bavarian Nordic A/S for Smallpox (Modified Vaccinia Ankara) Vaccine, Live, Non-replicating (JYNNEOS)

Proposed indication(s): For prevention of smallpox or monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection

PDUFA goal date: September 24, 2019

In preparation for this meeting, FDA issued the Late-Cycle Meeting Materials on July 18, 2019.

## **DISCUSSION**

### **1. Discussion of Substantive Review Issues**

PRNT assay (LLOQ): Based on review of information submitted on July 5, 2019, we request that you set the LLOQ at a titer of ~20. We further request that you recalculate the immunogenicity results that are to be included in the Package Insert to reflect the change in LLOQ. We anticipate communicating requested package insert revisions, which will inform the immunogenicity data that needs to be recalculated using the new LLOQ, at the end of July 2019. Please refer to the information request (IR) #30 sent on July 15, 2019 for further details.

#### **Meeting Discussion:**

CBER acknowledged receiving BN's email dated July 17, 2019, in response to IR #30 and BN's proposal to reset the LLOQ to 20 (instead of (b) (4)) for version (b) (4) of the vaccinia PRNT assay, to impute PRNT titer values below 20 by (b) (4) and to recalculate the immunogenicity data that will be included in the package insert to reflect this change in LLOQ. CBER informed BN that their proposal is still being discussed. CBER anticipates providing comments on the package insert by the end of July, and these comments will include revisions to data impacted by the change in LLOQ.

### **2. Discussion of Minor Review Issues**

None.

#### **Meeting Discussion:**

BN acknowledged that there are no minor review issues.

### **3. Additional Applicant Data**

None.

#### **Meeting Discussion:**

BN acknowledged that there is no additional applicant data required.

### **4. Information Requests**

Pending responses to the following information requests (IRs):

- IR #29 sent on July 5, 2019 requesting information on (b) (4) filling facility. BN updated CBER on July 9, 2019 that they will not be able to provide responses to all the items in the IR #29 by July 19, 2019, as requested. CBER agreed with BN that submission of a complete response by July 31, 2019 will be acceptable.
- IR #30 sent on July 15, 2019 requesting BN to:

- Reset the LLOQ of the PRNT assay to a titer of 20, and recalculate the immunogenicity data tables that are included in the package insert. A response to this item is requested along with the response to labeling comments, which will be communicated by the end of July 2019.
- Provide information related to Drug Substance manufacturing at Denmark facility. A response to this item is requested by July 31, 2019.

**Meeting Discussion:**

BN acknowledged the two pending IRs.

BN informed CBER that they are actively working to address the 21 questions for (b) (4) in IR #29, and are on track to submit a response to CBER by July 31, 2019. BN noted that there may be a delay in submission of some of the reports which require a translation from German to English. CBER agreed that BN could provide summaries in English for any reports requiring translation, with English translations of full reports submitted at a later date.

BN informed that the response to the IR # 30, related to the DS manufacturing facility at Denmark, will be submitted to CBER by July 31, 2019.

5. Current assessment of risk management activities, e.g., REMS

A discussion is not planned as we do not anticipate the need for a REMS.

**Meeting Discussion:**

BN acknowledged that CBER does not anticipate the need for a REMS.

6. Postmarketing Requirements/Postmarketing Commitments

Regarding study POX MVA 039: We have reviewed the protocol and agree with the proposed study. However, we may have a few minor comments on the protocol, which will be communicated to BN later. We strongly encourage BN to conduct this study, but it will not be considered as a post-marketing commitment/requirement.

**Meeting Discussion:**

BN acknowledged CBER's comments regarding study POX MVA 039.

7. Major Labeling Issues

We are targeting to communicate our first set of labeling comments to BN by end of July 2019.

The data demonstrating efficacy of JYNNEOS against monkeypox infection

needs to be included. We will provide guidance with our first set of labeling comments.

Carton labels:

- BN's request for a waiver of the Drug Supply Chain Security Act DSCSA requirement is still under review. Amendment 43 with responses to our information request regarding the request for the DSCSA waiver was received on July 10, 2019. This response is currently under review.
- BN's request to use one carton label with two storage conditions/expiration dates for both stockpiled and non-stockpiled product purposes is still under consideration

**Meeting Discussion:**

BN acknowledged CBER's comments regarding labeling. CBER anticipates providing a response to the DSCSA waiver request by the end of July or early August.

**8. Review Plans**

Labeling Discussions to begin by the end of July (targeted)

Additional Information Requests may be communicated

BN will be notified if any post-marketing commitment/requirement is identified

**Meeting Discussion:**

BN acknowledged CBER's review plans.

**9. Applicant Questions**

The following agenda-items for discussion were provided by BN on July 17, 2019:

- Status of FDA's review of BN's responses to information requests
- Status of serialization waiver request
- Status of pediatric waiver request for monkeypox
- Status of FDA's review of post-authorization -039 study
- Status of FDA's input regarding labeling for monkeypox indication
- Will any additional samples/reagent shipments be required?
- BN's update on information request 29 concerning (b) (4) information

**Meeting Discussion:**

BN acknowledged the agenda items that had already been discussed during the meeting. CBER noted that the pediatric waiver request for monkeypox had been reviewed, no additional information was required, and that an official response to pediatric waiver request would be communicated in the final action letter. CBER also confirmed that no additional samples or reagents would be required.

10. Wrap-up and Action Items

**Meeting Discussion:**

There were no additional discussion items.

This application has not yet been fully reviewed by the signatory authorities, Division Directors and Review Committee Chair and therefore, this meeting did not address the final regulatory decision for the application.