

**From:** [Jarvis, Candace](#)  
**To:** [James L'Italien, PhD \(jlitalien@avexis.com\)](#)  
**Cc:** [Nancy Boman](#); [Byrnes, Andrew](#); [Jarvis, Candace](#)  
**Subject:** BLA 125694/0 | AveXis, Inc | Information Request 32 (PLEASE RESPOND BY FEBRUARY 18, 2019)  
**Date:** Friday, February 01, 2019 9:28:38 AM  
**Attachments:** [image013.png](#)  
**Importance:** High

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Good morning Dr. L'Italien,

We have the following request for information regarding BLA 125694/0. Please respond by February 18, 2019. If you are unable to meet the established deadline, please let us know so that we can negotiate a timeline that is feasible for both parties.

1. Regarding your response to question 3 in submission number 30 (received 1/28/19): BLA section 3.2.P.5.6.10 states that the in vitro potency for lot (b) (4) is "result pending." While we understand that lot (b) (4) was not released using this test method, please state clearly whether lot (b) (4) has been tested for in vitro potency, and if so please provide the results. If not, please explain why the in vitro potency test for this lot has not been completed 4 months after it was listed as "result pending" in the original BLA submission.
2. Regarding the CPV plans (PLAN-176, PLAN-172 and PLAN-244) that were provided in submission number 21 (received 1/17/19):
  - a. Please explain why the DS acceptance criteria listed in section 5.2.3.7 of PLAN-172 do not match the DS specifications listed in 3.2.S.4.1.
  - b. For analysis of data from quantitative DS and DP specifications, please modify your CPV plans to incorporate a pre-defined approach to detecting non-random effects (for example, Nelson rules are one possible approach). We also recommend that you consider such an approach for analyzing data from process parameters and in-process controls, when appropriate.
3. MBRs have been updated multiple times subsequent to the manufacturing of the PPQ lots, and the information in the BLA is insufficient for us to determine whether any of these MBR updates involved major manufacturing process changes that might require additional performance qualification. Please provide the following information:
  - a. Please clarify whether the versions of the MBR that were submitted to section 3.2.R are current. If they have been updated after submission of the BLA, please provide the updated MBRs.
  - b. Please provide the MBR version numbers used for manufacturing each of the PPQ lots.
  - c. Please provide a version tracking summary for each of the DS manufacturing MBRs, describing the changes made to the MBR at each version number.

- d. Please provide the risk analyses and change controls associated with each DS manufacturing MBR version change.
- e. In some cases, key details of manufacturing procedures are contained in SOPs instead of MBRs (e.g., SOP-203, SOP-303). Changes to such manufacturing SOPs may also have significant impact on product quality, and such changes may require additional performance qualification. Please provide the risk analyses and change controls associated with these manufacturing SOPs (SOP-203, SOP-303 and all other SOP that contain instructions for manufacturing steps that may impact the quality of the product).
- f. The MBRs for DP manufacturing (MBR-(b) (4), MBR-(b) (4), MBR-(b) (4) and MBR-(b) (4)) are different than the MBRs that were used for performance qualification of the DP manufacturing process. Please clearly describe the differences between the current DP manufacturing MBRs and the MBRs that were used when manufacturing the PPQ DP lots. If relevant and informative, please also provide MBR and SOP version tracking summaries, risk analyses and change controls similar to those requested above for DS manufacturing process changes.

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)



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