

From: [Gildner, Jean](#)
To: ["jitalien@avexis.com"](mailto:jitalien@avexis.com)
Cc: [Jarvis, Candace](#); [Whatley, Angela](#); [Byrnes, Andrew](#)
Subject: BLA 125694/0 AveXis Information Request #21
Date: Friday, January 04, 2019 12:38:55 PM
Attachments: [image013.png](#)

Dear Dr. L'Italien,

Please see the following Information Request for BLA 125694/0. Please respond by January 31, 2019. Please acknowledge receipt of this request and the ability to meet the requested deadline. If you have any questions please feel free to contact me anytime today. Candace will be in the office again on Monday, January 7, 2019.

1. ***We note several raw materials used in the manufacture of the (b) (4) are not listed in tables 1 & 2 of section 3.2.s.2.3. Please update these tables and section 3.2.s.2.3 to include:***
 - a. ***all raw materials (including (b) (4), etc.) that are used in the manufacture of the (b) (4)***
 - b. ***all confirmatory testing and associated acceptance criteria, for the confirmatory inhouse QC tests completed on raw materials by AveXis or a contract laboratory on materials received by AveXis***
2. ***We note in table 62 of 3.2.s.2.3 several of the tests include specification of report results. We do not agree with these specifications. We recommend that you update your release specifications based on manufacturing experience of the (b) (4).***
3. ***Please provide the results for the (b) (4) stability testing referenced in table 69 of 3.2.s.2.3.***
4. ***We note that section 3.2.s.2.3 contains descriptions for (b) (4), and each (b) (4) was made with different reagents, and different release tests and specifications were used for each (b) (4). Clarify which procedures will be used to make new (b) (4) in the future.***
5. ***We note according to table 44 Specification for (b) (4) of section 3.2.s.2.3 the acceptance criteria for viral testing for (b) (4) antibody is Tested. We do not agree with this acceptance criteria. We recommend that the acceptance criteria be (b) (4), or that that you provide justification for the tested acceptance criteria and that you conduct additional incoming testing on (b) (4) entering your facility to ensure that it is free of (b) (4), or that you provide viral clearance studies that demonstrate that you manufacturing and purification procedures removes (b) (4) or similar viruses from your final product.***
6. ***Please explain how you control or qualify new lots of the following reference materials:***
 - a. ***(b) (4) standards (SOP-183)***
 - b. ***(b) (4) standard (SOP-182)***
 - c. ***(b) (4) standards (SOP-181)***
 - d. ***(b) (4) standards (SOP-287)***
 - e. ***Human DNA control (SOP-190)***
 - f. ***(b) (4) standard reference material (SOP-186)***

7. *SOP-184, section 2, indicates that the (b) (4) protein assay may be performed by either AveXis or (b) (4), but this assay is not listed in submission number 8 as being one of the assays that is performed by AveXis. Please clarify whether the (b) (4) protein assay is being performed at AveXis, and if so please provide evidence that this assay produces reproducible results after it was transferred from (b) (4) to AveXis.*
8. *Assay robustness was not evaluated for all assays during validation. Please provide data demonstrating the robustness of the following assays:*
 - a. (b) (4) (RPT-585)
 - b. (b) (4) (RPT-471)
 - c. (b) (4) (SOP-191)
9. *Section 5.3.1 of SOP-183 (b) (4) incorrectly lists the catalog number of the (b) (4) kit as (b) (4). Please correct this.*
10. *Regarding the (b) (4) assay procedure (SOP-191):*
 - a. *Section 8.2.5 incorrectly lists the slope criterion. Please correct this.*
 - b. *SOP-191 does not specify the amount of the test article. Please revise the SOP to state the volume and/or vg concentration of the test article used per (b) (4), and the number of (b) (4) that are exposed to the test article in each assay.*
 - c. *Please provide the detection limit of the assay in terms of IU per vg.*
11. *Your environmental assessment, section 14.6.2, states that “the virus is sensitive to all main detergents and can be eliminated through defined sanitation conditions.” Please provide support for this statement regarding detergent sensitivity, and please clarify what is meant by “defined sanitation conditions.”*

Sincerely, Jean for Candace Jarvis

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