

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Food and Drug Administration  
Center for Biologics Evaluation and Research

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DATE August 30, 2016

FROM Anthony Hawkins, Bioresearch Monitoring Branch  
Division of Inspections and Surveillance  
Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Chief, Bioresearch Monitoring Branch  
  
Gilliam Conley, Director, Division of Inspections and Surveillance

TO John Terrig Thomas, BLA Committee Chair  
Michael Yao, BLA Clinical Reviewer  
Jean Gildner, BLA RPM

SUBJECT Bioresearch Monitoring Final Discipline Review  
BLA: STN 125603 / 0  
PRODUCT: Matrix applied characterized autologous cultured chondrocytes  
SPONSOR: Vericel Corporation, Cambridge, MA

REVIEW SUMMARY

Bioresearch Monitoring inspections of three foreign clinical investigator study sites were conducted in support of this Biologics Licensing Application (BLA). Results from the inspections did not reveal substantive problems that impact the data submitted in the BLA.

BACKGROUND

Three foreign clinical investigator study sites under phase 3 study protocol MACI00206 were identified for Bioresearch Monitoring inspections. The BLA review committee concurred with the proposed sites. The sites were selected based upon numbers of enrolled study subjects, prior FDA inspection history and numbers and types of protocol deviations.

Protocol inspected:

*A Prospective, Randomized, Open-Label, Parallel-Group, Multicenter Study to Demonstrate the Superiority of Matrix-induced Autologous Chondrocyte Implantation (MACI® implant) versus Arthroscopic Microfracture for the Treatment of Symptomatic Articular Cartilage Defects of the Femoral Condyle including the Trochlea*

Protocol MACI00206 subjects were enrolled at 16 clinical study sites in seven European countries (three in the Czech Republic, four in France, three in the Netherlands, one in Norway, three in Poland, one in Sweden, and one in the United Kingdom). One study site in Poland, 1 in Sweden, and 2 in the United Kingdom were closed because no subjects were enrolled. A total of 189 subjects were screened and of those, 144 were randomized to study treatment. The three inspected sites comprise approximately 57% of the total study subjects randomized under the protocol.

The inspections were conducted in accordance with FDA’s Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators. Information submitted in the BLA was compared to source documents at each inspected site. The inspection assignment included specific questions concerning the clinical study.

### INSPECTIONS

Bioresearch Monitoring inspections were conducted at the following clinical study sites:

Study Site #	Site Name	Location	Form FDA 483 Issued?	Final Inspection Classification
5	Polyclinique Saint-Roch	Montpellier, France	No	VAI
11	University Medical Centre Utrecht	Utrecht, Netherlands	No	NAI
15	Wojewódzki Szpital	Piekary Śląskie, Poland	No	NAI

NAI = No Action Indicated    VAI = Voluntary Action Indicated

### INSPECTION FINDINGS

The results from the inspections showed only a few minor problems.

Protocol compliance:

The study **Site 5** clinical investigator re-screened one subject before the protocol-allowed timeframe; another subject had no screening or qualifying radiograph as required.

Study Records:

The Patient Information Sheet/Informed Consent Form document reviewed during the **Site 5 and Site 11** inspections did not contain a written statement noting the possibility that the Food and Drug Administration may inspect the study records.

### SPONSOR ISSUES

No sponsor or monitoring issues were noted.

### FINANCIAL DISCLOSURE:

The Clinical Investigator Compliance Program directs the FDA investigator to ask the clinical investigator if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children, as well as if and when the information was updated. The information submitted to the BLA was verified for each of the inspected clinical investigators.

ADMINISTRATIVE FOLLOW-UP:

We issued information letters to each of the above clinical investigators. Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at 240-402-8950.

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Anthony Hawkins  
Consumer Safety Officer

Distribution

Electronic Copies:

Upload to Application Folder in EDR

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Reviewed: Holobaugh: 8/30/16

Reviewed: Conley: 08/30/16