

## Isolagen BLA 125348 Review Team Meeting Minutes (9-17-09)

**Participants:** Donald Fink, John Thomas, Yao-Yao Zhu, Gang Wang, Stephanie Simek, Shiohjen Lee, Changting Haudenschild, Allen Ou, Raj Puri, Lisa Stockbridge, Craig Zinderman, Atm Hoque, Keith Wonnacott, Kimberly Benton, Ashok Batra, Lori Tull

### 1. Administrative

- Isolagen Technologies, Inc to emerge from chapter 11 bankruptcy
- New name – Fibrocell Technologies, Inc
- Proposed product proprietary name - Laviv™ (pending)
- Proposed USAN – azfibrocel-T (pending). *Accepted by company 9-23-09*

### 2. Review Status

- Report from DMPQ/DCGT inspection of Isolagen facility 8/31/09 – 9/4/09
  - Description of Isolagen facility re-start following “warm” shutdown in March  
Following bankruptcy filing the HVAC system remained on  
Facility was in “warm shutdown” from March 4 to July 30, 2009  
Manufacturing of lots for PLI began August 6
  - Form 483 citations – Sponsor required to provide response within 15 days
    1. The system for documentation of deviations and their subsequent investigation is inadequate.
    2. The media fill study performed is inadequate in that it does not simulate all of the critical aseptic processes such as -----(b)(4)-----  
----- executed during the production process.
    3. Environmental monitoring (EM) conducted during the manufacturing processes performed inside the -----(b)(4)-----  
----- Cleanroom ---(b)(4)--- is inadequate.
    4. Cleaning validations for the -----(b)(4)----- Cleanrooms have not been performed.
    5. Performance qualification of EM in the ---(b)(4)--- Cleanrooms is inadequate in that the worst-case locations for viable and non-viable particulates have not been identified.
    6. The qualification smoke study for ---(b)(4)----- conducted under dynamic conditions is inadequate in that the actual conditions of product manufacturing were not simulated. Maintenance of adequate airflow has not been demonstrated under such conditions.
    7. Sanitization effectiveness of the disinfectants used for cleaning the Cleanrooms and manufacturing equipment has not been performed.
    8. Currently, mycoplasma release testing of the Drug Substance – Cryovial is performed by the contract company -----(b)(4)-----  
however, the test method has not been validated by the contract company.

The significance of the above citations was discussed:

It is unlikely that the sponsor will not be able to fully address each issue prior to the BLA decision date.

If the sponsor responds with a reasonable assurance that each issue will be addressed either prior to the BLA decision date or as a post-marketing commitment, then they will most likely be allowed to initiate commercial

production according to their “soft launch” schedule of receipt and processing of ---(b)(4)--- per week.

This capacity was demonstrated to be feasible under the current manufacturing demonstrated during the inspection.

Further increases in the manufacturing capacity would require review and approval by the Agency.

- Other review updates
  - BIMO Inspections

-----Withheld Per Privacy Act-----  
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### 3. **Advisory Committee (CTGTAC)**

- **Meeting date – October 9<sup>th</sup>**
- Briefing document finalized
- AC panel Consumer Representative change:
  - The CTGTAC Consumer Rep, Peter Saltonstall’s appointment will not be finalized by the meeting.
  - Gail contacted and invited Karen Rue who was the CR for the November, 2008 CDRH AC meeting on Dermal Fillers
  - She has agreed to attend.
- AC Presentations – Discussion
  - As one hour has been allotted for FDA presentations the consensus was for the following order, presenters and times.
  - Product - Terrig 10 minutes
  - Clinical Efficacy – Agnes 20 minutes
  - Clinical Safety – Yao-Yao 20 minutes
  - (OBE will collaborate with clinical to provide suggestions)
  - Statistics - Shiohjen 10 minutes

On 9-16-09 the proposed redactions to the AC briefing document were received from OCOD. Many parts of the CMC section were affected. Concerns were raised about the redaction because it was felt that the AC would not be able to sensibly discuss the safety questions without knowing some of the redacted information. In particular redaction of keratinocytes, length of time in culture, passage numbers and impurities removed from the final product (cryopreservative, FBS, antimicrobials) were mentioned. Lori will arrange, through Gail, to discuss this concern with OCOD to express our concerns and see if they really feel these need to be redacted. If OCOD considers these redactions to be entirely up to the sponsor to waive, then it was suggested that we talk to the sponsor and express our concerns that it would be in their best interest to be as transparent as possible in the public setting of the AC.

**4. PVP/REMS – update**

- Next meeting with FDAAA SWG 10-14-09
  - Celia requested that there should be a team meeting after the AC but before the above date to discuss potential new suggestions/positions based on outcomes from the AC.

**5. Fibrocell Technologies, Inc**

- Future Plans

The presentation given by Jeanne Novak during the PLI was discussed

Manufacturing

- Sept. - Comparability study of -----(b)(4)-----
- October - New 48 hour stability study

Clinical

- Sept. Draft physician requalification/training program
- Oct. Establish Customer Complaint System and Customer Service Center