

**From:** [Jarvis, Candace](#)  
**To:** [James L'Italien, PhD \(jlitalien@avexis.com\)](#)  
**Cc:** [Nancy Boman](#); [Byrnes, Andrew](#); [Jarvis, Candace](#); [Wang, Wei \(FDA\)](#); [Whatley, Angela](#)  
**Subject:** BLA 125694/0 | AveXis, Inc | Information Request 27 (PLEASE RESPOND BY 1/25/19)  
**Date:** Friday, January 11, 2019 2:33:01 PM  
**Attachments:** [image013.png](#) **Importance:** High

---

Good afternoon Dr. L'Italien,

We have the following request for information regarding the review of BLA 125694/0. Please respond to this request by January 25, 2019 by 12 Noon. If you are unable to meet this deadline please let me know as soon as possible.

1. Validation of HVAC – Please provide a validation summary for the HVAC system with the following information:
  - A narrative description of the validation process (or protocol), including the acceptance criteria.
  - Certification that IQ, OQ and certification of filters has been completed.
  - Length of the validation period.
  - A validation data summary (include Performance Qualification data accumulated during actual processing).
  - Explanations of any excursions or failures, including deviation reports and summary of investigation results.
2. Deviations and Investigation – You indicated (in Section 3.2.S.2.5. Process Validation and/or Evaluation of STN 125694/0) that any deviations if encountered during Process Performance Qualification (PPQ) are mentioned following each table. You indicated that the PPQ lot (b) (4) was discarded shortly after (b) (4) of the (b) (4) due to contamination. The information of deviation investigation was not provided. Please provide summary of investigation results including the identification of possible route of cause and any corrective and preventative actions.
3. (b) (4) – You indicated (in Section 3.2.P.3.3 of STN 125694/0) that there are possible (b) (4) operations (b) (4) during the AAVXS-101 Drug Product manufacturing process. In the SOP-303 (Amendment, STN 125694/0.5), you did not specify (b) (4) the Sterile Filtration (b) (4) step is allowed to be (b) (4). We did not find written procedures for possible (b) (4) operations as per 21CFR211.115. Please provide detailed information for each (b) (4) procedure, including:
  - A description of the conditions or criteria which indicate the need for (b) (4)
  -

A description of the (b) (4) step and referenced Standard Operating Procedure for the step.

- A description of any additional or modified in-process controls or specifications which are included to monitor (b) (4) steps. A
- description of the modifications in batch numbers and documentation of (b) (4) in the Batch Production Record (BPR).
- The evidence derived from validation studies which assures that product identity, purity, potency, and stability is preserved for (b) (4) batches.

Please acknowledge receipt of this email.

*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.