



CBER REGULATORY REVIEW MEMORANDUM

Date 22 April, 2019

From Hyesuk Kong, Ph. D.
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Division of Biological Standards and Quality Control (DBSQC)
Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

To Biological License Application (BLA) Submission Tracking Number 125694/0

Subject BLA: Review of Bioburden, Mycoplasma, Sterility and Endotoxin Test Method Qualifications for AVXS-101 (onasemnogene abeparvovec)

Through James L. Kenney, D.Sc., Chief, LMIVTS
Maryna Eichelberger, Ph.D., Director, DBSQC

Applicant AveXis, Inc (AveXis).

Product Zolgensma™ (AVXS-101: onasemnogene abeparvovec)

Biological License Application Submission Tracking Number (STN) 125694/0

Submission Received by CBER 28 September, 2018

Review Completed 22 April, 2019

Material Reviewed

Method qualifications for mycoplasma and bioburden test (b) (4) sterility and bacterial endotoxin test (b) (4) methods performed on drug product (DP); and information request responses received 14 November of 2018, 22 January and 29 March of 2019 were reviewed.

Executive Summary

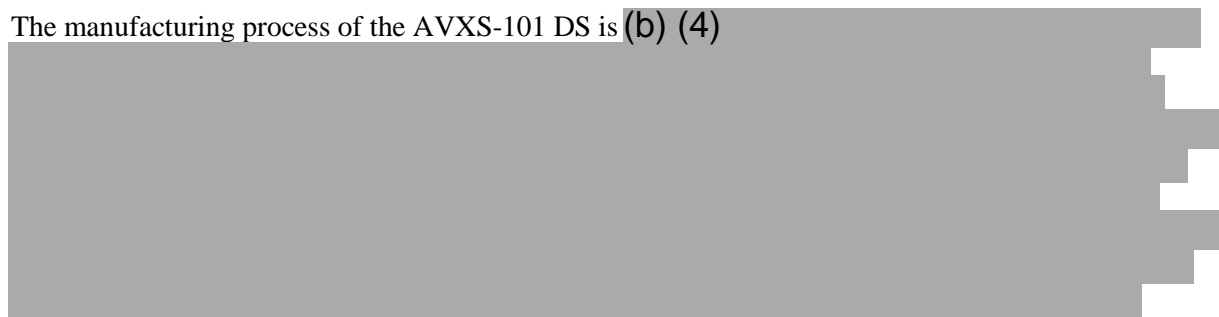
After a thorough review of this BLA, this reviewer finds the mycoplasma, bioburden, sterility and BET methods were qualified in accordance with (b) (4) respectively and the product matrixes for (b) (4) DP of AVXS-101 were demonstrated to be suitable for the intended test methods.

Background

On 28 September, 2018, AveXis submitted this BLA for AVXS-101 (onasemnogene abeparvovec), an adeno-associated virus (AAV) vector-based gene therapy indicated for the treatment of pediatric patients diagnosed with spinal muscular atrophy (b) (4) disease onset. AVXS-101 is proposed to be administered as a one-time-only intravenous infusion in pediatric patients with a body weight of 2.6 to (b) (4), at a dose of 1.1×10^{14} vector genomes (vg)/kg.

AVXS-101 is a sterile suspension of non-replicating, self-complementary recombinant AAV serotype 9 containing the human survival motor neuron (SMN) gene formulated at a target concentration of 2.0×10^{13} vg/mL. The matrix also contains: 20 mM Tromethamine, 1 mM Magnesium Chloride, 200 mM Sodium Chloride, and 0.005% w/v Poloxamer 188 (b) (4). AVXS-101 is provided in a kit containing 2 to 9 vials. Each vial of AVXS-101 contains (b) (4) 1.1×10^{14} vg in a 5.5 mL or (b) (4) in an 8.3 mL.




The manufacturing process of the AVXS-101 DS is (b) (4)



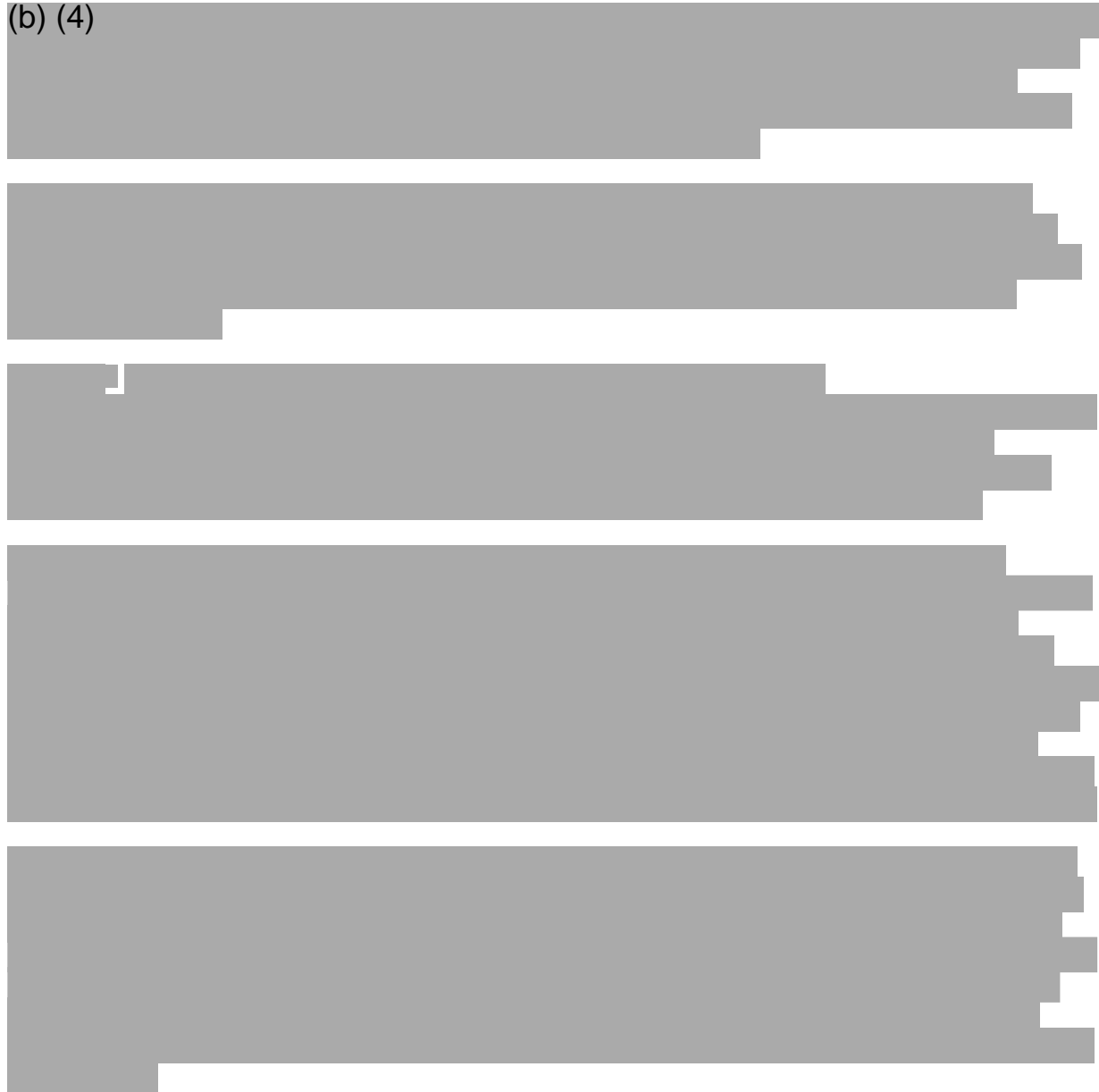
The DBSQC reviews BLAs and their supplements to ensure analytical methods are appropriate, properly validated and the product matrix is suitable for the intended test method. DBSQC also reviews release specifications for endotoxin testing to ensure they reflect process capability and meet regulatory compliance. These review activities support DBSQC's lot-release mission, which is the confirmatory testing of submitted product samples and review of manufacturers' lot-release protocols to ensure biological products are released per their product's licensed test method specifications. Therefore, this review will focus on the qualification of mycoplasma, bioburden, sterility and BET methods to ensure the tested product matrix is suitable for these intended test methods.

Review

(b) (4)



(b) (4)



Conclusions

After a thorough review of the information submitted in this BLA, this reviewer finds AveXis (b) (4) drug product matrixes are suitable for testing using their mycoplasma, bioburden, sterility, and endotoxin testing methods; these tests were qualified and performed in accordance with (b) (4) respectively. Therefore, this reviewer finds these methods acceptable for their intended purpose and recommends their approval.