



CBER REGULATORY REVIEW MEMORANDUM

Date 05 October, 2015

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Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

To Biologics License Application Submission Tracking Number # 125587/0

Subject BLA: Review of Bioburden, Sterility, Endotoxin, Diphtheria and General Safety Tests for PANZYGA® (NewGam 10%) Immune Globulin Intravenous, Human 10%

Through Dr. James L. Kenney, Chief, LMIVTS/DBSQC/OCBQ/CBER/FDA
Dr. William M. McCormick, Director, DBSQC/OCBQ/CBER/FDA

Applicant Octapharma

Product PANZYGA® (NewGam 10%) Immune Globulin Intravenous, Human 10%

Biologics License Application (BLA) Submission Tracking Number (STN) 125587/0

Submission Received by CBER 15 April, 2015

Review Completed 01 October, 2015

Material Reviewed

Method qualifications for: 1) bioburden; 2) sterility; 3) endotoxin; and 4) diphtheria tests performed on (b) (4) final container for NewGam 10%. In addition, procedure for general safety test and information request response received 15 June and 7 September of 2015 were also reviewed.

Executive Summary

After a thorough review of this BLA, this reviewer finds the bioburden, sterility, and endotoxin test methods were qualified in accordance with (b) (4), respectively. In addition, diphtheria potency test and general safety test are performed in accordance with 21 CFR 640.104 and 21 CFR 610.11, respectively, for NewGam10%.

Background

On 15 April, 2015, Octapharma submitted a BLA for production of NewGam a 10% human normal Immunoglobulin G (IgG) for intravenous administration. It is indicated for treatment of primary humoral immunodeficiency and chronic immune thrombocytopenic purpura in adults. The solution contains $\geq 96\%$ IgG and has a distribution of IgG subclasses closely proportional to native human plasma. The manufacturing process developed at Octapharma Pharmazeutika Produktionsges.m.b.H, Vienna, Austria (OPG) is where pilot scale batches for preclinical and clinical studies were produced. The manufacturing process was transferred and scaled up to commercial level at the Octapharma site in Lingolsheim, France (OSA) where the conformance batches were produced.

The manufacturing process for NewGam10% is a continuous process with no clear definition of drug substance (DS) and drug product (DP). The process includes (b) (4)

The bulk product is then sterile filtered via (b) (4) filter and filled into glass vials, visually inspected, labeled and packaged. The final container vials are tested for sterility, endotoxin, diphtheria potency and general safety prior to release.

The complete manufacturing of NewGam10% is performed at the OSA facility whereas bioburden testing, filling of bulk product and release testing of final containers is also performed at the OPG facility. Visual inspection, labeling and packaging of final container vials is performed at both the OPG and the Octapharma GmbH Germany (ODE) facilities.

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 microbial and endotoxin testing to ensure they reflect process capability and meet regulatory compliance. DBSQC also produces and calibrates CBER toxin and antitoxin reference standards used in *in-vivo* and *in-vitro* test methods; therefore DBSQC has expertise in these methods and reviews them to ensure regulatory compliance. In addition, DBSQC's review of toxin/antitoxin methods ensures reference standard use is appropriate for the intended test method and provides quality control production oversight of CBER potency standard replacement lots, if applicable. 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 according to licensed test methods and product specifications. Therefore, this review will focus on the qualification of bioburden, sterility and endotoxin test and procedure for general safety test performed on panzyga[®], to indicate if the product matrix is suitable for testing using the intended test methods.

Review

Bioburden Test Qualification for ^{(b) (4)} Product at OPG and OSA

(b) (4)


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Sterility Test Qualification for Final Container at OPG and OSA

(b) (4)

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(b) (4)



Conclusion

After a thorough review of the information submitted in this BLA, this reviewer finds Octapharma NewGam10% drug product matrix is suitable for testing using their sterility and endotoxin testing methods; these tests were qualified and performed in accordance with (b) (4), respectively. CBER also reviewed the diphtheria and general safety test SOPs for the DP and found them to be in compliance with 21 CFR 640.104 and 21CFR 610.11, respectively. In addition, the NewGam10% (b) (4) matrix is suitable for testing using their bioburden test method and the qualification was performed in accordance with (b) (4). Therefore, this reviewer finds these methods acceptable for their intended purpose and recommends their approval.