

From: Jarvis, Candace
To: [James L'Italien, PhD \(jitalien@avexis.com\)](mailto:jitalien@avexis.com)
Cc: [Jarvis, Candace](#); [Wu, Iwen](#); [Galivo, Feorillo](#); [Byrnes, Andrew](#)
Subject: BLA 125694/0| AveXis, Inc Information Request 2 Due October 12, 2018
Date: Friday, October 05, 2018 1:25:00 PM
Attachments: [image002.png](#) **Importance:** High

Good afternoon Dr. L'Italien,

While conducting preliminary review of your October 1, 2018 BLA submission to the agency, we have the following requested information regarding the Additional Nonclinical Comments from the pre-BLA meeting summary dated July 12, 2018.

Please respond to the following information request:

1. Due to the uncertainty over the vector dose levels evaluated in the original proof-of-concept studies conducted to support initiation of the Phase 1 trial, please submit the final audited study report for the subsequent studies that evaluated intravenous administration of AVXS-101 in SMNΔ7 mice, originally submitted as RPT-777-SN0091 under IND #15699/096 (received 6/6/18). As relayed to you previously during the pre-BLA meeting and in the meeting summary, due to discrepancies in the data submitted previously, the final study report should be reviewed by a Quality Assurance (QA) unit/person that is independent of the personnel responsible for the conduct of the study (21 CFR Part 58.35) to assure that the study was conducted according to sound procedures and to ensure the quality and integrity of the resulting data. The final study report should be reviewed by the QA unit for accuracy and a signed QA statement included in the final audited study report that is submitted to Module 4 of the BLA.
2. For each nonclinical study used to support the safety and scientific rationale for intravenous administration of AVXS-101 in humans, please provide the following:
 - a. Please specify the AVXS-101 vector lot administered and provide a tabulated summary of the similarities and differences between the product that was evaluated in each study and the intended clinical product.
 - b. Please specify the dose-determining assay used for each AVXS-101 vector lot evaluated in the animals. If the current validated (b) (4) assay was not used, please reanalyze any retained samples from each lot using the validated assay and recalculate the dose levels administered in each study based on this analysis.

Please respond by submitting an amendment to the BLA by October 12, 2018.

Please confirm receipt of this email.

Regards,

Candace N. Jarvis

Sr. Regulatory Project Manager

Center for Biologics Evaluation and Research

Office of Tissues and Advanced Therapies

U.S. Food and Drug Administration

Tel: 240-402-8315

candace.jarvis@fda.hhs.gov



THIS MESSAGE IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify the sender immediately by e-mail or phone.