

From: [Dana Weinberger](#)
To: [Schneider, Bruce](#); [Zhu, Yao-Yao](#);
cc: [Tull, Lori](#); [Jay Merritt](#); [Ann Remmers](#); [Jeanne Novak](#);
[Lim, Agnes](#);
Subject: RE: Safety Data Issues for Discussion
Date: Monday, April 04, 2011 2:15:26 PM
Attachments: [emfalert.txt](#)

Dear Drs. Schneider and Zhu,

I just touched base with our clinical team, and we have an update to the below plan --

Data from the (b)(4) and vocal studies WILL be included. Please note, however, that safety data from one of the (b)(4) are still being located, and we may not be able to include these data in the integrated analysis. We are doing everything we can to obtain this data set in a timely way.

Please feel free to let me know if you have any questions or requests (by email or phone number below), and we look forward to your reply to Jeanne's request below.

Kind regards,
Dana

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-----Original Message-----

From: Jeanne Novak

Sent: Monday, April 04, 2011 7:51 AM

To: Bruce.Schneider@fda.hhs.gov; Yao-Yao.Zhu@fda.hhs.gov

Cc: Dana Weinberger; Jeanne Novak; Tull, Lori; Jay Merritt; Ann Remmers

Subject: Safety Data Issues for Discussion

Importance: High

Dear Drs. Schneider and Zhu,

Thank you for the call last week regarding efficacy and safety labeling topics for Fibrocell's BLA 125348 for azficel-T.

This email includes a description of what we are preparing in response to the FDA request for additional safety data for clinical studies performed (b)(4) (i.e., for the vocal, (b)(4) and acne indications). We propose to submit the below information. If you could please confirm that this information will meet your needs, we can do the analyses this week and submit the results on or before Friday, April, 8th.

Proposed for submission to BLA 125348:

1. Safety data from clinical studies IT-A-008 (acne; n=122) and IT-H-001 (histology; n=29)

a. These data will be provided as an integrated set for these two studies only (i.e., not integrated with pivotal study data from Studies IT-R-005 and 006). Note that adverse events for this integrated analysis will be coded using the MedDRA version 10.0 dictionary (because the IT-A-008 data were originally coded to this version), whereas the data from Studies IT-R-005 and 006 were coded using MedDRA version 9.0.

b. Data from the (b)(4) and vocal (b)(4) studies will not be included. The rationale is that we feel that the acne and histology data are the most relevant to the proposed indication and represent the majority of the available additional data. Additionally, datasets for the (b)(4) and vocal studies are not currently available in electronic format, and would

require additional time to prepare. Of course, please let us know if the (b)(4) and vocal data will be vital for your review.

2. Descriptive titles for the proposed data tables are included below (additional "mini" ISS)

- Extent of exposure for the integrated safety population by treatment group
- Disposition of subjects (withdrawals due to AEs, and other reasons)
- Demographic characteristics of the integrated safety population by treatment group
- Treatment-emergent adverse events occurring in ≥1% of subjects in either treatment group by SOC and preferred term for the integrated safety population
- Treatment-emergent adverse events occurring in ≥1% of subjects in either treatment group for the integrated safety population by treatment group and severity
- Treatment-emergent adverse events occurring in ≥1% of subjects in either treatment group for the integrated safety population by treatment group and relationship to study treatment
- Adverse events leading to premature study termination or treatment discontinuation, and serious adverse events for the integrated safety population
- Listings of other significant adverse events for the integrated safety population
- Possibly, probably, and definitely related TEAEs by system organ class
- Treatment emergent adverse events in the system organ class immune system disorders by treatment group for the integrated safety population

3. Does the set of analyses provide the data in the best output for FDA review? If not, can you please advise us on what would best suit the

Agency reviewers?

4. We intend to provide these data as tables in a "response to request" format and submit to the BLA as an amendment. Please confirm this is acceptable.

5. At this time, we are preparing CDs with SAS files for submission. However, submission of the electronic files on CD may be delayed to the following week. Is that acceptable?

6. Finally, we plan to submit a response to the FDA request for additional efficacy analyses (e.g., time to sustained response) in the follow weeks.

Thank you in advance for your consideration, and we look forward to your feedback. [Note: I am on international travel so we request that your primary contact be Dana Weinberger this week.]

Best regards,

Jeanne

Jeanne M. Novak, Ph.D.

CEO and Principal Consultant

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