BLA 761340/Original 1

BLA APPROVAL

Samsung Bioepis Co., Ltd.
c/o Biologics Consulting Group, Inc.
Attention: Yelena Vaydman, MS, RAC
US Agent
100 Daingerfield Road
Suite 400
Alexandria, VA 22314

Dear Yelena Vaydman:

Please refer to your biologics license application (BLA) dated and received April 21, 2023, and your amendments, submitted under section 351(k) of the Public Health Service Act for Epysqli (eculizumab-aagh) intravenous (IV) injection.

We acknowledge receipt of your major amendment dated April 8, 2024, which extended the goal date by three months.

This BLA seeks licensure of Epysqli (eculizumab-aagh) 300 mg/30 mL (10 mg/mL) injection, for IV use in a single-dose vial (vial) as (b) (4) US-Soliris (eculizumab) 300 mg/30 mL (10 mg/mL) injection, for IV use in a vial.

Epysqli seeks licensure as (b) (4) US-Soliris for the following indications:

- The treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis, and

- The treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

For administrative purposes, we have split BLA 761340 into the following applications:

- BLA 761340/Original 1 – Epysqli (eculizumab-aagh):

    - Epysqli 300 mg/30 mL (10 mg/mL) injection, for IV use in a vial seeking biosimilarity to US-Soliris 300 mg/30 mL (10 mg/mL) injection, for IV use in a vial.

(b) (4)

LICENSING

We have approved your BLA for Epysqli (eculizumab-aagh) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Epysqli under your existing Department of Health and Human Services U.S. License No. 2046. Epysqli is indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis and the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture eculizumab-aagh drug substance at (b) (4). The final formulated drug product will be manufactured and filled at Samsung Biologics Co. Ltd., Incheon, Republic of Korea. The filled drug product will be labeled and packaged at (b) (4). You may label your product with the proprietary name, Epysqli, and market it in 300 mg/30 mL (10 mg/mL) single-dose vial, injection, for IV use.

DATING PERIOD

The dating period for Epysqli shall be 36 months from the date of manufacture when stored at 5 ± 3ºC, protected from light. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored (b) (4) (b) (4).

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Epysqli to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Epysqli, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As (October 2009)*.[2]

The SPL will be accessible via publicly available labeling repositories.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761340**." Approval of this submission by FDA is not required before the labeling is used.

[1] See http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

This product is appropriately labeled for use in all relevant pediatric populations. Therefore, no additional pediatric studies are needed at this time.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4619-1 Perform real-time drug product commercial container closure system leachate studies using appropriate test methods to identify and quantify volatile organic compounds (VOC), semi-VOC, non-VOC, and trace metals at regular intervals through the end of shelf life. The study results will be updated annually in the BLA Annual Report. The final results of this study and the toxicology risk evaluation for the levels of leachates detected in the drug product will be provided in the final study report to the BLA.

Final Report Submission: 07/2026

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the Food Drug Cosmetic Act (FDCA) authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks.

In accordance with section 505-1 of FDCA, we have determined that a REMS is necessary for Epysqli to ensure the benefits of the drug outweigh the risk of serious meningococcal infections.

Your proposed REMS must also include the following:

Elements to assure safe use: Pursuant to 505-1(f)(1), we have also determined that Epysqli can be approved only if elements necessary to assure safe use are required as part of the REMS to mitigate the risk of **serious meningococcal infections** listed in the labeling of the drug.

Your REMS includes the following elements to mitigate this risk:

- Healthcare providers have particular experience or training, or are specially certified
- Pharmacies or health care settings that dispense the drug are specially certified
- The drug is dispensed to patients with evidence or other documentation of safe-use conditions

Implementation System: The REMS must include an implementation system to monitor, evaluate, and work to improve the implementation of the elements to assure safe use (outlined above) that require: pharmacies or health care settings that dispense the drug be specially certified **and** the drug be dispensed to patients with documentation of safe use conditions.

Your proposed REMS, submitted on April 21, 2023, amended and appended to this letter, is approved.

The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your REMS must be fully operational before you introduce Epysqli into interstate commerce.

The REMS assessment plan must include, but is not limited to, the following:

For each metric, provide the two previous, current, and cumulative reporting periods (where applicable) unless otherwise noted.

Program Implementation and Operations

1. REMS Implementation (for the first REMS assessment only)
    a. Date of first commercial distribution of Epysqli
    b. Date of Epysqli REMS launch
    c. Date when the Epysqli REMS website became live and fully operational
    d. Date when healthcare providers (HCPs) who can prescribe could become certified in the Epysqli REMS
    e. Date when healthcare settings and pharmacies could become certified in the Epysqli REMS
    f. Date when wholesalers/distributors were authorized to distribute the drug (i.e., first order placed)
    g. Date of first healthcare prescriber certification
    h. Date of first healthcare setting and pharmacy certification
    i. Date when the REMS Call Center was established and fully operational

2. REMS Certification and Enrollment Statistics
    a. Healthcare provider (HCP) Certification
        i. The number of HCPs certified: total, newly certified, and active (prescribed Epysqli at least once during the reporting period) stratified by credentials (e.g., Doctor of Medicine, Doctor of Osteopathic Medicine, Advanced Practice Registered Nurse, Physician Assistant), medical specialty (e.g., Hematology/Oncology, Immunology, Internal medicine, Nephrology, Neurology, Rheumatology, and Other), and geographic region (as defined by US Census)
        ii. Method of certification (e.g., fax, online)
        iii. Number of HCPs who were unable to become certified, accompanied by a summary of the reason(s) why they were unable to be certified
    b. Healthcare Setting and Pharmacy Certification
        i. Identity and numbers of each healthcare setting and pharmacy certified: total, newly certified and active (dispensed Epysqli at least once during the reporting period) stratified by pharmacy or healthcare setting type, (e.g., hospital, specialty pharmacy), and geographic region (as defined by US Census)
        ii. Method of healthcare setting and pharmacy certification (e.g., fax, online)
        iii. Number of healthcare settings and pharmacies that were unable to become certified, accompanied by a summary of the reason(s) why they were unable to be certified
    c. Wholesaler/Distributors
        i. Numbers contracted: total, newly contracted, and active (distributed Epysqli at least once during the reporting period)

3. Patient Statistics
    a. The number and percent of new patients treated with Epysqli
    b. The number of patients treated with Epysqli stratified by sex, age, diagnosis, and geographic region (as defined by US Census)

4. Epysqli Utilization Data
    a. The number of Epysqli shipments sent to healthcare settings and pharmacies, overall, and stratified by quantity per shipment and by geographic region (as defined by US Census)

b. For certified healthcare settings and pharmacies, number of prescriptions dispensed stratified by:
    i. Prescriber specialty, degree/credentials, and geographic region
    ii. Patient demographics (e.g., age, sex), and geographic region (as defined by US Census)
    iii. Whether the prescription was new or a refill
c. Percentage (%) of Epysqli dispenses corresponding to prescriptions written by REMS certified HCPs
d. The number of prescriptions not dispensed, accompanied by a listing and summary of all reasons for not dispensing the prescription (e.g., HCP not certified, REMS related issue)
e. For wholesalers/distributors, the number of orders distributed

5. REMS Compliance
    a. A summary report of non-compliance identified, associated corrective and preventive action (CAPA) plans, and the status of CAPA plans. Provide a summary of non-compliance identified, including, but not limited to:
        i. A copy of the non-compliance plan, including the criteria for determination of non-compliance for each stakeholder, actions taken to address non-compliance for each case, and what events led to suspension or decertification from the REMS
        ii. The number of instances of noncompliance accompanied by a description of each instance and the reason for the occurrence (if provided). For each instance of non-compliance, report the following information:
            a) The unique ID(s) of the stakeholder(s) associated with the noncompliance event or deviation to enable tracking over time
            b) The source of the noncompliance data
            c) The results of root cause analysis
            d) What action(s) were taken in response
        iii. The number and percentage of prescribers who prescribed Epysqli but were not certified
        iv. The specific reasons why prescribers were not certified at the time of prescribing (e.g., emergency use, etc.), and whether these prescribers subsequently became certified

v. The number and percentage of drug distributions to healthcare settings and pharmacies who obtained Epysqli that were not certified

vi. The specific reasons for the drug distributions to healthcare settings and pharmacies that were not certified

vii. The number of healthcare settings and pharmacies who became decertified, accompanied by a summary of reasons for decertification

6. Audits: Summary of audit activities including but not limited to:

   a. A copy of the audit plan used for each audited stakeholder type (i.e., healthcare settings, pharmacies, REMS Call Center, and wholesalers-distributors)

   b. The number of audits expected, and the number of audits performed for each stakeholder

   c. The number and category of observations noted, stratified by category

   d. A unique ID for each stakeholder that had observations to track observations by stakeholder over time

   e. Documentation of completion of training for relevant staff

   f. A summary report of documented processes and procedures for complying with the REMS requirements including how certified healthcare settings and pharmacies obtain patient vaccination status

   g. Verification that at each audited healthcare setting and pharmacy, a designated Authorized Representative is certified, and certification is up to date. If the Authorized Representative changes, include the number of new Authorized Representatives and verification of the healthcare setting's and pharmacy's recertification.

   h. Describe any corrective actions taken for any non-compliance (audit observation) identified during the audits as well as preventative measures that were developed from uncovering these non-compliance events

      i. For those with deficiencies noted, report the number that successfully completed a CAPA plan by the due date

      ii. For any that did not complete the CAPA by the due date, describe additional actions taken

7. REMS Infrastructure and Performance

   a. REMS Website

      i. Number of visits and unique visits to the REMS Website

      ii. Number of REMS materials downloaded or printed for each material

b. REMS Call Center Report

i. Number of contacts by stakeholder type (patient/caregiver, healthcare provider, healthcare setting, pharmacy, etc.)

ii. A table summarizing the reasons for calls (e.g., certification question) by stakeholder type

iii. If the reason for the call(s) indicates a complaint, provide details on the nature of the complaint(s), and whether they indicate potential REMS burden or patient access issues

iv. A summary report of corrective actions resulting from issues identified

Safe Use Behaviors

8. Safe Use Behaviors

Determination of patients' vaccination and antibacterial drug prophylaxis compliance is made using data collected via the certified healthcare settings and pharmacies documenting the patient's vaccination status.

a. Methods utilized to determine whether or not patients received meningococcal vaccinations in accordance with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients receiving a complement inhibitor. Include vaccine serogroup, dosing (i.e., first vaccine dose, second vaccine dose and booster doses), and timing of the vaccinations, when the information is provided.

b. Data on the number and percentage of new patients treated with Epysqli who report receiving meningococcal vaccination(s) out of the total number of patients who received Epysqli. Of those who reported receiving meningococcal vaccinations, provide the number and percentage of patients who:

i. Received vaccinations in accordance with the most current ACIP recommendations for meningococcal vaccinations in patients receiving a complement inhibitor

ii. Did not receive vaccinations in accordance with the most current ACIP recommendations for meningococcal vaccinations in patients receiving a complement inhibitor

c. Data on the number and percentage of new patients treated with Epysqli who reported not receiving meningococcal vaccination(s) out of the total number of patients who received Epysqli

d. Whether the patient received antibacterial drug prophylaxis, and timing of antibacterial drug prophylaxis in relation to the dosing of Epysqli (if available)

e. If any of the above information is missing, the reasons why this information is missing such as:
    i. Healthcare provider records do not include this information
    ii. Healthcare provider declined to provide information
    iii. Healthcare provider did not respond to healthcare setting/pharmacy queries

f. The number and percentage of new patients treated with Epysqli who completed or were up to date with meningococcal vaccinations (against all of the following serogroups: A, C, W, Y, and B), as per the most current ACIP recommendations in patients receiving a complement inhibitor at the time of first dose

g. Number and percentage of patients dispensed Epysqli who received at least one dose of meningococcal vaccines (against all of the following serogroups: A, C, W, Y, and B) according to the most current ACIP recommendations in patients receiving a complement inhibitor and antibacterial drug prophylaxis, if needed, before the first dispense

h. For patients who were not initially up to date with meningococcal vaccines when starting treatment, report the number and percentage who, up to 6 months after the first dose:
    i. Completed meningococcal vaccines
    ii. Did not complete meningococcal vaccines but were receiving antibacterial drug prophylaxis
    iii. Vaccination status was unknown after completed follow-up attempts

Health Outcomes and/or Surrogates of Health Outcomes

9. Summary of cases of meningococcal infections in patients receiving Epysqli
    a. For US cases of meningococcal infections, cases are summarized as follows:
        i. In the most recent Periodic Safety Update Report (PSUR) submitted to the Epysqli Biologics License Application (BLA) with a link to that PSUR corresponding with the reporting interval
        ii. Cumulative listing of all U.S. cases of meningococcal infections from approval to include cases identified during the current reporting period
    b. For each US case of meningococcal infection, provide the following information:
        i. MedWatch or other case report number

ii. Date of event and date of report to FDA

iii. Patient age, race, and sex

iv. Indication for Epysqli treatment

v. Meningococcal vaccination status:

a) Date of vaccine(s) (i.e., all of the meningococcal vaccines doses (serogroups: A, C, W, Y, and B) that a patient receives including the first vaccine dose, second vaccine dose, and booster doses)

b) Name of vaccine(s)

c) Timing in relation to Epysqli (i.e., the dates or duration that a patient receives Epysqli in relation to the meningococcal vaccine(s))

d) ACIP compliance and antibacterial drug prophylaxis status

1) Antibacterial drug prophylaxis regimen

2) Timing (i.e., include the dates or duration that a patient receives Epysqli in relation to antibacterial drug prophylaxis)

e) Clinical course

1) Outcome and causative meningococcal serogroup

2) Source of the vaccine information when available. For information that is not available (listed as “unk” or “unknown”) the number and type (patient, prescriber, etc.) of outreach attempts made to obtain the information for each case. Also, if the information is not available, a narrative is presented explaining why the information is unknown (“unk”) or unavailable for each reported case.

vi. Whether or not the patient was administered antibacterial drug prophylaxis and if so:

a) The specific antibacterial drug, antibacterial drug regimen (dose/frequency/duration), and route(s) of administration

b) The timing of the course of the antibacterial drug prophylaxis in relation to Epysqli treatment

vii. Summary of clinical course and the outcome; specifically whether the patient:

a) Was admitted to an intensive care unit

b) Experienced any organ system failure, such as (but not limited to) requiring mechanical ventilation or medication (vasopressors) to support blood pressure

c) Died

viii. The length of time between onset of symptoms and when the patient presented for medical evaluation (if available)

ix. Causative meningococcal serogroups

x. Whether the **Patient Safety Card** was presented during the process of the patient seeking treatment

c. For each non-US case of meningococcal infection, provide the following information:

i. Case report number

ii. Patient age and sex

iii. Indication for Epysqli treatment

iv. Meningococcal vaccination status if known

v. Outcome

vi. If associated with any clinical trials

10. Meningococcal Infections Rate (per year and cumulatively)

a. Among patients who received Epysqli in the US and worldwide:

i. The number of reported cases of meningococcal infections per 100,000 patient-years of postmarketing exposure to Epysqli; reporting rate will be summarized cumulatively since the approval of Epysqli and stratified by year and relevant age subgroups (≤ 18 years, 19-55 years, and >55 years)

Knowledge

11. Knowledge

a. Stakeholder surveys for prescribing HCPs and patients (beginning with the 1-year REMS Assessment Report and provided for each reporting period annually thereafter)

i. Assess HCP and patient awareness regarding:

a) Patients are vaccinated against meningococcal infections caused by *Neisseria meningitidis* serogroups A, C, W, Y, and B prior to starting therapy according to the most current ACIP recommendations in patients receiving a complement inhibitor and receive antibacterial drug prophylaxis if needed

b) The early signs and symptoms of meningococcal infections

c) The need for immediate medical evaluation

Overall Assessment of REMS Effectiveness

12. The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

If the information provided in an assessment is insufficient to allow FDA to determine whether the REMS is meeting its goals or whether the REMS must be modified, FDA may require the submission of a new assessment plan that contains the metrics and/or methods necessary to make such a determination. Therefore, FDA strongly recommends obtaining FDA feedback on the details of your proposed assessment plan to ensure its success. To that end, we recommend that methodological approaches, study protocols, other analysis plans and assessment approaches used to assess a REMS program be submitted for FDA review as follows:

i. Submit your proposed audit plan and non-compliance plan for FDA review within 60 days of this letter.

ii. Submit your proposed protocol for the knowledge survey(s) for FDA review within 90 days of this letter.

Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

BLA 761340 REMS ASSESSMENT METHODOLOGY
(insert concise description of content in bold capital letters, e.g., **ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT PLAN, DRUG USE STUDY)**

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A). This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new, proposed indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of the last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing a REMS modification*, provide a rationale for why the REMS does not need to be modified.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

BLA 761340 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR BLA 761340/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 761340/S-000

PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 761340/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 761340/S-000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISION FOR BLA 761340

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling*.

For additional information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements at 21 CFR 600.81.

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

If you have any questions, call May Zuwannin, Regulatory Project Manager, at 301-796-7775.

Sincerely,

{See appended electronic signature page}

Tanya Wroblewski, MD
Deputy Director
Division of Nonmalignant Hematology
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling
- REMS

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

TANYA M WROBLEWSKI
07/19/2024 08:56:00 PM