



Center for Biologics Evaluation and Research Laboratory Quality System

Laboratory Quality Product Testing Plan (TP)

Title: MACI (Vericel) Autologous Cultured Chondrocytes on a Porcine Collagen Membrane

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Testing Plans document how CBER currently anticipates regulating licensed products including the circumstances under which CBER testing may be used to evaluate a lot of licensed product. It is the responsibility of each Product Office to develop Lot Release Testing Plans for the licensed products under its purview.

Product Trade Name:	MACI
License Product Name (Proper Name):	Autologous Cultured Chondrocytes on a Porcine Collagen Membrane
Product ID (LQDB):	002410
License Number:	2010
STN (RMS-BLA):	125603
Applicant (Supplier):	Vericel Corporation

Signatures Required to Approve or Update this Testing Plan

Director, DBSQ/OCBQ	William McCormick, Ph.D.
Product Office Director (or designee):	Celia Witten, Ph.D., M.D.
Director, DMPQ/OCBQ:	John A. Eltermann, Jr., M.S., R.Ph.
Center Lab Quality Mgr:	Sheila Smith

<p>Mode of Product Regulation</p> <p>Based upon Product Office assessment of the product, including relevant manufacturing, safety, clinical and other considerations, determine which form of CBER review and or release of manufactured product lots is necessary.</p> <p>Lot Release – Manufacturer may not distribute product until receiving lot-specific release from CBER.</p> <p>Surveillance – Manufacturer may distribute product without lot-specific release from CBER. Manufacturer is required, according to the terms of the license, to periodically provide CBER with lot-specific testing information and possibly samples.</p> <p>Exempt – Manufacturer is free to distribute product post-licensure without supplying any additional information or samples to CBER.</p>	<p>Lot Release</p> <p>Protocol Review <input type="checkbox"/></p> <p>Protocol Review and Confirmatory CBER Testing <input type="checkbox"/></p> <p>-----</p> <p>Alternative to Lot Release</p> <p>Surveillance <input type="checkbox"/></p> <p>Exempt <input checked="" type="checkbox"/></p>
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Justification for Mode of Regulation:

Briefly, describe how the indicated Mode of Regulation supports CBER's mission to ensure the purity, potency, safety, efficacy, and availability of this biological product including justification for any confirmatory CBER product testing, per 21 CFR 610.2(a). Additionally, for products on Surveillance, summarize the requirements for submission of lot-specific information and sample (if required) as described in the license.

Brief description: MACI consists of autologous cultured chondrocytes, expanded ex vivo and seeded on a 14.5 cm² resorbable porcine (b) (4) -derived Type I/III collagen membrane at a density of 500,000 to 1,000,000 cells per cm².

Indications and Usage: MACI™ is an autologous cellular product indicated for the repair of symptomatic, full-thickness cartilage defects (single or multiple defects) of the knee with or without bone involvement (b) (4) in adults.

Dosage and Administration: For Autologous Use Only

- MACI should be administered only by a surgeon specifically trained in the use of MACI.
- MACI is implanted with the cell-side down. The implantation is performed using sterile surgical techniques and requires both the preparation of the defect bed and the application of fibrin sealant to the base and rim of the defect in order to secure the implant.

Dosage Forms and Strengths: Each implant consists of autologous cultured chondrocytes on a resorbable Type I/III collagen membrane, at a density of 500,000 to 1,000,000 cells per cm² to be trimmed by the surgeon to the size and shape of the defect.

The following discussion forms the rationale for the testing plan for mode of lot release of this fractionated Blood Product. MACI™ will be exempt from lot release with no requirement for submission of lot release protocols or product samples to CBER. No testing is performed at CBER for the following reasons:

- MACI™ is an autologous product. Each patient receives a single autologous implant generated from an initial biopsy. Occasionally there may be a second implant from the lot.
- Single lot failure has a minimal impact on public health.
- The cellular product is administered fresh and has only a (b) (4) shelf life. This does not allow enough time for CBER to test the product before expiry.
- The cellular component of this product is (b) (4) .
- Vericel will submit release test results from all lots in BLA annual reports; tabulated data from released lots will be reviewed for data trends and potential problems.

Safety and Purity – Final product may be evaluated from the information provided in the lot release protocol only if a lot release protocol is submitted to CBER. In the event of protocol review, the specifications will be confirmed or provided by the product office for protocol review.

Potency and Identity – Final product may be evaluated from the information provided in the lot

release protocol only if a lot release protocol is submitted to CBER. In the event of protocol review, the specifications will be confirmed or provided by the product office for protocol review.

Anticipated CBER product testing:

List laboratory evaluations to be performed at CBER.

Document ID number	Test Method	Test Specifications	Testing Frequency
	N/A		

Lot Testing algorithm(s):

For each Test Method listed above describe how the indicated frequency of testing supports the assurance of product quality.

For each method with testing frequencies other than 100%, describe how lots are pre-selected for testing, i.e. random number table, every nth lot submitted, first X lot(s) submitted per time period, decision tree, etc.

N/A

Conditions anticipated to require temporary over-ride of algorithm:

Specify conditions justifying algorithm over-ride; i.e. Public Health Considerations (e.g. temporary product shortage, sudden increase in demand), Operational Considerations (e.g. temporary unavailability of resources), Lot-specific Compliance Considerations (e.g. questions raised during lot release protocol review).

- Public Health Considerations (e.g. temporary product shortage, sudden increase in demand)
- Operational Considerations (e.g. temporary unavailability of resources)
- Lot-specific Compliance Considerations (e.g. questions raised during lot release protocol review)

Changes since the last revision

N/A New Document