

RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125582/0 Office: OBRR
Title/Product: Coagulation Factor IX (Recombinant), Albumin Fusion Protein
Sponsor/Applicant: CSL Behring Recombinant Facility AG (CSLB)

Telecon Date / Time: Wed 2/10/2016 at 4 P.M. Initiated by FDA? Yes

Communication Category: ADVICE (AD)

Drafted: Edward Thompson
Revised: Lisa Faulcon
Bindu George

Telecon Summary: To discuss and provide clarification for the information request sent on February 9, 2016 on dosing regimen and testing assays.

FDA Participants:

Howard Chazin, MD, MBA, Acting Director, Division of Hematology Clinical Review, OBRR

Bindu George, MD, Acting Branch Chief, Clinical Review Branch, Division of Hematology Clinical Review, OBRR

Lisa Faulcon, MD, Medical Officer, Division of Hematology Clinical Review, OBRR

Iftekhhar Mahmood, PhD, Clinical Pharmacologist, Division of Hematology, OBRR

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Edward Thompson, RPM, OBRR

Non-FDA Participants:

CSLB

Debra Bensen-Kennedy, MD, Therapeutic Area Head, Clinical Research and Development

Nicole Blackman, PhD, Associate Director, Global Biostatistics, Clinical Research and Development

Paula Clark, Associate Director, Regulatory Regional Lead, NA

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Iris Jacobs, MD, Senior Global Clinical Program Director, Clinical Research and Development

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Yanyan Li, PhD, Global Statistical Scientist, Clinical Research and Development

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Monica Richardson, Regulatory Affairs Regional Manager, North America, Global Regulatory Affairs

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Kevin Darryl White, MBA, RAC, Senior Director, Regional Head North America, Global
Regulatory Affairs
Jian Ye, MD, Director, Clinical Safety Physician, Global Clinical Safety

Telecon Body:

This teleconference was requested by FDA to provide clarification for the information request sent on February 9, 2016 on dosing regimens and testing assays.

FDA stated that the review of the draft labeling for the dosing regimen is on-going. FDA expressed concerns that the proposed routine prophylaxis dose of 35-50 IU/kg for patients <12 years of age may not be adequate because a large percentage of subjects treated in the pediatric study required higher than recommended dosing, and because the pharmacokinetic data showed significant increases in clearance. This was particularly true of subjects <6 years. CSLB stated that the reasons for higher dosage for prophylaxis were not a result of bleeding, and that the study protocol allowed for discretionary dosing. FDA stated that the recommended dose should be based on observed clinical and PK data. Therefore the dose should not be restricted to 50 IU/kg and a higher than 35 IU/kg starting dose may be required for the low end of the dosing range. CSLB clarified that the driver was the bleeding events for trauma and not for spontaneous bleeds. CSLB agreed to provide a justification for their proposed dose in their formal justification of the selected pediatric dose.

FDA stated that additional efforts, other than describing the issue in the Prescribing Information, were needed to inform the public of the assay variability observed with the use of different assay reagents. FDA requested that CSLB provide a DHP to alert prescribers and care givers to these issues. FDA also suggested that CSLB maintain a dedicated phone line to assist clinical labs address issues with assay variability. CSLB stated that the proposed language in the draft labeling is aligned with factor IX products such as ALPROLIX. FDA stated that based on the field studies of IDELVION with different reagents, there are concerns for over and under-dosing. These concerns may not be adequately conveyed in the PI. CSLB stated that the systematic variability demonstrated by the field sites is not specific to this product. FDA stated that the intent is not to single this product out; similar efforts will be undertaken for other products in which this variability is seen.

End