

APPROVED

By Jean Gildner at 2:58 pm, Dec 07, 2016

From: [Yong, Carolyn](#)
To: [Gildner, Jean](#)
Cc: [Thomas, John](#)
Subject: MF (b) (4) IR request
Date: Monday, June 20, 2016 1:13:05 PM
Importance: High

Jean,

We have the following IR request for the master file holder, Matricel. The point of contact according to my records is (b) (6)

Please also cc the Vericel point of contact on the email communication:

1. Please provide the following additional information to ensure the safety of the animal tissue derived collagen product:

a. The master file states the slaughterhouses have been inspected by the USDA. Please identify the methods used to ensure compliance with USDA inspection requirements.

b. Please identify quarantine procedures for tissues until they have met/failed release criteria.

c. Please provide certification the manufacturing facility has not processed animal tissues that came from countries with bovine spongiform encephalopathy or transmissible spongiform encephalopathy risk.

2. The (b) (4) is measured using (b) (4). The acceptance criterion of (b) (4) is stated to be based on process monitoring results of batches manufactured during the design phase of the product. Please provide the data supporting a justification for the (b) (4) acceptance criteria.

3. The (b) (4) specification is based on the (b) (4). Please provide additional justification supporting the (b) (4) specification to include a (b) (4) the methods described in (b) (4) or similar method.

4. The (b) (4) test reports are dated from 2002 to 2005. Please confirm the collagen membrane evaluated in these (b) (4) studies is representative of the current collagen mesh product using the same manufacturing processes with the same final (b) (4) specifications.

5. The collagen membrane product is being evaluated for (b) (4) testing;

(b) (4)

on a manufacturing process-validation basis with periodic determinations.

6. (b) (4)

7. Package integrity appears to be evaluated using standards that are not recognized by FDA. Please cite conformance to FDA recognized standards. Alternatively, please provide a justification explaining why the standards are equivalent to FDA recognized package testing standards.

8. Please provide complete test reports for the (b) (4) analysis used to evaluate collagen product (b) (4) for review.

Quality Systems Information:

Provide the summaries listed below, or indicate the location of this information in your master file that was intended to satisfy the elements below:

9. A summary of the firm's management structure with executive responsibility who manage, perform, and assess work affecting quality of the product and related controls to ensure that the firm's quality policies are appropriately implemented and followed, and the product appropriately designed and manufactured in conformance with quality system requirements as per 21 CFR 820.20.

10. A summary of the firm's design control system under 21 CFR 820.30 must be included for the device constituent. The design control information should include initial design, planning and development, design input, design output, design review, design transfer, design verification, design validation that meets the proposed intended use of the device, design changes, and design history file. All the design control activities must be documented in the Design History File (DHF) and subjected for design reviews. In addition, the location of DHF should be provided to the Agency for the facility inspection determination.

11. Summary of information pertaining to the Purchasing Control as per 21 CFR 820.50 to demonstrate controls and documentation for components, products, or services (example (b) (4)) received at the sponsor's facility for use in the manufacture of the device. The summary should include the applicant's evaluation process of their suppliers that meet the manufacturing acceptance criteria of the device specifications. Notification of changes by

the suppliers should be considered in the firm's Purchasing/Supplier agreement as changes to incoming specification can impact the safety and effectiveness of the device.

12. Summary of information related to Corrective and Preventive Actions (CAPA) as per the requirement of 21 CFR 820.100. CAPA procedures are used to determine the cause of problems and non-conformances, and the appropriate measures used to correct and prevent such problems and non-conformances from recurring. The CAPA system must account for investigations into failures in the device constituent. CAPA activities for the analysis of sources of quality data to identify existing and potential cause of nonconformances, related investigations, and actions considered to correct and prevent recurrences of problems and non-conformances, including the verification or validation of the actions should be documented under the firm's CAPA System as described in 21 CFR 820.100.