Date: **August 23, 2018**

To: BLA 125661/0 File

Subject: Draft Labeling Discussion

FDA Attendees:
Candace Jarvis
Kay Owosela
Bindu George
Megha Kaushal
Robert McElwain
Kimberly Benton
Wilson Bryan
Iftekar Mahmood
Ramani Sista
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Sponsor Attendees:
Michelle Meng
Maria Wang
Lisa Michaels
Anita Shah
Monika Mass Enriquez
Joel Krasnow
Olubunimi Afonja
Todd Paporello
Audrey Anderson
Silvana Schumacher
Gabriele Braeunlich
Chi Li
Kim Quaintance-Lunn

Meeting Summary:

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

Bayer wanted this discussion as they were still not in agreement with the twice weekly dosing regimen as the initial starting regimen, and would like to have an every 5 day dosing regimen as the initial dosing regimen, with an increased/decreased frequency

and/or dose titration for bleed control, as needed. They explained that the ABR rates for the "forced" twice weekly regimen were comparable to the every five day dosing.. They also stated that a provider could gauge the dosing from the patients prior regimen. FDA stated that their position remains the same. The trial was based on higher frequency dosing to low frequency dosing in a carefully selected group and the dosing recommendations should be based on the findings from the study, that switching from low frequency to high frequency exposes more patients to bleeds. Furthermore, those subjects in the "failed" twice weekly regimen were on the highest dose and had an unacceptable ABR rate. This underscores that those with high bleeding phenotypes would need a more frequent regimen.

Bayer agreed to FDA's position and proposed the language in the package insert to reflected what was discussed.