

RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125523/0 Office: OBRR

Product:

Fibrin Sealant, Human Fibrinogen Human Thrombin

Applicant:

ProFibrix, BV.

Telecon Date/Time: 7-Apr -2014 10:00 AM Initiated by FDA? No

Telephone Number: (b) (4)

Communication Category(ies):

1. Other - To obtain clarification on question 1 on the information request dated March 26, 2014

Author: TRACY TILGHMAN

Telecon Summary:

To obtain clarification on question 1 on the information request dated March 26, 2014

FDA Participants:

Alfred DelGrosso

Tracy Tilghman

Non-FDA Participants:

ProFibrix/ The Medicines Company:

Eliane Schutte, MSc. VP Global Product Development

Laurens van Pinxteren, Ph.D. Director Manufacturing and Supply

Sabine Snaar, Ph.D., Director Quality Assurance

Linda Zuckerman, Ph.D. VP Clinical Development

Sabrina Gu, Manager, Regulatory Affairs

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

The purpose of this teleconference to obtain clarification on question 1 on the information request dated March 26, 2014 in which it was requested that ProFibrix commit to adoption of test methods and specifications for the control of Trehalose

(b) (4) and Calcium Chloride (b) (4) in the final product. ProFibrix stated that they would like to have an understanding of this question so they know how to address it. ProFibrix asked why this is a requirement and why it is important to the product.

FDA stated that trehalose and calcium chloride are considered major components of the Drug Product that serve roles in product stability and efficacy and that it is critical that specifications be set and content controlled by testing. ProFibrix stated that they have had several conversations with the FDA regarding this product and there were three conversations regarding the drug product specification. ProFibrix received feedback that their specifications were appropriate. ProFibrix stated that during the March 23, 2013 CMC meeting, there was no note of this information, nor at their recent pre-BLA meeting. Trehalose is a (b) (4) of the product. It is added, and it has never been considered as a test method by ProFibrix. Product potency is measured throughout the manufacturing process, which the firm claimed provided a good measurement of trehalose function. ProFibrix stated that the calcium chloride is in the (b) (4). FDA stated that even if these are not directly involved in the activity of the product, they can have influence on the product stability and there should be a control in the final drug product. These could be important secondary components. ProFibrix discussed the relationship of calcium and citrate in the role of clotting activation.

FDA reiterated that these (b) (4) should be controlled in the Drug Product. ProFibrix stated that some of the assays will be difficult to do on the final dried product due to the fact that the combined thrombin and fibrinogen material clots immediately if reconstituted in water of neutral pH. For this reason they stated that would like to do the measurements on the (b) (4). FDA recommended that ProFibrix provide a justification for testing at (b) (4) on the final drug product. FDA would be willing to consider this. ProFibrix asked about the timing of this submission, and would like to know whether they could respond in a separate amendment to question 1 and commit to the timeline. FDA stated that this approach is acceptable.