BLA 125400
1/27/2012

Clinical Reviewer: Agnes Lim, M.D.

Re: The Applicant will conduct a deferred postmarketing pediatric study (submission#25).

1/27/2012, 2:56pm email from Organogenesis (Kristine Riley)

Dear Agnes:

As promised, please find attached the partial waiver, pediatric plan, and draft pediatric study protocol. This will be submitted today (1/27) to BLA 125400 under Sequence 0025. Please let me know if you have any questions. Have a nice weekend!

Best regards,
Kristine

From: Lim, Agnes [mailto:Agnes.Lim@fda.hhs.gov]
Sent: Wednesday, January 25, 2012 4:37 PM
To: Kristine Riley
Cc: Barash, Faith; Schneider, Bruce; Irony, Ilan; Lee, Mark H (FDA); Thomas, Terrolyn
Subject: RE: Organogenesis Post-AC, follow-up

Kristine,

Thank you for sending the summary. Much appreciated! I will look for the submission on Friday.

Regards,
Agnes

From: Kristine Riley [mailto:KRiley@Organo.com]
Sent: Wednesday, January 25, 2012 4:14 PM
To: Lim, Agnes
Subject: RE: Organogenesis Post-AC, follow-up

Dear Agnes:

We will be providing a response on or before this Friday (1/27) regarding pediatrics and other safety concerns expressed at the AC meeting.

The submission will be summarized in a Q&A document located in Section 1.11. This document will link to the request for a partial waiver (provided in Section 1.9.1) and the pediatric plan

(provided in Section 1.9.6). The Q&A document will also address any additional post-marketing plans outside of pediatrics which will consist of the PVP and routine pharmacovigilance.

The request for partial waiver will be for children younger than 12 years of age . The pediatric plan will address ages covered in the plan, pediatric formulation, additional nonclinical studies, and clinical studies. The pediatric plan will also contain a draft pediatric clinical study synopsis for FDA review/input.

When this response has been finalized, I will send it to you via email. For completeness, this response will also be submitted to the BLA via the Gateway most likely on Friday (1/27).

I hope this summary helps.

Best regards,
Kristine

From: Lim, Agnes [mailto:Agnes.Lim@fda.hhs.gov]
Sent: Friday, January 20, 2012 2:49 PM
To: Pat Bilbo; Kristine Riley
Subject: RE: Organogenesis Post-AC, follow-up

Patrick and Kristine,

As a follow-up, has your group developed any post-marketing protocols or outlines to address the pediatric and other significant clinical concerns expressed at the AC meeting? It would help facilitate my review of this portion of the BLA if I knew how you plan to proceed to address these issues.

Thank you,
Agnes

From: Lim, Agnes
Sent: Monday, January 09, 2012 8:50 AM
To: 'Pat Bilbo'
Subject: RE: Organogenesis Post-AC, follow-up

I mentioned the pediatric population and longer-term follow-up in adults as examples of clinical issues that may need to be addressed in post-marketing plan(s). Based on feedback from the AC panel, your team should determine what post-marketing clinical issues need to be addressed. The pediatric population will likely be a potential issue; in your action plan proposal, please take the different pediatric age categories (newborn infants, toddlers, children, and adolescents) into consideration. Thank you.

Congratulations to Kristine.

Regards,
Agnes

From: Pat Bilbo [mailto:PBilbo@Organo.com]
Sent: Friday, January 06, 2012 1:48 PM
To: Lim, Agnes
Subject: RE: Organogenesis Post-AC, follow-up

Thank you for forwarding Agnes. Kristine is on ---b(6)----------! We have had discussions around the pediatric population and longer-term follow-up in adults. I will regroup with the Clinical/Medical team on Monday and we will discuss providing an outline of a post-market plan. Is the scope of your Clinical concerns limited to these two issues, the pediatric population and longer-term follow-up in adults?

Best regards
Patrick

From: Lim, Agnes [mailto:Agnes.Lim@fda.hhs.gov]
Sent: Friday, January 06, 2012 1:02 PM
To: Pat Bilbo
Cc: Thomas, Terrolyn; Lee, Mark H (FDA)
Subject: RE: Organogenesis Post-AC, follow-up

Good afternoon,

Since Kristine is out of her office until 1/12, I thought I'd go ahead and forward this to you. Thank you.

Agnes

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From: Lim, Agnes
Sent: Friday, January 06, 2012 12:55 PM
To: 'Kristine Riley'
Cc: Thomas, Terrolyn; Lee, Mark H (FDA); Schneider, Bruce; Irony, Ilan; Barash, Faith
Subject: Organogenesis Post-AC, follow-up

Hi Kristine,

I am writing to inquire whether your clinical team has formulated any action plans in response to the AC panel's comments and discussions, such as proposing a pediatric study to address the potential clinical use of Apligraf in the pediatric population and any associated safety concerns, or a registry study for long term follow-ups for any safety issues in the proposed adult population.

We are internally discussing significant clinical issues that were raised at the November 17, 2011 AC meeting. No official decision has been made on any issue yet by the Agency. If your group has drafted any post-AC plans/study protocols, it would be helpful for us to review them and take these proposals into consideration as we continue our review of your BLA.

Thank you, and Happy New Year.

Agnes