

Ko, Hon Sum

From: Ko, Hon Sum
Sent: Friday, August 14, 2009 8:15 PM
To: 'Paula.Hines@csllbehring.com'
Cc: Rana, Pratibha
Subject: RE: STN 125350/0 Information Request

Dear Dr. Hines:

1. If we provide a rationale as to why we think 10 pediatric subjects are enough to support use in children and adolescents, then does that mean we do not need a Deferral? Or should we do both (provide rationale and request Deferral)? In other words, we can seek approval based on 10 children (get this approved in the label) and then commit to provide additional pediatric data from the European study as soon as it's available?

- The 10 pediatric subjects include 3 children and 7 adolescents. The amount of information is not likely to support use in either age subgroup. Labeling presumably will mention their data with some qualifier that this is not adequate information (this is my tentative projecture and is not representing official verdict). If CSLB agrees that would be the case, CSLB can simply request Deferral and submit the remaining data post-approval as soon as they are available. There is no further need of providing a rationale.

2. Is this adequate time for FDA's assessment and incorporation into the IgPro20 label? Or will this automatically result in an extension of the review period (it is less than 3 months before the action due date of 28Feb10)?

- The purpose of Deferral is not to hold up approval if the adult data are adequate. The new information can be the subject of a supplement to change the label. If CSLB insists labeling with the additional information by submitting the assessment shortly before the due date (Feb 28), there are two possibilities. One is an extension as mentioned in the email, but it is more likely that it will not be reviewed at the present cycle, because that may hold up approval. It is important to note that the new data must not be simply available, but integrated with the existing data in order for the labeling to be complete. Thus having them available in January is not the only bar, but there is work in the integration, to the extent of updating the ISS and ISE.

3. Further a Pediatric Plan document is requested in Q #3 with the Deferral. We have submitted a Pediatric Assessment, including a request for a partial waiver in neonates and infants, in Module 1.9.1 of our BLA. What additional information is required to fulfill the Pediatric Plan document? We refer to the FDA guidance: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079756.pdf>

- I do understand CSLB has a Pediatric Assessment document in Module 1. This cannot be taken as the Pediatric Plan per se. FDAAA has established the Pediatric Review Committee which now reviews all PREA Deferrals, and they require to see a specific document by the title "Pediatric Plan". You have rightly referred to the guidance and in Section V.A., you will find the following recommendation: "A Pediatric Plan is a statement of intent that outlines the pediatric studies (e.g., pharmacokinetics/pharmacodynamics, safety, efficacy) that the applicant plans to conduct. The plan should also address the development of an age-appropriate formulation. Furthermore, it should address whether and, if so, under what grounds, the applicant plans to request a waiver or deferral under PREA." CSLB has essentially the needed information in Module 1 of the BLA, but simply needs to reorganize to fit the guidance and make the appropriate changes, especially if request for Deferral is to be made.

If you need any further clarification, please do not hesitate to be in touch with us.

Thank you.

Hon-Sum Ko.

From: Rana, Pratibha
Sent: Friday, August 14, 2009 6:57 PM
To: Ko, Hon Sum
Subject: Fw: STN 125350/0 Information Request

From: Paula.Hines@cslbehring.com <Paula.Hines@cslbehring.com>
To: Rana, Pratibha
Cc: Alaine.Zumpino@cslbehring.com <Alaine.Zumpino@cslbehring.com>
Sent: Fri Aug 14 16:21:42 2009
Subject: RE: STN 125350/0 Information Request

Dear Pratibha,

Concerning Q #3 below:

I would like to clarify with FDA what is meant by a Deferral in terms of the proposed label. If we provide a rationale as to why we think 10 pediatric subjects are enough to support use in children and adolescents, then does that mean we do not need a Deferral? Or should we do both (provide rationale and request Deferral)? In other words, we can seek approval based on 10 children (get this approved in the label) and then commit to provide additional pediatric data from the European study as soon as it's available?

Additionally in regards to timing, we know that the final clinical study report for the European study, which will include data from an additional 18 children and 5 adolescents, will not be available until Jan 2010. Is this adequate time for FDA's assessment and incorporation into the IgPro20 label? Or will this automatically result in an extension of the review period (it is less than 3 months before the action due date of 28Feb10)?

Further a Pediatric Plan document is requested in Q #3 with the Deferral. We have submitted a Pediatric Assessment, including a request for a partial waiver in neonates and infants, in Module 1.9.1 of our BLA. What additional information is required to fulfill the Pediatric Plan document? We refer to the FDA guidance: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079756.pdf>

Therefore, we seek advice on how to appropriately respond to Q #3 and would like to discuss our options with FDA.

Best regards,

Paula

P.S. Please copy Alaine Zumpino on any email to me. I will be working from home on Monday, Aug 17 and cannot read secure email from FDA from home.

From: Rana, Pratibha [mailto:Pratibha.Rana@fda.hhs.gov]
Sent: Wednesday, August 12, 2009 4:43 PM
To: Hartmann, Paul US/KOP; Hines, Paula US/KOP
Subject: STN 125350/0 Information Request

To: Paul Hartmann
CSL Behring AG
Date: August 12, 2009

This is regarding your BLA submission STN 125350/0 for Immune Globulin Subcutaneous (Human), 20% Liquid, submitted to the Agency on April 30, 2009. FDA continues with the review of the referenced submission and requests CSL Behring AG to provide the following information.

1. To facilitate reviewing the submission, please submit electronic files in Microsoft Word for

Sections 1 to 13 of each clinical study report (ZLB04_009CR, ZLB04_008CR, and ZLB06_003CR) in Microsoft Word.

2. Please provide an additional xpt file for adverse events showing (a) start time of immediate preceding infusion, (b) end time of immediate preceding infusion, (c) whether the event started between start time and within 48 hours of end of the infusion, and (d) whether event started between start time and within 72 hours of end of the infusion.
3. Please provide your rationale why 10 pediatric subjects' data are sufficient to support use of IgPro20 in children and adolescents. Since you will have additional data from European studies that include children and adolescents, please request a Deferral for submission. Please submit a Pediatric Plan document when you request for a PREA deferral for pediatric data submission.

Please submit a response to this request as an amendment to the file by August 21, 2009.

Thank you.

Pratibha Rana

Pratibha Rana, M.S.

Regulatory Project Manager

FDA/CBER/OBRR

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