

# Telecon #1, October 20, 2009 - Laviv

- 9-10 AM October 20, 2009
- RE: Isolagen
- Participants:

AC Panel member-Lynn Drake, MD (Dermatologist/Dermatopathologist)  
FDA-Changting Haudenschild, Bruce Schneider, Yao-Yao Zhou, Agnes Lim, Mercedes Serabian

## Dr. Drake's responses/comments:

- We do not know what is going on with the injected cells. From a safety standpoint, we want to know that something bad is not going to happen. For example, scarring and granulomas may form at injection sites. We want to know about the tissues/cells after injection. The sponsor did not look, therefore we do not know. This should be the minimum standard, and the sponsor failed to meet it.
- Conduct biopsy study for up to 6 months can provide some answers as to what the injected cells have done and what tissues are found at the injection sites.

## Clinical study:

- Facial biopsies have been done before, e.g. photoaging studies. The alternative is the forearm (ante-lateral cubitus), which is not the same as the face but it is acceptable
- Recommend forearm (antecubitus) biopsies
- It is acceptable to follow the "3/3/3/6 phase rules" of wound healing
  - Small sample size study, ~ 20 subjects
  - Multiple biopsies. No more than 3 biopsies in a patient

10 subjects: day 3, week 3 Dr. Drake later suggested 10 subjects for 3 month; 10 subjects for 6 months, to simplify the study and directly answer the questions of the structure changes.

10 subjects: mo 3, mo 6

- Biopsies @ 3 or 6 mo would be adequate for safety concerns; OK to do in different subjects
- Recommend biopsy evaluations by dermatopathologist
- Histologically, collagen and elastin in scars can be distinguished from normal collagen and elastin due to their altered architecture (curled, clumped, acellularity)
- Dr. Drake is not concerned if the fibroblast is there or not
- Recommend focusing biopsies in subjects < 65 yo because younger patients have more robust reactions
- Would not specifically perform biopsies in racial subgroups

- Location matters
  - The face heals well whereas chest scars are very prominent
  - Different kinetics between face and arm; could affect results
- Difference between wrinkles vs folds vs contour. Once approved, product will be used for other indications, and Tx around the eyes and glabellar could lead to additional potential AEs. For this biopsy study, recommend keeping it to wrinkles

#### **Animal models:**

- Xenograft models to provide guidance for the time points to do the biopsies.
- Markers could be used in animal models
- Possibly skip animal studies by conducting a “3(days) ,3 (weeks) ,3 (months)” clinical study
- To check cell fate
- To study how long injected fibroblasts last and what they secrete.
- These mechanism issues could be addressed by labeling studies in animals

#### **Additional issues:**

- Residual components in the product (to be addressed by CMC)
- Suggested talking to cell experts regarding how long fibroblasts persist