



AMERICAN ACADEMY OF
ORTHOPAEDIC SURGEONS

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April 15, 2009

Joshua Scharfstein, M.D.

Acting FDA Commissioner
Division of Dockets Management (HFA-305)
Food and Drug Administration (FDA)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket Number FDA-2008-D-0659

Dear Dr. Scharfstein,

The American Academy of Orthopaedic Surgeons (AAOS/Academy), representing over 17,000 Board certified orthopaedic surgeons, welcomes the opportunity to comment on the FDA's Current Good Tissue Practice and Additional Requirements for Manufactures of Human Cells, Tissues, and Cellular and Tissue-based Products Draft Guidance. The proper manufacturing of human cells, tissues and cellular and tissue-based products is critical in preventing the introduction, transmission, or spread of communicable disease. It is imperative that specific measures are implemented to ensure the safety of patients.

The AAOS appreciates the efforts of the FDA to develop this guidance with recommendations for manufacturers to practice standardized recovery, processing, storage, labeling, packaging, or distribution of any human cell or tissue, and screening or testing of cell or tissue donors. Orthopaedic surgeons are frequent users of bone graft substitutes, bone growth factors used alone or in combination with other products, and autologous or allograft cells for regrowth of musculoskeletal tissues. The Academy encourages the FDA to consider the following suggestions prior to the release of the final draft guidance.

III. CGTP Requirements – Subsection C

How do I ensure that another establishment with which I have a contract or agreement complies with CGTP requirements?

Recommendations in the document state that in order to adequately audit a supplying tissue procurement agency, the next of kin should be contacted to assure the accuracy of provided information. This would, in fact mean that the recovery agency would have to reconnect with the donor family, requiring them to undergo some process of repeat questioning, which is inappropriate and intrusive, especially during a time of

bereavement. In addition, the criteria for the audits are much too broad and non-specific. There should be explicit language outlining what will be audited (appropriate storage temperatures, records, testing information, proper storage, equipment, recovery process measures, facility upkeep).

V. Establishment and Maintenance of a Quality Program – Subsection E

With whom must an establishment share information pertaining to the possible contamination of or potential transmission of communicable disease by a Human Cell, Tissue and Cellular and Tissue-based Product (HCT/P)?

If an agency or tissue bank receives information regarding serological or other tests that put the tissue at risk for communicable disease, this information needs to be communicated to other agencies or facilities that have received tissue from that particular donor or from a specific facility that is being investigated for contaminated tissue. However, caution should be exercised in alerting facilities, agencies and recipients without substantiated evidence or confirmation of an adverse reaction, such as an infection that was caused by allograft tissue or HCT/Ps. If the recovery establishment receives information that a confirmed adverse event involves their tissue, this information must then be shared with any other processing establishment which received the HCT/Ps from the same donor. Every recovery establishment encourages and receives notification of possible adverse reactions that are then investigated. If, at the end of the investigation, there is no association between the possible adverse event and the tissue, this information does not have to be shared with other agencies. On the other hand, if the possible adverse event is investigated and there appears to be a causal relationship between the tissue and the adverse event. All involved agencies and processors should be informed as soon as possible.

XIII. Processing and Process Controls – Subsection D

Why are pre-processing microbiological cultures important?

The recommendations made for pre-processing microbiological cultures should be more specific. Stipulations that validate processes must be in place to assure disinfection or sterilization of tissues that are processed depending on the bioburden present as detected on pre-processing cultures. These tissues may include tissues that have cultures positive for *Clostridium*, *Streptococcus pyogenes* or other microorganism determined to pose difficulty in elimination. As an example, if fresh tissue is to be used from a donor that has any positive cultures on other tissues for *Clostridium* or *Streptococcus*, there must be a validated process in place to prevent the possibility of transference of these microorganisms via the fresh grafts, which include zone recovery, aseptic processing and companion tissue destructive cultures.

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If the fresh grafts grow pathogens, they would need to be discarded or secondarily sterilized and used in other materials.) In an instance where a facility receives a donor in which there is *Clostridia* growth on several grafts and the facility has no validated system in place to assure the prevention of possible disease transmission through processes and/or sterilization, all of the tissue must be discarded.

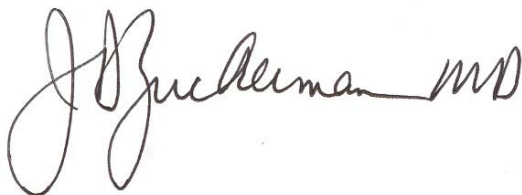
XVII. Storage – Subsection B

How do I determine appropriate storage temperatures for my HCT/Ps?

The recommendation to store HCT/Ps at an “appropriate temperature” is a vague statement. There should be suggested temperatures to lessen opportunity for contaminating the products. The Academy encourages tissue storage facilities to follow standards required by the Joint Commission. Providing additional information regarding what temperatures are appropriate should be considered. Since many hospitals, which serve as short-term storage facilities prior to implantation, are accredited by the Joint Commission and must comply with their standards in order to maintain their accreditation, referencing those standards in this guidance would provide consistency and encourage uniform practices.

The American Academy of Orthopaedic Surgeons strives for the safest practices for our patients. It is of extreme importance that manufacturers of human cells, tissues, and cellular and tissue-based products are held to the highest standards. Furthermore, standardized processes must be in place to ensure that proper steps are taken to prevent transmission, introduction, or spread of communicable disease. The Academy looks to working with the FDA to ensure the safe and proper manufacturing of human cells, tissues, and cellular and tissue-based products.

Sincerely,



Joseph Zuckerman, MD
President