

**From:** [Jarvis, Candace](#)  
**To:** [James L'Italien, PhD \(jlitalien@avexis.com\)](#)  
**Cc:** [Nancy Boman](#); [Byrnes, Andrew](#); [Jarvis, Candace](#); [Lin, Xue \(Mary\)](#)  
**Subject:** 125694/0| AveXis, Inc | Information Request 31 (PLEASE RESPOND BY JANUARY 24, 2019)  
**Date:** Tuesday, January 22, 2019 11:24:26 AM **Attachments:**  
[image013.png](#)

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Hello Dr. L'Italien,

We have the following statistical request for information regarding BLA 125694/0. Please Respond by COB January 24, 2019. If you are unable to meeting this deadline, please let us know soon as possible so that we can negotiate a new timeline that is feasible for both FDA and your team.

In review of your Jan 18th response to FDA's statistical IR sent on Jan 15th, we have the following comments. Please address those comments/questions.

1. In your response to IR #1, you stated that "The evaluations of the motor milestones came from two sources, the Developmental Milestone form and the Gross Motor Skills checklist" and "the results from both sources were used to count the numbers of patients in the table that summarizes the motor milestone achievements (Table 14.2.3.1.1-24)." Though "prone: hold head to vertical axis and legs extended " is an item in the Developmental Milestone form, Gross Motor Skills checklist does not have such an item. It is not clear how you determine a subject who did not reach this milestone based on Developmental Milestone form alone, however reached this milestone based on Gross Motor Skills checklist. Please describe the algorithm you used in this determination.
2. In your response to IR #1 and #2, you stated that milestone achieved at an Unscheduled visit was not considered to be part of the analysis data set and therefore was not in Table 14.2.3.1.1-24. However, in your protocol data sets definition, you did not define analysis sets based on unscheduled visit or not. A milestone achieved on an unscheduled visit should be counted the same way as scheduled visit.
3. In explaining the discrepancies between Table 14.2.3.1.1-24 and Listing 16.2.6.624, you stated that Table 14.2.3.3.1-24 is a summary table of the motor milestone findings that had been documented on video and subsequently reviewed and confirmed by a trained Central Reviewer. Please explain the sources of the video that's used for milestone determination in Table 14.2.3.1.1-24 . If they were videotapes of study visits, then why the determination of milestone achievement was different from Listing 16.2.6.6-24 which was based on observation made at study visits.

Please acknowledge receipt.

*Regards,*

***Candace N. Jarvis***

*Regulatory Project Manager*

*Center for Biologics Evaluation and Research*

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