

**From:** [Jarvis, Candace](#)  
**To:** [James L'Italien, PhD \(jlitalien@avexis.com\)](#)  
**Cc:** [Nancy Boman](#); [Jarvis, Candace](#); [Byrnes, Andrew](#); [Galivo, Feorillo](#); [Wu, Iwen](#)  
**Subject:** BLA 125694/0| AveXis, Inc| Information Request 18 (PLEASE RESPOND BY JANUARY 21, 2019)  
**Date:** Thursday, December 20, 2018 10:38:34 PM  
**Attachments:** [image013.png](#) **Importance:** High

---

Good evening Dr. L'Italien,

We have the following request for information regarding BLA 125694.

1. Single-dose toxicology in neonatal mice

Regarding the studies administering AVXS-101 as a single IV dose in neonatal FVB mice, please provide an explanation for the differences in the safety profile for AVXS-101 reported in Study No. 8384031 and Study No. 20122446 at the dose levels evaluated. This should include a discussion of the differences in the cardiovascular, liver, and lung toxicity findings and potential factors, including any differences between the product lots, that may be contributing to the disparities in the adverse findings observed across the two studies.

2. Biodistribution data for Subject (b) (6)

During the BLA Applicant orientation meeting with the FDA on November 30, 2018, you presented data on the tissue biodistribution of AVXS-101 vector genome and SMN transgene expression for Subject (b) (6). Please submit a comprehensive report which should include the clinical vector lot and dose level administered, complete list of tissues and organs collected, justification for exclusion of tissues not collected or analyzed, detailed description of methods used to process and analyze post-mortem tissues, gross and microscopic tissue observations, if available, and background information/description of the tissue sources from non-treated SMA subjects used as comparator.

3. Please submit the final autopsy report for Subject (b) (6)

Please provide your response via email by COB Monday, January 21, 2018. The information should also be submitted as an amendment to the BLA.

Please confirm receipt.

*Regards,*

**Candace N. Jarvis**  
*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](mailto: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.