

## Isolagen BLA 125348 Midcycle Meeting Minutes (8-13-09)

**Participants:** Donald Fink, John Thomas, Yao-Yao Zhu, Gang Wang, Stephanie Simek, Shiojwen Lee, Changting Haudenschild, Raj Puri, Lisa Stockbridge, Craig Zinderman, Atm Hoque, Keith Wonnacott, Kimberly Benton, Lori Tull, Jane Liedtka, Janette Alexander, Charles Durfor, Celia Witten, Alan Ou, Aileen Buckler, Janet White, Agnes Lim

### 1. Overview (5 min)

- Updated timeline
- Advisory Committee
- Milestones

### 2. Status of Product Review (20 min)

Issues

-----b(4)-----

-----b(4)-----

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*How is the issue of protocol deviations to be addressed post-licensure?*

*Is there a correlation between lots that deviate from the process at the -----b(4)-----*

*----- with those that deviate at the --b(4)--*

#### Shipping Validation

*Shipping is not validated for the 48 hour specification. Additional studies are needed*

### 3. Status of Pharm/Tox Review (5 min)

### 4. Status of Clinical/Statistical Review (5 min)

- Clinical review status
- Issues
  - Efficacy of Isolagen beyond 6 months was not studied
  - Isolagen in combination with other cosmetic Tx was not studied
  - Safety concerns – PMR 505(o) or PMC
    - Long-term safety concern
    - Tumor formation

- Hypertrophic scars/keloid
  - Abnormal pigmentation
  - Unknown safety profile in non-white population – *labeling*
  - Unknown safety profile in age group > 65 *Labeling*
  - Risks of the product application – REMS 505-1
  - Postmarket Registry Study- PMR 505(o) to assess signals of serious risks
  - Risk Evaluation and Mitigation Strategies – REMS 505-1 to ensure that the benefits outweigh the risks of the product application (Injection site reactions)
- Statistical review status
  - Issues
    1. Primary investigators at sites 5100, 5300, 5600 and 6400 participated in other studies under IND(b)(4).
      - Account for 65.5% enrollment in study 005
      - Account for 16% enrollment in study 006
    2. Success rates in EWSA are considerably low for Isolagen group at sites 6100, 6300 and 6600 (5%, 5% and 10%).
      - Account for 55% enrollment in study 006
5. Status of Facility Reviews and Inspections (15 min)
- The aseptic processing validation / media fill simulation studies (EX-PRT-120 and Ex-GTR-120) only covered the -----b(4)----- Drug Product-Injection stages of the Isolagen Process, and are not adequate.
  - Studies are needed to capture worst case scenarios:
    - Maximum capacity
    - Occupancy
    - Interventions
    - Maximum number of concurrent manufacturing process
  - The -----b(4)----- method is used to demonstrate container closure integrity so as to prevent contamination.
  - Additional information needed:
    - Demonstrate sensitivity of method
    - Demonstrate CCI following freezing/thawing (simulate freezing of the cryovial – drug substance)
    - Demonstrate CCI at 2-8°C to simulate the storage conditions of the Drug Product-Injection

**6. Status of BIMO inspections (15 min)**

**7. AC meeting (20 min)**

- Latest agenda