

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: 05-Jun-2014 11:30 AM Initiated by FDA? Yes

Telephone Number: (b) (4)

Communication Categorie(s):

1. Other - Telecon to discuss IR

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Telecon Summary:

Telecon to discuss IR

FDA Participants:

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Non-FDA Participants:

(b) (4), (b) (6)

Linda Zuckerman, Ph.D., VP Clinical Development

Sabine Snaar, Ph.D. Director Quality Assurance

Eliane Schutte, MSc., VP Product Development

Sabrina Gu, Regulatory Project Mgr

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

The teleconference was scheduled on June 5, 2014 at the request of the sponsor to clarify the information requests (IR) sent to ProFibrix by emails on May 30, 2014 and June 4, 2014.

FDA pointed out that RSD of the results from (b) (4) is about (b) (4) and one of the analysts from (b) (4) is between (b) (4) in the Method Transfer Report MET 1250. These results are above the acceptance criterion ((b) (4)) in Method Transfer Protocol MET 1245 as well as in the validation report. Therefore, the sponsor's method transfer data are inconsistent with the method validation and did not meet the acceptance criteria. However, the sponsor used SD as the acceptance criterion in Method Transfer Report MET 1250. FDA was unclear as to why two different criteria were used in method validation vs method transfer. The sponsor explained that they used different samples in method validation vs method transfer. In method validation the sponsor used a sample that contained about (b) (4). However, they used a sample that contained approximately (b) (4) in method transfer. When FDA asked that their results are showing values between (b) (4), the sponsor responded that this was due to assay variability and any result below (b) (4) is due to assay variability.

FDA pointed out that same or equivalent material should have been used for method validation and method transfer because, if the material was not equivalent, it is not possible to compare the results. The sponsor responded that equivalent material was used because both lots were produced by the same manufacturing process. FDA felt that the method validation was not consistent with the manufacturing capability and recommended that the sponsor should look into this issue internally. ProFibrix agreed to look into the deficiencies in their method transfer protocol and report, per the information request sent on May 30th and June 4th.

When asked about the negative (b) (4) results, ProFibrix stated that (b) (4) samples for samples containing (b) (4) are in the negative values, which can happen because the accuracy is (b) (4). FDA stated that the sponsor should not report meaningless negative values.

ProFibrix stated that they would propose that (b) (4) can be seen as an LOQ level. FDA stated that the sponsor have not submitted any result with samples containing less than below (b) (4), which met acceptance criteria for method validation. Therefore, as per the validation report, the assay LOQ is (b) (4). Hence the sponsor should carry out method transfer using materials that contain more than (b) (4). In addition, any result below (b) (4) should not be expressed quantitatively but as (b) (4) (method LOQ). FDA also offered that it would be happy to consider any supporting data which were generated under GMP environment even if it was obtained outside of the scope of the validation protocol to evaluate the sponsor's claim that the LOQ of the assay is (b) (4).

Regarding the moisture content assay, ProFibrix stated that they would work on obtaining requested data to cover entire assay range. FDA also stated that the data should be

obtained using the actual product samples. Such product samples may be (b) (4), if necessary, with a (b) (4) standard to study the entire range.

In response to sponsor's question, FDA stated that they prefer to obtain requested information in one amendment. However, FDA would need data from ProFibrix submitted within a reasonable time-frame prior to the action due date. ProFibrix stated that they can provide the timeline for submission of requested data to the FDA by June 13th.