MEMORANDUM

Date: May 26, 2021

From: Marie J. Anderson
Quality Assurance Branch (QAB)
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: Biologics License Application Submission Tracking Numbers 125659/0

Subject: Review of Lot Release Protocol (LRP) Template for Plasminogen (Human) Intravenous

Through: Maryna Eichelberger, PhD, Director, DBSQC/OCBQ/CBER/FDA

Cc: Alexey Khrenov, PhD, Chair, BLA Review Committee,
DPPT/OTAT/CBER/FDA
Crystal Menendez, Regulatory Project Manager, DRPM/OTAT/CBER/FDA

Applicant: Prometics Biotherapeutics Inc.

Products: Plasminogen (Human) Intravenous
Trade Name - Ryplazim

1 General Information

1.1 CMC Review Identifiers and Dates

1.1.1 **Biologics License Application (BLA) Submission Tracking Number (STN):** 125659/0

1.1.2 **Submission received by CBER:** August 14, 2017; response to Complete Response (CR) letter: September 4, 2020

1.1.3 **Review completed:** May 26, 2021

1.1.4 **Material Reviewed:** BLA 125659/0 Module 3, Quality

1.1.5 **Related Master File, INDs and BLAs:** N/A

2 Executive Summary: The LRP template for Plasminogen (Human) Intravenous submitted in BLA 125659/0.30 on May 25, 2021 is acceptable for use. This product is for replacement therapy in pediatrics and adults with plasminogen deficiency.

3 Review

3.1 Documents Reviewed

LRP template for Plasminogen (Human) Intravenous submitted in BLA 125659/0 on August 14, 2017.

LRP template for Plasminogen (Human) Intravenous submitted in amendment 125659/0.27 on May 7, 2021

LRP template for Plasminogen (Human) Intravenous submitted in amendment 125659/0.30 on May 25, 2021

3.2 Review

On August 14, 2017 Prometics Biotherapeutics Inc. submitted BLA 125659/0 for Plasminogen (Human) Intravenous. The LRP template was reviewed by representatives of OTAT/DPPT and OCBQ/DBSQC. Comments were not made due to the issuance of the CR letter.

An IR for a revised LRP template was sent to Prometics Biotherapeutics Inc. on May 5, 2021.

CBER Comments

Please submit a revised lot release protocol template to include the revised drug product specifications as submitted in amendment 125659/0.25 on April 25, 2021.

Sponsor response

A revised lot release protocol was submitted.

The revised LRP template was submitted to amendment 125659/0.27 on May 7, 2021. This template was reviewed by OCBQ/DBSQC with comments.

CBER Comments

Throughout the document

Please include the following information at the top left corner of each page of the protocol:

cc: line – 125659 – 0/2065/FC or B
Licensed Name of Product - Plasminogen (Human) Intravenous tvmh
Lot Number –

Page 1

Please add a Reason for submission section in the upper right-hand corner of the protocol:

a) Reason for Submission

___ Release
___ Surveillance
___ Licensing Action,
STN – 125659/Supplement Number
___ Corrected Protocol

b. All tests conducted on this lot are reported and pass specifications as required.

Signature: _____ Date:_____

Printed name: _____ Title: Authorized Official

Please refer to Lot Release Protocol Template Page 1 example (Attachment 1)

Endotoxin

Please revise the endotoxin table to include the information per the attached template. (Attachment 2)

Sterility

Please revise the sterility table to include the information per the attached template. (Attachment 3)

3.3 Conclusions

The LRP template received May 26, 2021 in amendment 125659/0.30 is acceptable for use. This template may be used for future lot release submissions.

Attachment 1

cc: 000000 _0/Lic #/*C or –B or –FC*

Lot Number:
License Name of Product:

Submission

Reason For

__ For Release
__ For Surveillance
__ For Licensing Action
STN:
__ Corrected Protocol

Manufacturer Name:

Manufacturer Address:

Trade name:

Date of Manufacturing: 00/00/0000 Expiration Date: 00/00/0000

Label Strength: 00%

Source Material:

Processing Method:

Stabilizer:

Stabilizer:_____
Manufacturer / Lot Number

Other:

Reprocessing/Heating:

Fill Information

Filling Date: 00/00/0000

Location:

Total Volume: 000 mL Volume per Vial: 000 mL

Number of Vials filled: 0000 Number of Rejected Vials: 0000

Recommended Reconstitution Volume:

Storage Temperature:

All tests conducted on this lot are reported and pass specifications as required.

Signature: _____ Date:_____

Printed name: _____ Title: Authorized Official

Attachment 2

(b) (4)

Method ☐ **Turbidimetric** ☐ **Chromogenic**

Test date _____

Name of (b) (4) **Manufacturer** _____

(b) (4) **Lot number** _____

Standard Curve Information

Endotoxin lot number _____

Endotoxin Mfr/Supplier_____

Standard Curve *(performed for each analytical session)*

	Standard Endotoxin Concentration IU/mL	Mean Onset Time (seconds)	CV%
1			
2			
3			
4			
5			
6			

Correlation coefficient (r): _____ Intercept: _____ Slope: _____

Product Test Summary

MVD _____

	Results IU/mL	Test Dilution	Mean Onset Time	CV%	% Spike Recovery
Beginning					
Middle					
End					

Results (IU/mL): _____ Specifications: _____

Calculations or additional comments

Attachment 3

Sterility

Method used: _____
Type: for example, Viral Harvests, Bulk, Final Container
B&F Test Date:

On Test Date	Medium/Temperature	Tested Quantity	Off Test Date

Result:
Specification: