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Division of Documents Management (HFZ-305)
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Federal Register Docket Number 2006D-0363

Written Comments on FDA Draft Guidance for Industry and FDA Staff – Class II Special Controls Guidance Document: Absorbable hemostatic Device; Issued October 31, 2006

Dear FDA Representative,

St. Jude Medical (SJM) is providing comments to FDA regarding the above referenced document as requested by FDA.

Additionally, SJM hereby requests that an open public hearing be held to discuss this draft guidance document, especially in regards to the bovine spongiform encephalitis requirements proposed in the document.

Two (2) copies of this document are provided as specified in the Federal Register Notice. The content of this letter is truthful and accurate to the best of my knowledge and nothing of material fact has been omitted. If you have any questions regarding the information contained herein, please contact the undersigned. You may also contact Ann Graves, Director of Regulatory Affairs, at 763-383-2639.

Best Regards,



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Written Comments on FDA Draft Guidance for Industry and FDA Staff –
Class II Special Controls Guidance Document: Absorbable Hemostatic
Device; Issued October 31, 2006

St. Jude Medical (SJM) is hereby providing comments to FDA regarding the above referenced document as requested by FDA. SJM is pleased that FDA has researched and prepared this draft Guidance Document for absorbable hemostatic devices.

SJM understands that this draft guidance is the first public document in several years that to provide insight to FDA's thinking regarding bovine spongiform encephalopathy (BSE) and medical devices. Given the importance of this subject matter, SJM believes that if this proposed guidance is implemented by FDA, the individual subsection regarding BSE controls will likely be used as a reference for any device that incorporates non-viable tissue of animal origin. It is also likely that other foreign regulatory agencies will adopt these same requirements for their own use when considering the review, approval and control of such medical devices. For example, the Chinese State Food and Drug Administrations' (SFDA) uses the FDA (outdated) 1998 Guidance Document, "Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices)".

FDA has proposed a recommendation in this draft guidance that a device manufacturer provide a certification for any animal material of bovine origin used in a medical device "that the animal is from a country free of bovine spongiform encephalopathy." Both the United States Department of Agriculture (USDA) and FDA have confirmed that the United States has two documented cases of BSE^(a,b), and thus the US is no longer a "BSE free country" and would not be considered BSE free in many other geographies.

(^a) USDA News Release; Statement by USDA Chief Veterinary Officer John Clifford (DVM) Regarding Positive BSE Test Results March 13, 2006.
http://www.aphis.usda.gov/newsroom/content/2006/03/bsestatement3-13-06_vs.shtml

(^b) FDA Statement on USDA Announcement of Positive BSE Test Result (March 13, 2006).
<http://www.fda.gov/bbs/topics/NEWS/2006/NEW01333.html>

To ensure that an adequate supply of bovine source material remains available for use in medical devices, SJM recommends that FDA consider alternative criteria for minimizing the risk of BSE transmission through animal materials. As discussed in greater detail below, SJM recommends that FDA adopt criteria that is consistent with FDA's proposed rule on the "Use of Materials Derived from Cattle in Medical Products Intended for Use in Humans and Drugs Intended for Use in Ruminants," 72 Fed. Reg. 1582 (January 12, 2007) (referred to herein as "Proposed Bovine Material Source Rule").

General Overview Comments

Great benefits are provided by the use of non-viable animal tissue in medical devices. Both FDA and industry seek to protect and enhance the public health through minimizing the risk of exposure to BSE. SJM believes that the shared goal of ensuring that BSE-free animal source material remains available can be met by allowing manufacturers to provide alternative assurances of safety with respect to BSE infectivity to meet FDA's requirements. Based on the significant experience garnered in the last 10 years on reducing the risks of BSE transmission, FDA has recognized more efficient, less burdensome approaches to ensure public health and safety with respect to BSE infectivity. For example, the United States (US) has lowered the risk of BSE occurrence by placing restrictions and controls on: (1) animal feed of mammalian origin; (2) animal rendering practices and (3) by increasing the testing of cattle during the slaughter process. The current controls have had a very positive impact, as is evidenced by only two (2) documented cases in US cattle since the initial reports in the UK in 1997. Through the use of the current controls the risk of BSE infection in any cattle sourced from the US is significantly reduced. Accordingly, the related non-viable tissue used for medical devices sourced from US cattle has an overall significantly reduced BSE risk. Indeed, there have been no reports of vCJD in humans associated with BSE transmission in the US.

SJM respectfully suggests that FDA's revise the draft guidance to provide alternative means to achieve FDA's goals in the manufacture of medical devices for the US. Restricting the sourcing of bovine-derived materials only to BSE-free countries is no longer justified and unnecessarily burdensome, and, therefore, would have a significant negative impact on public health and safety by significantly limiting the availability of certain medical devices.

The following two sections provide SJM's detailed comments and corresponding recommendations.

Comments and Recommendations on Specific Document Statements

FDA Statement:

Collagen or Animal Derived Material

If collagen or other animal-derived material is a device component, we recommend that you describe the species and tissue from which the animal material was derived, including the specific type of collagen or another material used.

If the animal material is of bovine origin⁷, we recommend that you include:

- **Certification that the animal is from a country free of bovine spongiform encephalopathy.**

(⁷) See also List of USDA-Recognized Animal Health Status of Countries/ Areas Regarding Specific Livestock or Poultry Disease, <http://www.aphis.usda.gov/vs/ncie/country.html>

SJM Comment:

While this statement references the USDA's specific country listing, it is SJM's opinion that this statement will be interpreted by foreign regulatory bodies that the material source country must be '*from a country [completely] free of (BSE)*'.

Considering that both the USDA and USFDA have themselves determined that the US has itself found two documented cases of BSE^(a,b), it is SJM's belief that foreign regulatory agencies will not consider the US to be a "BSE free country".

In addition, the FDA requirement for 'certification' does not explicitly provide manufacturers with alternative methods of compliance with FDA's requirements. Alternative methods, as outlined in FDA's Proposed Bovine Material Source Rule, would ensure material safety and purity without increasing any risks to the patient.

Potential alternative methods of control include: (1) certification that the animals are sourced from a 'closed herd'; (2) that the non-viable tissue derived material is from tissue defined as having no detectable levels of infectivity, e.g., bovine hide or heart tissue; or (3) where potential cross-contamination is controlled. The manufacturer also should be allowed the option of certifying that it is in conformance with internationally accepted BSE control and sourcing standards. See e.g., Animal tissues and their derivatives utilized in the manufacture of medical devices; Analysis and management of risk (EN12442-1); Controls on sourcing, collection and handling (EN12442-2); Validation of the elimination and/ or inactivation off viruses and transmissible agents (EN12442-3).

Finally, based on experience, effective US controls, and the different missions of the FDA and the USDA, use of the USDA BSE-free country list as criteria for determining

and limiting the appropriate bovine source countries is no longer supportable. Specifically, the list of BSE-free countries prepared by the USDA is to control entry of unacceptable products into the food chain and FDA's mission includes facilitating the advancement of innovated medical products, as evidenced by the mission statements set forth below:

| US FDA's Mission Statement | USDA's Mission Statement |
|---|--|
| <p>The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.</p> | <p>We provide leadership on food, agriculture, natural resources, and related issues based on sound public policy, the best available science, and efficient management.</p> |

FDA's mission includes "**helping the public get the accurate, science-based information they need to use medicines**". Given its mission and expertise FDA need not rely solely on the USDA's country list as the consideration for sourcing cattle and other animal tissue sources. There are other criteria available to FDA including internationally accepted standards such as the EN12442 standards series; Animal tissues and their derivatives utilized in the manufacture of medical devices.

Recommendations

In light of the above, SJM recommends that the language regarding certification of BSE free source country be modified from its current state.

| From | To |
|--|---|
| <p>If the animal material is of bovine origin⁷, we recommend that you include:</p> <ul style="list-style-type: none"> ➤ Certification that the animal is from a country free of bovine spongiform encephalopathy. <p>(⁷) See also List of USDA-Recognized Animal Health Status of Countries/ Areas Regarding Specific Livestock or Poultry Disease, http://www.aphis.usda.gov/vs/ncie/country.html</p> | <p>If the animal material is of bovine origin⁷, we recommend that you include:</p> <ul style="list-style-type: none"> ➤ Self-certification that the animal is either from a country free of bovine spongiform encephalopathy (BSE), sourced from a ‘closed herd’, or derived from tissue defined as having no detectable levels of infectivity (e.g., bovine hide or heart tissue), where potential cross-contamination is controlled, and/ or where the sponsor is in conformance with international BSE control and sourcing standards^{7a}. <p>(⁷) See also List of USDA-Recognized Animal Health Status of Countries/ Areas Regarding Specific Livestock or Poultry Disease, http://www.aphis.usda.gov/vs/ncie/country.html</p> <p>(^{7a}) For example: Animal tissues and their derivatives utilized in the manufacture of medical devices; Analysis and management of risk (EN12442-1); Controls on sourcing, collection and handling (EN12442-2); Validation of the elimination and/ or inactivation off viruses and transmissible agents (EN12442-3).</p> |

SJM believes that the proposed wording set forth above is consistent with FDA’s Mission as well as the Proposed Bovine Material Source Rule and should replace the current draft’s BSE statement. Alternatively, SJM recommends that FDA explicitly acknowledge in the guidance document the criteria set forth in the proposed rule and/or the existence of other criteria to demonstrate that bovine source material is a low-risk for BSE transmission. We recognize that FDA guidance is not intended to establish

requirements but rather provides recommendations and FDA's "current thinking" for compliance with regulatory requirements. Although the Proposed Bovine Materials Source Rule is not final, it appears to represent FDA's "current thinking" on this subject. At the very least, the proposed rule recognizes that alternative criteria for ensuring the safety of bovine-derived materials for medical products indeed exists. Therefore, any guidance document recommending the criteria for sourcing bovine-derived materials should be consistent with such thinking. SJM thanks the FDA for its time and consideration of this comment.