DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Ombudsman
5600 Fishers Lane
Room 14B-03, HF-7
Rockville, MD 20857

Food and Drug Administration
Rockville MD 20857

March 11, 2002

[redacted]

Re: Request for Designation
Musculoskeletal Transplant Foundation
DBX®
Our file: 2001.018

Dear [redacted]

The Food and Drug Administration has completed its review of the request for designation (RFD) you submitted on behalf of Musculoskeletal Transplant Foundation. The request covers DBX® and was filed by this office on July 5, 2001. On August 17, 2001, MTF extended the designation deadline for this request to provide the agency with sufficient time to fully consider the issues raised. The agency met with representatives of MTF on October 2, 2001, and MTF supplemented its RFD with additional information on November 8, 2001.

DBX® consists of allograft [redacted] human demineralized bone matrix (DBM) in a sodium hyaluronate / [redacted]. It is used to replace or supplement the recipient's bone in orthopaedic, reconstructive, and [redacted] bone grafting procedures. According to MTF, DBX® acts as a scaffolding or matrix for new host bone formation.

As explained by MTF, freeze-dried DBM is friable and difficult to place into a bony defect. If water is added to it to make it easier to handle, it degrades quickly. Therefore, according to MTF, surgeons frequently mix DBM with saline, blood, and/or autologous bone chips at the time of surgery in order to create a more viscous, paste-like material. According to MTF, the sodium hyaluronate turns the DBM into its two forms: a putty and a paste, both of which are easier to insert into bone voids than powdery DBM. MTF states further that the [redacted] which allows the sodium hyaluronate to be hydrophilic and keep water away from the DBM. According to MTF, because of sodium hyaluronate's hydrophilic characteristics, DBX® remains osteoinductive after storage for 18 months at ambient temperatures. In summary, MTF states that the addition of sodium hyaluronate [redacted]

solution is intended to improve the handling characteristics of DBM and provide surgeons with the convenience of a premixed product that can be stored for several months before using it.

MTF argues that DBX® is a human tissue product that may be regulated solely under section 361 of the Public Health Service Act and 21 CFR Part 1271 rather than the drug or device provisions of the Federal Food, Drug, and Cosmetic Act (the Act). After extensively considering the matter, the agency concludes that DBX® does not meet the all the criteria for regulation solely under section 361 of the Public Health Service Act and 21 CFR Part 1271.

On January 19, 2001, FDA issued a final rule called Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing.[1] Among other things, this rule listed four criteria that must all be met for human cells, tissues, and cellular and tissue-based products (HCT/P's) to be regulated solely under section 361 of the Public Health Service Act.[2] These criteria are:

1. The HCT/P is minimally manipulated;
2. The HCT/P is intended for homologous use only;
3. The manufacture of the HCT/P does not involve the combination of the cell or tissue component with a drug or device, except for a sterilizing, preserving, or storage agent, if the addition of the agent does not raise new clinical safety concerns with respect to the HCT/P; and
4. Either:
    - i The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
    - ii The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and:
        a. is for autogolous use
        b. is for allogeneic use in a first or second degree relative; or
        c. is for reproductive use.

DBX® does not meet the third criterion for regulation solely under section 361 of the Public Health Service Act. As MTF has explained, although the sodium hyaluronate / [redacted] is added as a preservative agent, it is also intended to affect the structure or function of the body – that is, to make demineralized bone easier to insert into bone voids. Accordingly, the agency concludes that within the meaning of 21 CFR 1271.10(a)(3), DBX® combines an HCT/P with a drug or device that is not a sterilizing, preserving, or storage agent. Therefore, DBX® is not eligible to be regulated solely under section 361 of the Public Health Service Act, but instead is regulated under the

[1] See the Federal Register of January 19, 2001 (66 FR 5447).
[2] 21 CFR 1271.10(a).

Federal Food, Drug, and Cosmetic Act. Further, consistent with the agency's review and regulation of other products containing DBM and having similar composition and mode of action, DBX® is appropriately reviewed and regulated under the medical device premarket notification provisions of the Act.

We are aware that other currently marketed demineralized bone products may also fail to meet the third criterion that HCT/P's must meet in order to be regulated solely under section 361 of the Public Health Service Act. In the very near future, the Center for Devices and Radiological Health will notify you, and all other known manufacturers of similar products, of the requirements for bringing such products into compliance with the Act. If you would like to discuss these requirements in the meantime, please call Mr. Mark Melkerson, Deputy Director, Division of General, Restorative and Neurological Devices at 301-594-1184.

If you have any questions about this matter, please call Suzanne O'Shea, of this office, at 301-827-3390.

Sincerely,

Suzanne O'Shea

Steven H. Unger
Ombudsman