

**From:** [Jarvis, Candace](#)  
**To:** [James L'Italien, PhD \(jlitalien@avexis.com\)](#)  
**Cc:** [Jarvis, Candace](#); [Byrnes, Andrew](#); [Kong, Hyesuk](#); [Garnepudi, Varsha](#); [Wang, Wei \(FDA\)](#)  
**Subject:** BLA 125694/0| AveXis, Inc| Information Request 5 (PLEASE RESPOND BY 10/31/18)  
**Date:** Thursday, October 18, 2018 9:06:40 PM  
**Attachments:** [image002.png](#) **Importance:** High

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Good evening Dr. L'Italien,

We have the following request for information regarding BLA 125694/0.

Please be aware that we will be sending a series of information requests (IRs) as we identify missing elements of the BLA. Your BLA was expected to be complete upon receipt because we did not discuss and agree on submission of late components during the pre-BLA meeting. The IRs will contain items that are required to make the BLA scientifically complete, and failure to submit will preclude filing of the BLA.

Since late component items were not agreed upon during the pre-BLA meeting, depending on the nature, volume or time of your response of the requested items, the amendment may be designated as a Major amendment, which will extend the review clock by three months.

1. We note that during the pre-BLA meeting on June 14, 2018 you agreed to submit reports and the lot release protocol in the BLA, but we are unable to find these. Please submit the following items to the BLA:

a. Mycoplasma Test:

- i. CBER requests the (b) (4) for type (b) (4) to include the inhibitory substances test results data for the mycoplasma (b) (4) listed in (b) (4); to demonstrate their ability to (b) (4) of mycoplasma on each (b) (4) in the presence and absence of the product to be examined.
- ii. CBER requests that AveXis, Inc., submit the (b) (4) method qualification assay results for the (b) (4) to show the test samples meet their qualification acceptance criteria according to (b) (4)

b. Sterility Test:

- i. CBER expects qualification of the sterility test to ensure known environmental isolates can be detected in the tested matrix. Therefore, CBER requests bacteriostasis and fungistasis qualification using known environmental isolates in your manufacturing facility for AVXS-101 drug product.

c. Lot Release Protocol Template:

- i. Please provide a lot release protocol template in your BLA. The template should include results of release tests for the Drug Product and the Drug Substance lot(s) used to formulate the Drug Product, together with specifications for each test.
2. Please provide a list containing the drug product batch number(s) administered to each subject in studies AVXS-101-CL-303 and AVXS-101-CL-304.
  3. For each testing site in 3.2.S.2.1 and 3.2.P.3.1, please list every test that is performed at each site (i.e., list the individual test names, not the test category).
  4. Please explain why there are so many in vitro relative potency test results listed as "NP" in

3.2.P.8.3.

5. Please provide NCR-965.
6. In 3.2.P.5.6.6 (DP justification of specifications for (b) (4)), there are discrepancies between the data in table 7 and figure 4. Please resolve these discrepancies and explain exactly how the mean (b) (4) were calculated for these (b) (4) data.
7. Please provide the upstream sampling plan (samples acquired prior to (b) (4)).

Please respond to this request by October 31, 2018.

Please kindly acknowledge receipt of this email.

*Regards,*

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