

**OCBQ SBRA Template as per CBER template T910.07, for STN  
[125755/0/0], [elivaldogene autoemcel], [bluebird bio, Inc.]**

**OCBQ review committee members:**

OCBQ/DBSQC reviewer(s) (or LIB Representative) (section 3.b and c): **Esmeralda Alvarado Facundo, Marie Anderson, Tao Pan, Most Nahid Parvin, Seth Schulte**

OCBQ/DMPQ reviewer(s) (section 3.d and e): **Wei Wang**

OCBQ/BMB reviewer(s) (section 6.b): **Colonious King**

OCBQ/APLB reviewer(s) (section 8): **Benjamin Cyge, Sonny Saini**

**Approved by Office Director:** August 18, 2022 (8/18/2022)

**From:** Debra Vause, RPM, OCBQ/DMPQ

**Forwarded to Product Office:** August 18, 2022 (8/18/2022)

**SBRA Section 3: Chemistry Manufacturing and Controls (CMC)**

**b) Testing specifications**

**DBSQC**

The analytical methods and their validations and/or qualifications reviewed for the SKYSONA drug substance and/or drug product were found to be adequate for their intended use, except for the outstanding issue for testing (b) (4) of the drug product. bluebird bio, Inc. has provided written commitment to resolve the issue as a Postmarketing Commitment.

**c) CBER Lot Release**

**DBSQC – CBER Lot Release**

An exemption has been granted from CBER Lot Release testing, including no requirement for submission of product samples to CBER. The basis for this decision is that SKYSONA is an autologous product; as such each lot will treat a single patient. Failure of a single lot will have minimal potential impact on public health.

**d) Facilities review/inspection**

**DMPQ**

Facility information and data provided in the BLA were reviewed by CBER and found to be sufficient and acceptable. Inspection histories and activities for facilities involved in the manufacture of eli-cel are summarized below.

**Manufacturing Facilities for SKYSONA**

<b>Name/Address</b>	<b>FEI Number</b>	<b>Waiver or Inspection</b>	<b>Justification and Results</b>
(b) (4)  <i>drug substance critical intermediates, BB305 LVV, manufacturing and testing</i>	(b) (4)	Waived	ORA (b) (4) VAI
<b>Lonza Houston, Inc.</b> 14905 Kirby Drive Houston, TX 77047 USA  <i>beti-cel drug substance and drug product manufacturing and testing</i>	3013629214	PLI	CBER February 14 -18, 2022 NAI
(b) (4)  <i>Drug product release testing</i>	(b) (4)	Waiver	ORA (b) (4) VAI
(b) (4)  <i>Drug product release testing</i>	(b) (4)	Waiver	ORA (b) (4) VAI
(b) (4)  <i>Drug product release testing</i>	(b) (4)	Waiver	ORA (b) (4) VAI
(b) (4)  <i>Drug product release testing</i>	(b) (4)	Waiver	ORA (b) (4) NAI
(b) (4)	(b) (4)	Waiver	ORA

Name/Address	FEI Number	Waiver or Inspection	Justification and Results
(b) (4)  <i>Drug product release testing</i>			(b) (4) VAI

CBER conducted a pre-license inspection (PLI) of the Lonza Houston, Inc. facility in February 2022. No FDA Form 483 was issued, and the inspection was classified as No Action Indicated (NAI).

Office of Regulatory Affairs (ORA) performed a surveillance inspection of (b) (4). All 483 issues were resolved, and the inspection was classified as voluntary action indicated (VAI).

ORA performed a surveillance inspection of (b) (4). All 483 issues were resolved, and the inspection was classified as VAI.

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ORA performed a surveillance inspection of (b) (4). No Form FDA 483 was issued, and the inspection was classified as NAI.

ORA performed a surveillance inspection of (b) (4). All 483 issues were resolved, and the inspection was classified as VAI.

#### e) Container Closure System

##### **DMPQ**

The container closure system (CCS) for eli-cel consists of a primary package container (a 20 mL (b) (4) Cryopreservation bag), a secondary package container (a (b) (4) Overwrap bag), and a tertiary metal package container (cryocassette). The eli-cel drug product (DP) is filled into (b) (4) bag(s) (e.g., 1 bag for 20 mL DP, or 2 bags for 40 mL DP). The (b) (4) bag is sterile and read-to-use (RTU, manufactured by (b) (4)). The product transfer tubing and sample tubing are sealed by (b) (4). Following visual inspection, a product label is applied to the bag, and the product bag is placed inside of a sterile RTU (b) (4) Overwrap (manufactured by (b) (4)). The overwrap bag is (b) (4). The product bag is inserted into a metal cassette that has been labeled with a label containing both product and patient

information. The container-closure integrity (CCI) was tested using a (b) (4) method by (b) (4) to determine the primary package container is able to maintain the container integrity under normal use, storage and transportation conditions.

The BLA was missing information about the (b) (4) Cryopreservation bag, which resulted in several PMCs and a PMR.

## **SBRA Section 6: Clinical /Statistical**

### **b) Bioresearch Monitoring (BIMO) – Clinical/Statistical/Pharmacovigilance**

#### **BIMO**

Bioresearch Monitoring (BIMO) inspection assignments were issued for the Sponsor and two clinical investigators (CI) participating in the conduct of Protocols ALD-102 and ALD-104 in support of this original Biologics License Application (BLA). The CI inspection reports are still pending. A review of the EIR for the Sponsor inspection did not reveal problems that impact the data submitted in this BLA.

## **SBRA Section 8: Labeling**

#### **APLB**

The proposed proprietary name, SKYSONA, was reviewed by the Advertising and Promotional Labeling Branch (APLB) on December 2, 2021, and was found acceptable. CBER communicated the acceptability of the proprietary name to the applicant on December 8, 2021.

The Advertising and Promotional Labeling Branch (APLB) reviewed the proposed Prescribing Information, Patient Package Insert, and package and container labels on August 9, 2022, and found them acceptable from a promotional and comprehension perspective.