July 30, 2019

Mr. Val Bias
Chief Executive Officer
National Hemophilia Foundation

Ms. Kimberly Haugstad
President & CEO
Hemophilia Federation of America

Dear Val and Kimberly,

Thank you once again for your July 26, 2019 letter regarding the recent recall of two lots of Kogenate FS in the U.S. We fully understand your concerns and appreciate that you and many in the community have questions.

As I stated in my initial response to you, we are deeply disappointed that this mislabeling error has potentially put patients at risk. As part of our commitment to patient safety, our quality practices and manufacturing protocols must be maintained at all times. In this case, that did not happen. Since confirming the error and reporting it to FDA, we have been working to understand how it happened and putting measures in place to prevent it from occurring ever again.

We also wanted to clarify some key overarching points about the recall. A total of 10,678 vials of the two recalled lots of Kogenate FS (#27118RK and #27119CG) were distributed. Approximately 10% of the vials in the two distributed Kogenate FS lots incorrectly contained the Jivi product; the remaining 90% of the vials were properly labeled and are within expiration. In total, 986 of the distributed recalled vials were mislabeled.

We appreciate the need for additional information, and with that in mind, following are answers to the questions NHF and HFA posed in your letter.

1. **The recall notice indicated that the lots being recalled were both mislabeled and had expired in August, 2018 – this leads to the following questions:**

a. Since Jivi was approved in August 2018, were these vials used in the clinical trials? Were there any differences between these trial drugs and the final approved versions?

The Jivi batch associated with the mislabeling was not used for clinical trials. This lot was one of several commercial quality batches produced to generate data for the regulatory approval process for Jivi. There is no difference between this Jivi batch and the commercial Jivi product.

b. Is it typical for remaining vials of study drug to be put into circulation once the product has been approved for distribution?

The Jivi product associated with the mislabeling was not used for clinical trials. Product produced to generate data for the regulatory approval process can be distributed once the product is approved.

c. What is Bayer's process for handling or disposing of expired product and the timeframe for this process?

Bayer's manufacturing site in Berkeley, California has a process for handling and disposing of expired product. The Jivi batch involved in the mislabeling, although expired, was undergoing additional testing to gather product data past expiration date.

2. Jivi was not approved for patients under the age of 12. Has it been confirmed if any of the recalled lots were distributed to anyone under the age of 12?

At this time, we have no information that any patient under the age of 12 received the recalled product. Currently we are working with our distribution partners to capture information on patients who received product from the recalled lots. If anyone has information about a patient of any age who received product from the affected two lots, they should call their physician and contact Bayer Medical Communications at 1-888-84BAYER.

3. Bayer indicated to the FDA that it would conduct the recall to the end user. Have all impacted patients been identified and notified of the recall? How many patients were impacted? What have you directed patients to do with affected products?

Because Bayer does not distribute product directly to patients, we took steps to notify the general public, the hemophilia community and healthcare professionals through various

channels. In addition, we rely on our distribution partners, which do have direct contact with patients, to provide the recall notification directly to patients who received the impacted lots.

Bayer notified all 54 of its distribution partners that received impacted product and provided the instructions on what to do with the affected product. Currently we are working with our distribution partners to capture information on the extent of their outreach to patients. We will provide more information as we gather it.

The instructions given to our distribution partners and in turn to patients are as follows:

- *Bayer is initiating a patient level voluntary recall. As such, we ask that Specialty Pharmacies/Specialty Distributors/HTCs please:*
  - *Immediately quarantine inventory of the affected product under your direct control*
  - *Immediately notify your individual patients or customers with instructions to coordinate the return and replacement of their affected product through their specialty pharmacy*
  - *Complete the attached business reply card and contact the Bayer Recall Coordinator, Inmar, at 855-707-7518 to arrange for return of the identified product from your current inventory and returns coming from your patient customer base for reimbursement credit.*

4. Have all specialty pharmacies been notified? As of early this week, we heard from pharmacies who did not yet know about the recall.

Bayer has contacted all distribution partners who purchased the recalled product. We have asked that they quarantine any recalled product remaining in their inventory, contact patients who they have distributed recalled product to, provide new product to patients who have recalled product, and work with Inmar (the recall vendor coordinating returns) to return recalled product to Bayer. Following that notification, the distribution partners communicate the information to their affiliates.

5. Have all affected products been returned to Bayer? If not, in what timeframe do you expect that this will occur?

Bayer's first priority is patient safety and our initial focus has been to stop the use of the recalled product. All distribution partners have been notified of the recall, instructed to stop distribution of impacted lots. Distribution partners were instructed to notify their customers

and return impacted product to the recall center. Return and reconciliation of impacted product is ongoing and will likely take several weeks to fully reconcile.

6. Does Bayer provide any information to the impacted patients or their providers on the potential medical implications of the mislabeled product? Can this information be shared?

In addition to the information shared with the FDA, the recall press release and notifications to distributors and Specialty Pharmacies, Bayer contacted more than 2,800 healthcare providers to notify them of the recall, necessary next steps and potential medical implications.

The letter to healthcare providers outlined the following:

- *Reason for recall and recalled lot numbers with instructions for next steps*
- *Indications and contraindications for Kogenate FS and Jivi with accompanying full Prescribing Information for both products*
- *Differences between Kogenate FS and Jivi and potential efficacy and safety implications of the affected lots*
- *Guidance to advise the patients who have affected product to discontinue the use of the affected product and contact pharmacy where they obtained the products to arrange for returns*
- *Directions to report any complications or side effects to Bayer at 1-888-84-BAYER (1-888-842-2937) and FDA (www.fda.gov/medwatch, or 1-800- FDA-1088)*
- *Availability of Bayer Medical Communications for any questions about the recall and the products.*

Bayer sent the letter to healthcare providers via electronic mail and followed up with a hard copy. In addition, our team contacted 400 HCPs and a number of patient organizations and advocates. The Bayer Call Center (1-888-84-BAYER (1-888-842-2937) is continuing to be available to answer any questions about the recall.

Patient and caregivers who have contacted Bayer Medical Communications have been advised to stop using product from the recalled lots. They are informed about the potential safety risk and advised to contact their physician for their individual care and treatment.

7. When did Bayer inform PPTA's Patient Safety Notification System of the recall? The alert was not sent out until Wednesday, July 24.

Bayer initially made contact with PPTA (Plasma Protein Therapeutics Association) and Stericycle, the Patient Notification System (PNS) vendor, on Friday July 19 to obtain details on the submission process. On Monday July 22, we electronically completed the alert forms so Stericycle could format for their multiple communication channels.

Stericycle sent Bayer their completed alert materials on Tuesday July 23 for review and approval. Bayer made modifications to the materials to ensure accuracy, and thoroughness. Stericycle updated the materials, and distributed the PNS alert on Wednesday July 24.

Moving forward, we will incorporate PNS instructions directly into our procedures to shorten communication timelines.

8. The Bayer press release indicates that the last manufactured date of lots was July 15 but the recall did not occur until July 19th. Why the 4 day delay and what steps were taken during that time?

We appreciate your concern about the timeframe between the confirmation of the last distribution date and initiation of the recall. To clarify, Bayer immediately halted distribution of the two impacted lots on July 16, upon confirmation of the mislabeling. Voluntary drug recalls of this nature are conducted in conjunction with the FDA. In accordance with FDA policy and regulation, Bayer conducted an expedited investigation, safety evaluation and impact assessment to determine any potential impact on patient safety. In alignment with the FDA, Bayer issued the voluntary recall on July 19. A high-level timeline of the week follows:

- July 16 – Confirmed mislabeling in Berkeley, CA supply center; halted all shipments
- July 17 – Bayer's Product Quality & Safety Committee made decision to recall; Notified FDA and submitted biological product deviation report (BPDR); during this time Pharmacovigilance records were reviewed and initial medical assessment was conducted.
- July 18 – Submitted recall package and communications materials to FDA
- July 19 – FDA aligned with recall plan; recall initiated at approximately 1:00PM EST.

9. Have any adverse events (including breakthrough bleeding) been reported to Bayer?

A thorough review of all adverse events reported to Bayer after the release of the impacted Kogenate FS 2000 IU lots through July 17, 2019 has not confirmed any safety issue due to the affected lots.

Since the voluntary recall on July 19, 2019 Bayer has received new reports potentially related to the affected lots. These reports are currently in the process of being assessed by Bayer Pharmacovigilance for adverse events and whether they are related to the impacted lots. They will be reported to FDA according to FDA regulatory requirements. Bayer will continue to monitor and assess all incoming adverse event reports associated with this recall.

We appreciate the opportunity to work with the hemophilia community leadership to improve how we address these matters and to ensure timely and transparent communication. As new information becomes available, we are committed to providing updates on the recall and related topics. If there are new questions that come up, please feel free to reach out to us.

Kind regards,

Paul Bedard
Senior Vice President, Specialty Franchise