Our STN: BL 125822/0

BLA APPROVAL
September 26, 2025

Kedrion S.p.A.
Attention: Erin Stokes, PhD
Parker Plaza
400 Kelby Street, 11th Floor
Fort Lee, NJ 07024

Dear Dr. Stokes:

Please refer to your Biologics License Application (BLA) received September 26, 2024, submitted under section 351(a) of the Public Health Service Act (PHS Act) for immune globulin intravenous, human-kthm 10% solution.

LICENSING

We have approved your BLA for immune globulin intravenous, human-kthm 10% solution effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, immune globulin intravenous, human-kthm 10% solution under your existing Department of Health and Human Services U.S. License No. 1851. immune globulin intravenous, human-kthm 10% solution is indicated for the treatment of adults with primary humoral immunodeficiency.

The review of this product was associated with the following National Clinical Trial (NCT) number: NCT01581593.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture immune globulin intravenous, human-kthm 10% solution drug substance at Kedrion S.p.A. (referred also as Kedrion (b) (4) . The final formulated product will be filled, labeled, and packaged at Kedrion S.p.A. (referred also as Kedrion BOL), Via Provinciale, Bolognana, Lucca, Italy 55027.

You may label your product with the proprietary name QIVIGY and market it in 50 mL and 100 mL fill sizes.

ADVISORY COMMITTEE

We did not refer your application to the Cellular, Tissue, and Gene Therapies Advisory Committee because our review of information submitted in your BLA, including the

clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for immune globulin intravenous, human-kthm 10% solution shall be 36 months from the date of manufacture when stored at 2°C -8°C (36°F - 46°F). The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency.

FDA LOT RELEASE

Please submit protocols showing results of all applicable tests. You may not distribute any lots of products until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, 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 the Director, Office of Compliance and Biologics Quality, electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations :

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of immune globulin intravenous, human-kthm 10% solution or in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including the Package Insert submitted via email on September 26, 2025 and the draft package labels submitted under amendment 77 dated September 25, 2025, and container labels submitted under amendment 73, dated September 23, 2025 .

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert submitted via email on September 26, 2025. 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* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

PACKAGE AND CONTAINER LABELS

Please electronically submit final printed package and container labels identical to the package labels submitted on September 25, 2025 and container labels submitted on September 23, 2025 according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA, 125822/0 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112

Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and you must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports and FDA's Adverse Event reporting System website at https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at https://www.fda.gov/vaccines-blood-biologics/lot-release/lot-distribution-database-ldd.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages < 2 years of age because necessary studies are impossible or highly impracticable. This is because primary humoral immunodeficiency is rarely diagnosed in this age group.

We are deferring submission of your pediatric study for ages 2 to less than 17 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) is a required postmarketing study. The status of this postmarketing study must be reported according to 21 CFR 601.28 and section 505B(a)(4)(C) of the FDCA. In addition, section 506B of the FDCA and 21 CFR 601.70

require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

Label your annual report as an "**Annual Status Report of Postmarketing Study Requirement/Commitments**" and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. This required study is listed below:

1. Deferred pediatric study under PREA for the treatment of primary immune deficiency in pediatric patients ages 2 years to less than 17 years.

   Final Protocol Submission: December 30, 2025

   Study/Trial Completion: April 30, 2026

   Final Report Submission: July 30, 2026

Submit the protocol to your IND 18648, with a cross-reference letter to this BLA, STN BL 125822 explaining that this protocol was submitted to the IND.

Submit final study reports to this BLA STN BL 125822. In order for your PREA PMR to be considered fulfilled, you must submit and receive approval of either an efficacy or a labeling supplement. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated as **Required Pediatric Assessment.**

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

We acknowledge your written commitments as described in your letter of March 17, 2025 as outlined below:

2. Kedrion commits to providing validation of (b) (4) as a Post Marketing Commitment (PMC). The validation report will be submitted as a "Postmarketing Commitment – Final Study Report by December 31, 2025. Please include the (b) (4) in your final study report.

   Final Study Report Submission: December 31, 2025

We acknowledge your written commitment as described in your letter of July 24, 2025, as outlined below:

3. Kedrion commits to establish a final container action limit for (b) (4) using (b) (4) methodology. These limits will be determined following evaluation of at least (b) (4) lots collected over a (b) (4). When action limits are exceeded, Kedrion commits to investigating root cause and determining corrective and preventative actions as applicable. (b) (4) in final container will be measured and reported for information only. The method procedure for quantitation of (b) (4) will be submitted for evaluation in a Postmarketing Commitment – Status Update by December 31, 2026. The method validation and the action limits for (b) (4) in final container will be submitted as a Prior Approval Supplement Postmarketing Commitment - Final Study Report by December 31, 2027.

   Final Study Report Submission: December 31, 2027

We acknowledge your written commitments as described in your letter of August 5, 2025, as outlined below:

4. Kedrion commits to performing a concurrent (b) (4) validation study for the (b) (4). The interim results of the studies will be submitted annually in an Annual Report. Kedrion commits to notifying the FDA of any (b) (4) failures within 45 days of the occurrence, as a *Postmarketing Commitment Submission – Status Update*. The final validation study reports will be submitted as a Changes Being Effected (CBE) supplement no later than December 31, 2026

   Final Study Report Submission: December 31, 2026

5. Kedrion commits to submitting a final validation study report to confirm the proposed maximum (b) (4) as a Changes Being Effected (CBE) supplement by December 31, 2026. Kedrion commits to notifying the FDA of any (b) (4) failures within 45 days of the occurrence as a *Postmarketing Commitment Submission – Status Update.*

   Final Study Report Submission: December 31, 2026

6. Kedrion commits to (b) (4) method for (b) (4) for Drug Product. The method standard operating procedure (SOP) and the final validation study report will be submitted as a Prior Approval Supplement (PAS) no later than March 31, 2027.

Final Report Submission: March 31, 2027

We acknowledge your written commitments as described in your letters of August 19, 2025, as outlined below:

7. Kedrion commits to submitting stability study data for lots (b) (4) annually as a Post-marketing Commitment Submission-Status Update. Within three months after the completion of the study, a final stability report will be submitted as a Post-marketing Commitment Submission-Final Study Report by 30 June 2027.

   Kedrion commits to reporting all stability failures within 45 days of the occurrence as a Post-Marketing Commitment Submission - Status Update.

   Final Study Report Submission: June 30, 2027

8. Kedrion commits to providing the (b) (4) by December 31, 2025. The analytical results for (b) (4) samples will be provided as well in the qualification summary report.

   Kedrion commits to providing the available results of the long-term (b) (4) months) and accelerated stability study (b) (4) months, completed) for these samples by June 30, 2026. The complete stability results for long term stability study (36 months) these samples will be provided at the end of the study (Reference document STS-186-R, expected due date by 31 July 2028).

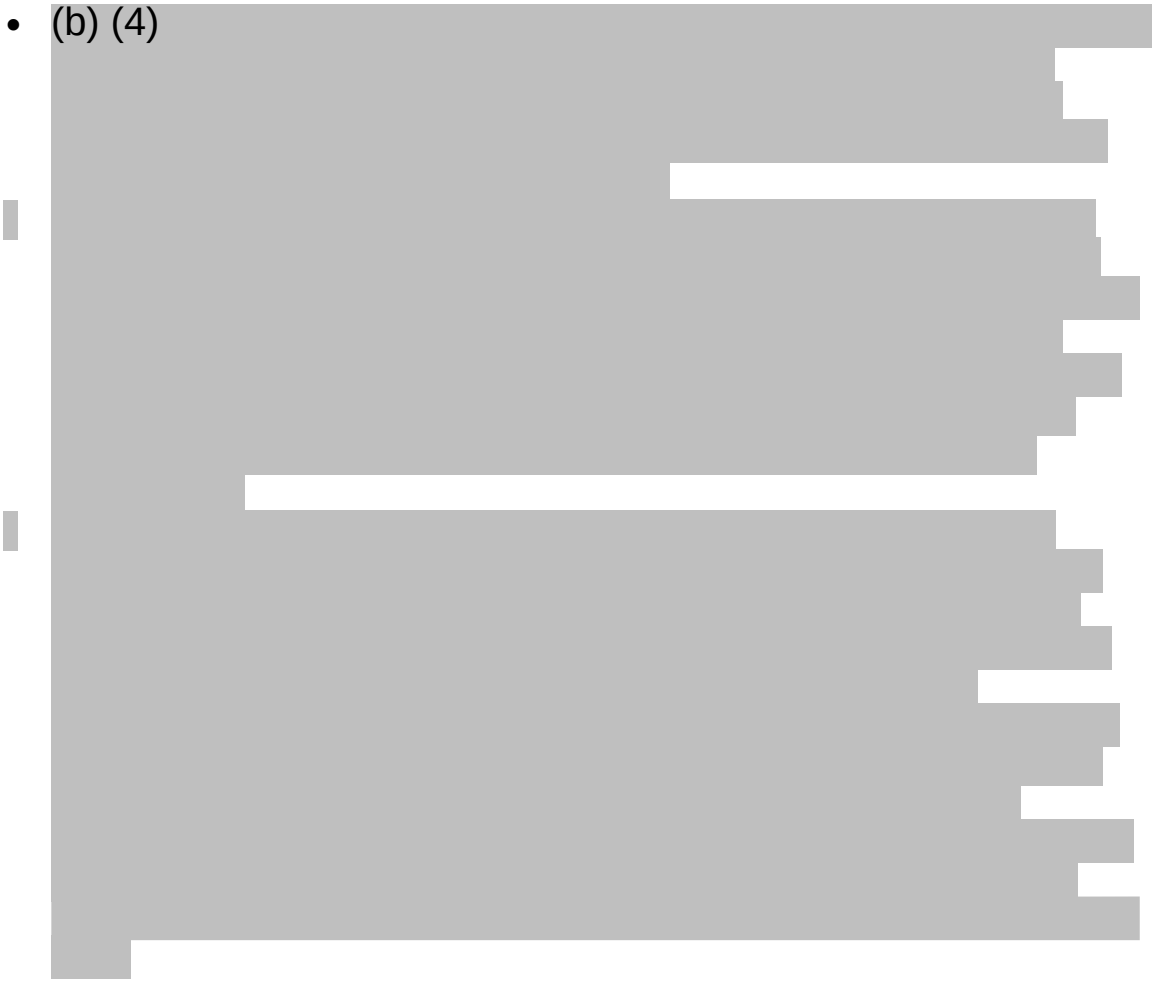
   Final Study Report Submission (qualification summary report (b) (4)-1427-R): December 31, 2025

   Final Study Report Submission (stability study report STS-186-R): July 31, 2028

We acknowledge your written commitment as described in your letter of August 22, 2025, as outlined below:

9. Kedrion commits to performing an (b) (4) validation under worst-case conditions. A final study report will be submitted as a Post-marketing Commitment Submission-Final Study Report by February 28, 2027. The validation study will include but not be limited to the following information:
   - (b) (4)

- (b) (4)



Final Study Report Submission: February 28, 2027

We acknowledge your written commitment as described in your letter of August 28, 2025, as outlined below:

10. Kedrion commits to evaluate (b) (4) . Kedrion proposes to submit data on (b) (4) and the relevant assessment as a Post-Marketing Commitment by December 31, 2026.

    Final Study Report Submission: December 31, 2026

We request that you submit information concerning nonclinical and chemistry, manufacturing, and control postmarketing commitments and final reports to your BLA, STN BL 125822. Please refer to the sequential number for each commitment.

Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Postmarketing Commitment – Status Update**. The status report for each commitment should include:

- the sequential number for each study as shown in this letter;
- the submission number associated with this letter;
- describe what has been accomplished to fulfill the non-section 506B PMC; and,
- summarize any data collected or issues with fulfilling the non-section 506B PMC.

When you have fulfilled your commitment, submit your final report as **Postmarketing Commitment – Final Study Report** or **Supplement contains Postmarketing Commitment – Final Study Report**.

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

Asha Das, MD
Acting Director
Office of Clinical Evaluation
Office of Therapeutic Products
Center for Biologics Evaluation and Research