

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

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1. Overview (5 min)

- Updated timeline
- Advisory Committee
- Milestones

2. Status of Product Review (20 min)

Issues

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

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

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

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

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

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

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