Our STN: BL 125661/0

BLA FILING NOTIFICATION
October 23, 2017

Bayer Healthcare, LLC
Attention: Michelle Meng, MD
100 Bayer Boulevard
PO Box 915
Whippany, NJ 07981-0915

Dear Dr. Meng:

This letter is in regard to your Biologics License Application (BLA) received on August 30, 2017, under section 351(a) of the Public Health Service (PHS) Act for Antihemophilic Factor (Recombinant), PEGylated.

We also refer to your amendments dated October 4, 2017, October 10, 2017, and October 23, 2017.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Under 21 CFR 601.2(a), this application is considered filed today. The review classification for this application is **Standard**; the review action due date is August 30, 2018. This acknowledgment of filing does not mean that we have issued a license nor does it represent any evaluation of the adequacy of the data submitted.

This application is also subject to the provisions of "the Program" under the Prescription Drug User Fee Act (PDUFA) (refer to http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm)

We are reviewing your application according to the processes described in the guidance for review staff and industry: *Good Review Management Principles and Practices for PDUFA Products* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079748. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). We plan to hold our internal mid-cycle review meeting on February 12, 2018. Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by July 31, 2018.

At this time, we are still assessing if we will be discussing this application at an Advisory Committee meeting. We expect to notify you of a decision shortly.

While conducting our filing review, we identified the following potential review issues:

1. The following Information Requests (IRs) pertain to module 1.16, Pharmacovigilance Plan:

    a. Please elaborate on how the Pharmacovigilance Plan will address each of the "important identified risks" (development of Factor VIII inhibitors, hypersensitivity, immune response to PEG associated with loss of drug effect) and "missing information" (patients <2 years or previously untreated, severe hepatic impairment, renal insufficiency, elderly >65 years, potential long-term PEG-related adverse reactions) detailed in the table in section 1.

    b. Please provide "Standard Operating Procedures" referenced in section 2.1.

    c. Please submit the Specific Adverse Reaction Follow-up questionnaire referenced in section 2.1.1 and associated study protocol.

    d. Please submit the study protocol for each of the following studies:

        i. "Post-Marketing Study to assess safety and efficacy of BAY 94-902"
        ii. PROTECT KIDs – extension phase (study 15912)"

    e. Please submit the protocol for the information that will be reported to the referenced EUHASS registry.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our complete review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application. Following a review of the application, we shall advise you in writing of any action we have taken and request additional information if needed.

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge you have addressed PREA for this application.

If you have any questions, please contact the Regulatory Project Manager, Ms. Candace Jarvis, at (240) 402-8315.

Sincerely yours,

Kimberly Benton, PhD
Associate Director for Regulatory Management
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research