**Date:** **August 17, 2018**

**To:** BLA 125661/0 File

**Subject:** Draft Labeling Discussion

**FDA Attendees:**
Candace Jarvis
Kay Owosela
Bindu George
Megha Kaushal

**Sponsor Attendees:**
Michelle Meng
Lisa Michaels
Todd Paporello
Gabriele Braeunlich
Chi Li

**Meeting Summary**:

Bayer Healthcare requested a second teleconference with the agency to discuss the draft labeling document with FDA edits. In particular, the applicant wanted to discuss the dose and administration section of the PI.

The main discussion by the applicant for dosing was to start the every 5 day regimen and if patients bleed in excess, then to switch to the twice weekly regimen. The applicant stated that the twice weekly and every 5 day regimen had similar ABRs. The FDA stated that the trial conducted was based on higher frequency dosing and then randomizing to lower frequency dosing. This was done in a carefully selected group and the dosing recommendations should be based on the findings from the study. This dosing regimen should be reflected in the label and switching from low frequency to high frequency dosing will expose more patients to bleeds and the trial period to observe for bleeding before switching was only 10 weeks.

We agreed that the initial dosing in the first 10 weeks had significant bleeding. FDA recommended to start dosing at 30-40IU/kg and the applicant can write the language for any specific criteria for those patients who can start at every 5 day dosing and then titrate up to individualized dosing. We agreed on removing the every (b)( day dosing.

Bayer is going to "consider" revising the label, after an internal discussion, to revise it to begin all patients at the higher frequency (of 30-40 IU/kg q twice weekly) followed

by  titration to a lower frequency dose of 45-60 IU/kg q 5days if patients have a bleed rate below the pre specified threshold observed in the 10 wk period.
The applicant was also concerned that we hadn't included the text about individualized prophylaxis. This was a miscommunication from the Telecon held on 8/13/18 where they assumed we would do it, and we assumed that they would do it after we sent them the label. They agreed to include the text as the label is currently being reviewed by them.