

From: [Gildner, Jean](#)
To: ["jilitalien@avexis.com"](mailto:jilitalien@avexis.com)
Cc: [Jarvis, Candace](#)
Subject: BLA 125694 Information Request # 20
Date: Friday, December 28, 2018 9:31:21 AM
Attachments: [image013.png](#)

Dear James,

Candace is on leave and I am sitting in for her. Please see the following information request. Please respond to this request by January 11, 2019. Please acknowledge receipt of this email and the ability to meet the requested deadline. If you need any additional assistance please feel free to contact me.

1. ***Please describe the process for cleaning, testing and criteria to release equipment that is (b) (4) for manufacturing purposes at (b) (4).***
2. ***Provide the rationale for the (b) (4) specifications for the testing and release criteria for the equipment that is (b) (4) in (b) (4) manufacturing that was provided in submission 17 received on November 30.***
3. ***We note according to the updated Tables 58 & 59 in 3.2.S.2.3 Control of materials, additional testing conducted by AveXis for (b) (4) from (b) (4) is appearance at the AveXis (b) (4) site and Identity by (b) (4) performed by (b) (4). Please clarify:***
 - a. ***if the identity testing is conducted by (b) (4) for (b) (4) from (b) (4)***
 - b. ***if the identity testing is conducted after the (b) (4) lots are received by AveXis on the material that is shipped to AveXis.***
4. ***We note you have provided (b) (4) Qualification plan- 296; however this document does not contain sufficient information to determine that a new (b) (4) manufacturer is adequate please provide the following:***
 - a. ***Referenced documents DVP-001 & SPEC-284***
 - b. ***The plan (also known as Technical Specification) referenced in section 5.2.1 which details how the (b) (4) manufacturer will prepare a new (b) (4) which will be approved by AveXis.***
 - c. ***Please clarify how you will evaluate the ability of new (b) (4) suppliers to prevent cross contamination from other (b) (4) manufactured at their facility***
5. ***In RPT-472 attachment 1 (b) (4) validation report for the (b) (4) assay), the recovery calculations in the right-most column of table 5-5 appear to be incorrect, leading to incorrect determination of the range of the assay. Please either fix these errors or (if they are correct) provide a clear explanation of how the accuracy and range of the assay were calculated.***
6. ***The (b) (4) assay (SOP-328) includes a reference standard in (b) (4). There should be an assay validity criterion for (b) (4) to ensure that the (b) (4) of the reference standard falls within an appropriate range. Please define an appropriate (b) (4) range for your reference standard and add this as an assay validity criterion.***
7. ***According to information in submission number 8 (received on 11/20/18), certain assays are performed at both AveXis (b) (4). Development and validation of these assays were performed at (b) (4). Information on the transfer of***

these assays from (b) (4) to AveXis was not included in the BLA. Please provide evidence that the following assays produce reproducible results after transfer to AveXis:

- SOP-259 / (b) (4)
- SOP-181 / (b) (4)
- SOP-182 / (b) (4)
- SOP-183 / (b) (4)
- SOP-186 / (b) (4)
- SOP-190 / (b) (4)

Sincerely, Jean

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