

TEAM MEETING SUMMARY

Application number: 125694/0
Product name: onasemnogene abeparvovec-xioi
Proposed Indication: Treatment of infantile-onset Spinal Muscular Atrophy
Applicant: AveXis, Inc.
Meeting date & time: April 10, 2019, 3:00 PM – 4:00 PM
Committee Chair: Andrew Byrnes, PhD
Meeting Recorder: Varsha Garnepudi

Link to submission:

(b) (4)

Link to SharePoint site:

To follow up on our discussion at the April 5 BLA team meeting:

(b) (4)

Table 1: Review Committee and Discipline Attendees

Discipline/Organization	Name [with credentials (not title)]	Attended meeting
Chair/CMC Reviewer and Inspector	Andrew Byrnes, PhD	X
Other Attendee(s)		
OTAT/DCGT	Raj Puri, MD	X
OTAT/DCGT	Steven Oh, MD	X
OTAT/DCGT	Denise Gavin, PhD	X
OTAT/DCGT	Ramjay Vatsan, PhD	X
OTAT/DCGT	Zenobia Taraporewala, PhD	X
OCBQ/DMPQ	Jay Eltermann	X
OCBQ/DMPQ	Laurie Norwood	X
OCBQ/DMPQ/PRB	Joseph Quander	X
OCBQ/DBSQC	Maryna Eichelberger, PhD	X

Discipline/Organization	Name [with credentials (not title)]	Attended meeting
OCBQ/DBSQC/QAB	Suzanne Carter	X

Team meeting Agenda: Discussion of CBER lot release/ surveillance for the AveXis product

Meeting Summary

Andrew Byrnes explained DCGT's preference for quarterly surveillance instead of lot release due to the large number of lots (approximately 1 per week) and the risk to commercial supply that could be caused by delays in release. Andrew explained that given the relatively short shelf life (effectively only 8 months), routine lot release could delay distribution of the product.

Jay Eltermann expressed that all products are subject to lot release, but case by case exemptions have been granted, e.g., CAR-T cells. Jay explained that this product has attributes that support the need for routine lot release - it is not a patient specific product, it is a novel product from a manufacturer with little experience, and there appear to be testing issues. It therefore cannot be under surveillance. AveXis will need to establish an acceptable lot release history (longer than 5 years), accumulate stability data, and demonstrate the manufacturing process is well controlled before submitting a supplement to request surveillance as an alternative to routine lot release.

Maryna Eichelberger explained that lot release would give CBER confidence with the product, and regardless if the protocols are electronic or paper, they come to DPMQ/PRB. They are reviewed by the Product Office (PO) and DBSQC reviewers. Paper protocols are physically routed to sequential reviewers and therefore if paper protocols are submitted, it could delay the release. AveXis could send electronic protocols after BLA approval. The Testing Plan (TP), a CBER internal document, determines the LRS routing. There are no PDUFA time lines for lot release. However, the Lot Release Branch (LRB) is committed to releasing lots within 30 business days of protocol receipt. Jay mentioned that LRS captures tests which are released, but no test data is captured in LRS.

Maryna suggested that OTAT decide if additional information regarding lot release tests need to be included in the Lot release protocol. Andrew mentioned some additional information may be useful like chromatograms. Jay remarked that in the future if the product were to be considered for surveillance, this additional data may be helpful in the decision making.

OTAT needed clarification about deviation reports, to which Laurie Norwood mentioned generally the report is sent with the protocol. Maryna mentioned that if a reviewer finds a deviation/error in the submitted Lot release protocol the lot can be TRed (To be returned) where the reviewer would ask PRB to contact manufacturer to send additional information.

DMPQ explained that electronic protocols come through the Gateway. AveXis works with a 3rd party for Gateway submissions. Jay suggested that once the Lot Release Protocol (LRP) is finalized, AveXis should be asked to submit the LRP to PRB electronically. PRB would work with AveXis to accomplish this. Andrew to set up a meeting with AveXis and PRB.

Other items discussed:

- Routing of the LRP was discussed: DBSQC reg coordinator sends information regarding the names of reviewers for each test to PRB. To ensure LRPs are reviewed expeditiously, it may be important to identify back up reviewers. It was suggested that the supervisor of each reviewer serve as a backup.
- Launch lots: AveXis has (b) (4) lots available. It is currently not clear whether all are suitable for release. It was stated that there are typically 3 launch lots.
- Product Shortages: Joe Manick in OCBQ handles notifications of product shortages.

Timeline

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| • TARGET DATE | MAY 17, 2019 |
| • FIRST ACTION | MAY 31, 2019 |