

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**125431Orig1s000**

**MICROBIOLOGY / VIROLOGY REVIEW(S)**



Food and Drug Administration  
Center for Drug Evaluation and Research  
10903 New Hampshire Avenue,  
Building 51,  
Silver Spring, MD 20993

**Date:** April 08, 2014  
**To:** Administrative File, STN 125431/0  
**From:** Lakshmi Rani Narasimhan, Ph.D., CDER/OC/OMPQ/DGMPA/BMAB  
Bo Chi, Ph.D., CDER/OC/OMPQ/DGMPA/BMAB  
**Endorsement:** Patricia F. Hughes, Ph.D., Team Leader, CDER/OC/OMPQ/DGMPA/BMAB  
**Subject:** Addendum to New Biologic License Application (BLA) to address the issue related with the (b) (4)  
**Applicant:** GlaxoSmithKline, LLC  
**Mfg. Facilities:** GlaxoSmithKline, LLC, (b) (4), 893 River Road, Conshohocken, PA 19428 (FEI: 3004055938)  
(b) (4)  
**Product:** Albiglutide (Tanzeum)  
**Dosage:** Single-use, sterile lyophilized cake in a clear glass dual chamber cartridge (DCC) for subcutaneous delivery (30 mg or 50 mg of albiglutide)  
**Indication:** Treatment of Type-2 Diabetes Mellitus (T2DM) as an adjunct to diet and exercise to improve glycemic control in adults.  
**Due Date:** April 15, 2014

**Recommendation for Approvability:** This BLA, as amended, was reviewed from a product quality microbiology perspective and recommended for approval.

**SUMMARY:**

This addendum addresses the issue related with the (b) (4)

**Background**

Andrew Jones, Head of Quality for Biopharm supply Chain at GSK informed Dr. Patricia Hughes, Team Leader, Biotech Manufacturing Assessment Branch, on March 21, 2014, through telephone call, that the (b) (4) Following this, GSK provided additional information and data in the responses to Agency's information requests for the (b) (4) Official amendments of the responses were submitted on March 28, 2014 (sequence 0057) and April 08, 2014 (sequence 0058).

**Drug Substance**

(b) (4)

[Redacted] (b) (4)

*Reviewer's comment:* [Redacted] (b) (4)

**Drug Product**

It appears that most of the [Redacted] (b) (4)

[Redacted] (b) (4)

*Reviewer's comment:* [Redacted] (b) (4)

The product quality impact assessment review is deferred to DTP.

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/s/  
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LAKSHMI RANI NARASIMHAN  
04/10/2014

BO CHI  
04/10/2014

PATRICIA F HUGHES TROOST  
04/10/2014



Food and Drug Administration  
Center for Drug Evaluation and Research  
WO Bldg 51  
10903 New Hampshire Ave.  
Silver Spring, MD 20993

**Date:** 4/8/2014  
**To:** Administrative File, STN 125431/0  
**From:** Bo Chi, Ph.D., CDER/OC/OMPQ/DGMPA/BMAB  
**Endorsement:** Patricia Hughes, Ph.D., Team Leader, CDER/OC/OMPQ/DGMPA/BMAB  
**Subject:** Addendum to review memo for New Biologic License Applications (BLA) STN 125431/0 dated 12/19/2013  
**Applicant:** GlaxoSmithKline LLC  
**US License:** 1727  
**Facility:** [REDACTED] (b) (4)  
**FEI:** [REDACTED] (b) (4)  
**Product:** albiglutide (Tanzeum)  
**Dosage:** single-use, sterile lyophilized cake in a clear glass dual chamber cartridge (DCC) for subcutaneous delivery (30 mg or 50 mg)  
**Indication:** Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus  
**PDUFA date:** April 15, 2014

**Recommendation:** The drug product part of this BLA, as amended, is recommended for approval from sterility assurance and product quality microbiology perspective with the following post-market commitment (PMC):

Conduct studies to develop an understanding of the mechanism of low endotoxin recovery in the formulated drug substance and drug product. In addition, develop and validate a reliable endotoxin test for the albiglutide drug product in-process and release samples and include worst-case hold conditions in the relevant containers. Provide the information and data in accordance with 21CFR601.12.

This review amends the drug product microbiology product quality review memo for GSK's BLA STN125431/0 dated 12/19/2013 with new information submitted by the applicant (amendment dated 3/7/2014, Sequence 54) pertaining to the plan for understanding the mechanism of low endotoxin recovery and developing a reliable endotoxin assay.

GSK has conducted the following investigative studies to evaluate potential improvements to the endotoxin test:

- Evaluations of various combinations of [REDACTED] (b) (4) and Solvents for Excipient Solution

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/s/  
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BO CHI  
04/10/2014

PATRICIA F HUGHES TROOST  
04/10/2014



Food and Drug Administration  
Center for Drug Evaluation and Research  
WO Bldg 51  
10903 New Hampshire Ave.  
Silver Spring, MD 20993

**Date:** 12/19/2013  
**To:** Administrative File, STN 125431/0  
**From:** Bo Chi, Ph.D., CDER/OC/OMPQ/DGMPA/BMAB  
**Endorsement:** Patricia Hughes, Ph.D., Team Leader, CDER/OC/OMPQ/DGMPA/BMAB  
**Subject:** New Biologic License Application (BLA)  
**Applicant:** GlaxoSmithKline LLC  
**US License:** 1727  
**Facility:** [REDACTED] (b) (4)  
**Product:** albiglutide (Tanzeum)  
**Dosage:** single-use, sterile lyophilized cake in a clear glass dual chamber cartridge (DCC) for subcutaneous delivery (30 mg or 50 mg)  
**Indication:** Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus  
**PDUFA date:** April 15, 2014

**Recommendation:** The drug product part of this BLA, as amended, is recommended for approval from sterility assurance and product quality microbiology perspective with the following post-market commitments (PMC):

Develop and validate a reliable endotoxin test for the albiglutide drug product in-process and release samples and include worst-case hold conditions in the relevant containers.

Conduct studies to develop an understanding of the mechanism of low endotoxin recovery in the formulated drug substance and drug product.

The pending plan for future studies to understand low endotoxin recovery in endotoxin test for albiglutide will be evaluated in an addendum to this review memo.

**Review Summary**

GSK has submitted this Biologics License Application (BLA) for albiglutide, an agonist of the Glucagon-like peptide-1 (GLP-1) receptor for the treatment of adult type 2 diabetes mellitus (T2DM) patients, as an adjunct to diet and exercise. Albiglutide drug substance is manufactured at the GSK facility at Conshohocken, PA. Albiglutide drug product is manufactured at [REDACTED] (b) (4). This application contains CMC information in an eCTD format.

**Assessment**

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/s/  
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BO CHI  
01/06/2014

PATRICIA F HUGHES TROOST  
01/06/2014



Food and Drug Administration  
Center for Drug Evaluation and Research  
10903 New Hampshire Avenue,  
Building 51,  
Silver Spring, MD 20993

**Date:** December 17, 2013  
**To:** Administrative File, STN 125431/0  
**From:** Lakshmi Rani Narasimhan, Ph.D., CDER/OC/OMPQ/DGMPA/BMAB  
**Endorsement:** Patricia F. Hughes, Ph.D., Team Leader, CDER/OC/OMPQ/DGMPA/BMAB  
**Subject:** Biological License Application (BLA)  
**US License:** # 1727  
**Applicant:** GlaxoSmithKline, LLC  
**Mfg Facility:** (b) (4) 893 River Road, Conshohocken, PA 19428 (FEI # 3004055938)  
**Product:** Albiglutide (Tanzeum, proposed)  
**Dosage:** single-use, sterile lyophilized cake in a clear glass dual chamber cartridge (DCC) for subcutaneous delivery (30 mg or 50 mg of albiglutide)  
**Indication:** Treatment of Type-2 Diabetes Mellitus (T2DM) as an adjunct to diet and exercise to improve glycemic control in adults.  
**Due Date:** April 15, 2014

**Recommendation for Approvability:** The drug substance section of the BLA, as amended, is recommended for approval from a microbiology product quality perspective.

**SUMMARY:**

GlaxoSmithKline LLC submitted this BLA for albiglutide for the treatment of T2DM in adults. Albiglutide drug substance is manufactured by GlaxoSmithKline LLC, Conshohocken, Pennsylvania. The manufacturing of DCC albiglutide pen injector is performed at (b) (4). This review covers the evaluation of the drug substance aspects of the application from a microbiological control and microbiology product quality perspective.

This BLA was submitted in eCTD format and included Module 1.1.2 - FDA form 356h, Module 1.2-Cover letter, and Module 2 and 3. The original submission and the amendments submitted on March 5, 2013 (sequence # 0004), April 26, 2013 (sequence # 009), June 14, 2013 (sequence # 0019), July 12, 2013 (sequence #024), August 8, 2013 (sequence # 0026), August 16, 2013 (sequence # 028), and December 13, 2013 (sequence # 044) are also reviewed.

**INTRODUCTION**

GlaxoSmithKline LLC submitted a new biologics license application, STN 125431 to license albiglutide (Tanzeum, proposed) and the associated drug substance and drug product manufacturing facilities. Albiglutide, an agonist of the Glucagon-like peptide-1 (GLP-1) receptor acts on pancreatic beta cells to increase insulin production augmenting glucose-dependent insulin secretion. The proposed indication is for the treatment of adult T2DM patients, as an adjunct to diet and exercise (b) (4) to improve glycemic control. Albiglutide is administered via subcutaneous injection at a dose of 30 mg or 50 mg weekly.

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/s/  
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LAKSHMI RANI NARASIMHAN  
12/17/2013

PATRICIA F HUGHES TROOST  
12/18/2013