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Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

00N-1380
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Re: Docket No. 00N-1380 Human Bone Allograft: Manipulation and Homologous Use in Spine and Other Orthopedic Reconstruction and Repair

The Advanced Medical Technology Association (AdvaMed) is pleased to provide the following comments on Human Bone Allograft. AdvaMed, formerly known as the Health Industry Manufacturers Association (HIMA), is the largest medical technology association in the world. AdvaMed represents more than 800 manufacturers of medical devices, diagnostic products, and medical information systems. AdvaMed's members manufacture nearly 90 percent of the \$68 billion of health care technology products purchased annually in the United States, and nearly 50 percent of the \$159 billion purchased annually around the world. A number of AdvaMed members are involved in providing human bone allograft to the clinical community.

General Comments

For many years, human bone allograft has provided significant clinical benefit to thousands of patients for a variety of disease states. The use of allograft bone in clinical practice is well established and has evolved over time through surgeon use into many innovative and useful forms. AdvaMed advocates innovation for patient care through development of new medical technologies and products. However, AdvaMed recognizes that the regulation of these products is a challenging matter for the agency.

Specific Comments

Existing regulations need to be implemented

FDA has established regulations to address tissue products, including human allograft bone, under the authority of Section 361 of the Public Health Service Act and under applicable sections of the Food Drug and Cosmetic Act (the Act), as amended. AdvaMed supports the regulation of human bone allograft as either transplanted human tissues or medical devices.

Plainly, it is in the interests of the FDA, industry, the healthcare delivery system and, most importantly, patients, for these regulations to be administered in a fair manner to achieve safe and effective products. AdvaMed believes that FDA must take great care when more than one Center is involved with regulating human tissues or materials derived from such tissues to ensure that the designated means of regulatory control for each such product is in fact enforced. Only by doing so, can the public health be protected and a level playing field among companies be created.

Tissue Reference Group needs to be more effective

AdvaMed members report that despite efforts by the agency, and the combination product law and regulations, jurisdictional questions still abound regarding which FDA component has the lead for regulating human tissue and its derivative products. AdvaMed commends the agency for its effort to address this problem through the creation of cross-functional groups such as the Tissue Reference Group (TRG). However, we have a few suggestions for strengthening the effectiveness of the group.

Specifically, AdvaMed suggests improvements in the operation of the TRG. We encourage a more transparent and open process in its activities, including use of notice and comment rulemaking. Also, there is a need to ensure that product specific agency decision-making is more open to public participation when it involves creating precedent for a product type. This is particularly important with the TRG because the group makes recommendations on individual products that may be binding for an entire product class. Public meetings should be held prior to making binding decisions that affect a class of products.

Good Tissue Practices need to be implemented

Additionally, the proposed Good Tissue Practices regulation needs to be implemented as soon as possible. The proposed regulation is encouraging and will be helpful to the tissue banking and processing industry. When finalized, the proposed regulation will help to reduce confusion over the regulatory requirements necessary for companies working in this industry. AdvaMed is appreciative of the effort that must take place to establish this regulation, but it is urgently needed. We believe that finalizing this regulation is critical before FDA proposes additional tissue-related regulations because of the agency's tendency to revisit each outstanding proposed regulation in light of the newest proposal. In other words, proposed regulations become a moving target and are unlikely to be resolved as final until the target stands relatively still.

Moreover, standards such as the Tissue Engineered Medical Product (TEMP) standards, developed by American Society for Testing and Materials (ASTM) will be helpful in providing continuing guidance for industry. Generally, it appears that the regulatory framework for consistent, appropriate and equitable regulation of human bone allograft either exists or is in preparation, but there is an urgent need for these regulatory elements to be completed and appropriately applied.

Better definition for tissue-based products is needed

There is a need for a better and more encompassing definition of human bone allograft products to ensure that the TRG and regulated companies can more efficiently and predictably proceed in the future. AdvaMed recommends that the homologous use and minimally manipulated criteria for determining whether a human cellular and tissue-based product is subject to regulation as a medical device or tissue should be eliminated. These agency-proposed definitions fail to reflect the current FDA approach to regulating most tissue-based products as "tissue." For example, the definition for homologous tissue states that such tissue "fulfills in its native state, in a location where such structural function normally occurs." This language is very confusing. It appears to state that in order for a product to be regulated as tissue, it must be used in the same location from which it was removed and for the same purpose the tissue originally fulfilled.

The definition of minimal manipulation is imprecise, making it very difficult to draw a meaningful distinction between tissue-based products that are "minimally manipulated" and those that are "more than minimally manipulated." Moreover, the result of manipulation should be more important than the fact of manipulation. Specifically, the shaping of bone, for example, into screws, wedges, pins or dowels does not change the character or identity of bone and should be seen as manipulation of tissue that remains tissue and should be regulated as such. In other words, tissue-based products labeled or promoted for tissue replacement, reconstruction or restoration of function should be regulated under 21 CFR 1270 as Human Tissues. However, if false or misleading claims are made by the processor regarding the performance of the tissue, then the agency should enforce the Act against such person or product. In contrast, AdvaMed believes that tissue loses its identity when it is combined with a nontissue component, such as in combination products. For example, when bone is demineralized and combined with a device (e.g., collagen) or a drug, then it should fall outside of the tissue regulatory category.

From this, AdvaMed contends that FDA should consider deleting the homologous use and minimally manipulated concepts from the tissue definition and replacing them with a definition that reflects the current tissue versus device definitions. By doing so, the agency will provide enough breadth to fairly capture the products of the future and ensure the safety and effectiveness of current products and those still developing in innovators' minds.

If FDA is wedded to its proposed definition of "tissue-based products," AdvaMed strongly urges the agency to fully explore the meaning of its approach and include in the definition a range of examples that will clarify the scope of the term. This is important to ensure certainty and not create regulatory delays that deny physicians excellent and needed products and hurt consumers. AdvaMed requests the agency to return to the primary goal, as stated in the proposed rule for establishment registration and listing, to "improve protection of the public health without the imposition of unnecessary restrictions on research, development, or the availability of new products."

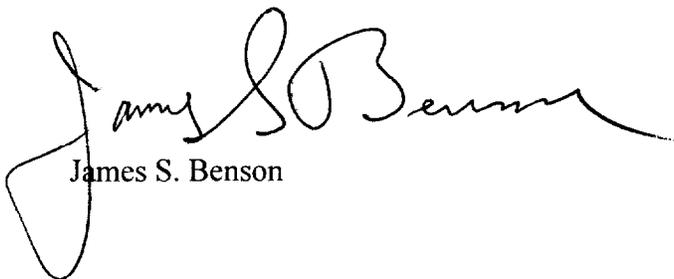
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AdvaMed recognizes that the agency is faced with a complex issue as it addresses the regulation of tissue. Because of the complexity of this issue, AdvaMed is willing to work with the agency in a cooperative manner to explore alternative approaches to tissue regulation. AdvaMed appreciates the opportunity to provide comments on human bone allograft.

Sincerely,

A handwritten signature in black ink, appearing to read "James S. Benson". The signature is fluid and cursive, with a large initial "J" and "B".

James S. Benson