From:	Ahmed, Narin
To:	Giordano, Erica; Patel, Manisha
Cc:	Riggins, Cindy
Subject:	RE: BL 125646 DSCSA Exemption Request
Date:	Tuesday, April 25, 2017 3:09:13 PM
Attachments:	response-fda-20170425.pdf
Sensitivity:	Confidential

Dear Erica,

Attached please find the response to FDA's below request for information. This will be submitted as an amendment to the BLA by the end of this week. We will also submit a revised DSCSA Exemption Request by next week.

Please let me know if you have any questions.

Best regards,
Narin

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From: Giordano, Erica [mailto:Erica.Giordano@fda.hhs.gov]
Sent: Monday, March 13, 2017 1:28 PM
To: Patel, Manisha <manisha.patel@novartis.com>
Cc: Riggins, Cindy <cindy.riggins@novartis.com>; Ahmed, Narin <narin.ahmed@novartis.com>
Subject: BL 125646 DSCSA Exemption Request
Sensitivity: Confidential

Good afternoon,

FDA's Center for Biologics Evaluation and Research (CBER) has reviewed the letter dated February 27, 2017 from Louis Francis to Connie Jung, R.Ph., Ph.D., Center for Drug Evaluation and Research (CDER), in which an exemption from the requirements of the Drug Supply Chain Security Act (DSCSA) was requested (letter attached below). We also reviewed related submissions to your Biologics License Application (STN 125646), including the draft Prescribing Information, the mock product label, and the document titled, "Overview of Chain of Identity."

Please be aware the DSCSA exemption request was sent to CDER. All future correspondence should be sent directly to the BLA in OTAT by the authorized contact. The FDA will not be able to provide a definitive answer by March 17, 2017, as requested, due to insufficient

information and clarify of the request. Our questions and requests for additional information relating to your DSCSA exemption request are detailed below.

The scope of Novartis' DSCSA exemption request is unclear. For example, it is not clear whether Novartis is requesting an exemption from all of the applicable requirements under the DSCSA or only certain labeling requirements.

We recommend that Novartis submit a revised exemption request to its BLA, as product correspondence, that specifies each requirement under DSCSA for which an exemption is being requested and provide a justification for each.

We note that the mock product label provided in your application contains a placeholder for a 2-D barcode, but there are no details as to what information will be embedded in the 2D-barcode. Please specify which data elements you intend to include in the 2D bar code data carrier. As you may be aware, section 582 (b)(2) of the DSCSA requires that manufacturers put a unique product identifier on prescription drug packages no later than November 27, 2017, that consists of the standardized numerical identifier (SNI) (meaning the National Drug Code combined with a unique alphanumeric serial number), the lot number, and the expiration number.

We note that the mock product label provided in your application does not include the lot number or expiration date, as required under 21 CFR 610.60 and 610.61. Please explain how these two data elements will be incorporated on the container label.

Although the Bar Code Label Requirements under 21 CFR 201.25 are referenced in your application, it is not clear whether Novartis is also requesting an exemption from these requirements. For example, your mock product label contains a placeholder for a linear barcode, but there are no details as to what information will be embedded in this linear barcode.

If Novartis is also seeking an exemption from the linear barcode requirements, we recommend that Novartis submit a separate exemption request to its BLA, as product correspondence, that, as required under 21 CFR 201.25(d), documents why:

compliance with the bar code requirement would adversely affect the safety, effectiveness, purity or potency of the drug or not be technologically feasible, and the concerns underlying the request could not reasonably be addressed by measures such as package redesign or use of overwraps; or

an alternative regulatory program or method of product use renders the bar code unnecessary for patient safety.

Figure 13-1, titled "Overview of Maintaining Chain of Identity in Commercial Setting," included with your submission to the BLA, appears to indicate the use of various patient and product identifiers such as:

Name and DOB

ISBT-DIN# or unique identifier

Non-ISBT hang tag

AplhaData form with Chain of Identification (COI), name, DOB, DIN

Batch ID #

Final product labeling and COI with name, DOB, Batch ID#

Group Batch ID

Certificate of conformance with batch ID and DIN

Because of these various identifiers, it is not clear whether Novartis has established a COI system that will ultimately provide a single unique identifier.
We recommend that Novartis include more detailed information to explain the data elements of each identifier, the rationale for use of ISBT DIN and non-ISBT DIN, why each variable identifier is needed (e.g., batch ID vs. group batch ID), and whether Novartis has established a COI system that will ultimately provide a single, unique identifier for the final product. Please explain at what time point the unique identifier is assigned, when and how it follows the product between facilities and patient services (e.g., does the unique identifier travel with the ISBT-128 or non-ISBT 128 label or does it replace these labels during each subsequent routing of product), the alpha-numeric character limits for the each identifier, and whether the unique identifier be provided in both human-readable and machine-readable format on the final product label.
It is unclear what information will be included in the "bill of materials" and whether Novartis intends for this record to serve as documentation for tracking and/or tracing the product. Moreover, in the letter February 27, 2017 Novartis explains that a "Bill of Lading" and the product labeling will contain a unique patient (but not product) identifier.

We recommend that Novartis provide detailed information to explain what information will be included on bill of materials and the intended purpose served by this documentation. Also, please explain whether the bill of materials and Bill of Lading are or are not the same document and if the intended purpose of each document (bill of materials and Bill of Lading) are or are not the same.

Novartis explains in the draft Prescribing Information that there will be a label on the product, and separate product and patient specific labels will be located inside the Dewar, however, there is no explanation regarding the type of information that will be included.

We recommend that Novartis provide detailed information to explain what information will be included on these internal package labels. Mock label(s) should also be included.

Novartis explains in their proposed Prescribing Information that the product "is shipped directly to the cell lab associated with the infusion center," and your letter dated February 27, 2017 states that Novartis "will drop ship each dose by courier directly to the hospital where it will be infused into the patient," however, the February 27, 2017 letter also states "Novartis plans to market CTL019 through a specialty wholesaler, but the specialty wholesaler will never take possession of the product."

Please explain the role of the specialty wholesaler. Is the specialty wholesaler also serving as a logistic center (e.g., responsible for scheduling of patient apheresis and shipments of product).

Please indicate whether there is a transfer of ownership to the specialty wholesaler.

Please confirm receipt of this notification and let me know if a teleconference is needed to

provide clarification on any of the comments above.

Thank you,

Erica Giordano
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