



Our STN: BL 125348/0

**May 19, 2009**

Isolagen Technologies, Inc.  
Attention: Dr. Jeanne M Novak  
2905 Wilderness Place, Suite 202  
Boulder, CO 80301

Dear Dr. Novak:

Please refer to your biologics license application (BLA), submitted under section 351 of the Public Health Service Act, and to our filing letter dated May 5, 2009. While conducting our filing review we identified the following potential review issues:

#### PRODUCT INFORMATION

1. Please submit a summary report for aseptic processing validation / media fill simulation studies for the manufacturing process. Please ensure that the aseptic processing validation/media fill simulation studies capture the worst-case scenarios such as maximum capacity, occupancy, interventions, environmental monitoring, and the maximum number of concurrent manufacturing processes.

#### CLINICAL INFORMATION

2. For each study (IT-R-005 and IT-R-006), please provide the following information by clinical site:
  - a. The number of patients enrolled
  - b. The number of patients who had biopsy performed
  - c. The number of patients for whom biopsies were deemed unacceptable. For this set of patients please state the reason(s) the biopsies were considered to be unacceptable.
3. For data validation of each study (IT-R-005 and IT-R-006), please submit results of the intra-rater and inter-rater variability assessments for individuals performing rating of clinical outcomes if the data are available.

4. Please comment on the significant imbalance of product manufacture failure rate between IT-treatment and placebo groups in both pivotal trials IT-R-005 and IT-R-006. These subjects did not receive any treatment.
5. Your protocols/amendments described a plan for re-biopsy and manufacturing of new product for patients withdrawn for lot release failures. Please comment on the reasons for patient withdrawals without treatment.

#### STATISTICAL INFORMATION

6. Regarding randomization:
  - a. You state that errors occurred for assigning treatments to patients during the course of studies IT-R-005 and IT-R-006 (Module 2, Volume 1, Section 2.7.3, pages 17-18; as well as individual Clinical Study Report). Please specify the site(s) and patient IDs involved.
  - b. In your Clinical Study Reports of studies IT-R-005 and IT-R-006, you included Randomization Scheme with treatment assigned in the Appendices (Module 5, Volumes 45 and 54). Please submit the original randomization lists generated prior to patient assignments.

#### IRB STATUS

7. -b(4)- IRB was recently issued a warning letter by FDA suspending their authority to approve new studies and banning enrollment of new subjects into existing studies. Please comment on the current status of Isolagen's IRB.

#### PROPRIETARY NAME REVIEW

8. The proposed product label currently states the name of the product as "Isolagen Therapy™ (Dermal Fibroblasts)," which is not acceptable because it does not follow the United States Adopted Names (USAN) scheme for cellular therapy products. Please comment on the status of the Proprietary Name Review.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our complete review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application. Following a review of the application, we shall advise you in writing of any action we have taken and request additional information if needed.

If you have any questions, please contact the Regulatory Project Manager, Lori Tull, at (301) 827-5102.

Sincerely yours,

Raj K. Puri, M.D., Ph.D.  
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Center for Biologics Evaluation and Research