

RECORD OF TELEPHONE CONVERSATION

Submission ID:

BLA 125694

Office:

OTAT

Product AVXS-101-onasemnogene abeparvovec;

Sponsor: AveXis, Inc.

Telecon Date/Time: 21- May-2019; 12:30PM **Initiated by FDA?:** yes

Telephone Number: () -

Author:

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Purpose: To discuss lot release of the AveXis product, specifically the information provided in BLA 125694 and IND 15699 which indicates that the bioburden assay SOP-085 is a (b) (4) compliant assay that includes (b) (4).

FDA Participants:

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Sponsor Participants:

James L'Italien, PhD, Senior Vice President and Chief Regulatory Office

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FDA Revised LRP -
added (b) (4) ref lot n

Summary of Discussion:

AveXis provide the attached slide deck prior to the meeting.

FDA noted during the review of the lot release protocols that was submitted on May 17, 2019 that the (b) (4) portion of the bioburden assay had not been performed since (b) (4). It had been noted previously, in both BLA 125694 and IND 15699, that the use of the bioburden assay for (b) (4) had been used. FDA wanted to clarify this discrepancy to determine why the testing of the (b) (4) was discontinued, why the agency was never notified

RECORD OF TELEPHONE CONVERSATION

of this change and why they are not following the testing procedures outlined in the IND and BLA.

AveXis explained that from January 2018 to August 2018, it was discovered that (b) (4) Bioburden samples recovered on (b) (4) were bacteria. It was the concern of under reporting the total aerobic microbial count. The AveXis -101 bioburden specification is based on a total (b) (4) and does not differentiate between bacteria, yeast and mold. AveXis further noted that they replaced (b) (4) to ensure the same total volume of the sample had not changed and (b) (4) period from (b) (4). There was not validation change to the method and every lot of (b) (4) is growth promoted per (b) (4), but they acknowledge that the bioburden method does not use a specific medium for recovery of yeast and mold as specified in (b) (4).

AveXis further noted that due to timing, change control (CCR-180) was assessed (March 2018) and implemented (August 2018) prior to submitting the BLA in September 2018 and plans to initiate a non-conformance report to investigate the root cause for the failure in updating the BLA and commits to amending the BLA to align with the IND. SOP-085 update has been submitted to the BLA.

FDA noted that the IND was not updated with the changes that were previously discussed with resulted in a data dump in the fall of 2018. Updating regulatory documents in a timely fashion. Will look at recently submitted SOP and will discuss internally.

Cleaning Validation:

Method of cleaning validation was tested on (b) (4), FDA recommends cleaning of wrap and fill lines before and after a fill or a full run to develop a cleaning matrix to validate cleaning SOPS, and compare the data to ensure your cleaning is accurate. Use a detergent for cleaning and not use a sanitizer. Team Bio will follow-up at the bi annual follow-up

Lot release protocol

Section 2 (b) (4) DNA by (b) (4), no entry for the PDC reference slot for the 5 lot release protocols, and please update. AveXis will update soon