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August 13, 2004

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket Number 2004N-0264: Federal Measures to Mitigate BSE Risks: Considerations for Further Actions

Dear Sir or Madam:

On behalf of the Advanced Medical Technology Association (AdvaMed), I submit these comments on the Food and Drug Administration's (FDA) and the United States Department of Agriculture's (USDA) advanced notice of proposed rulemaking regarding "Federal Measures to Mitigate BSE Risks: Considerations for Further Actions" announced in the July 14, 2004 *Federal Register*. AdvaMed is the world's largest association representing manufacturers of medical devices, diagnostic products, and medical information systems. AdvaMed's more than 1,200 members and subsidiaries manufacture nearly 90 percent of the $75 billion of health care technology products purchased annually in the United States, and more than 50 percent of the $175 billion purchased annually around the world. AdvaMed members range from the largest to the smallest medical technology innovators and companies. Nearly 70 percent of our members have fewer than $30 million in sales annually.

A substantial percentage of the products sold by AdvaMed members are manufactured from source materials derived from ruminants, sourced from countries around the world. Thus, efforts to strengthen the protections against the spread of bovine spongiform encephalopathy (BSE) in US cattle and against human exposure to the BSE agent are important issues for AdvaMed member companies. We applaud FDA's and USDA's continued effort in this regard. However, we are concerned that FDA allotted so little time (30 days) for interested parties to respond to the questions posed in the *Federal Register Notice*. We hope that there will be additional opportunities for input.

GENERAL COMMENTS

Medical technologies save and improve the lives of countless people everyday, and the innovative companies who research and develop them are vital to the nation's health care system and the economy. A wide range of critical medical technologies incorporate bovine-derived

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components from in vitro diagnostic (IVD) devices used for disease diagnosis and screening of the nation's blood supply to life-saving implantable medical devices. Medical technology companies are committed to assuring the continued safety of their products and will continue their cooperation with FDA and the USDA in this regard.

As FDA and USDA consider measures to continue to assure the safety of the human food and animal feed chains, potential implications to the manufacture of medical technologies must not be overlooked. Bovine-derived components, such as blood, tallow, milk-products, and enzymes from the small intestine, serve critical functions in many medical technologies.

It is difficult to predict with certainty the impact to the medical device industry of proposed rules designed to assure the safety of the human food and animal feed chains. However, in our past experience, measures taken to assure the safety of the human food and animal feed chains, such as general import bans of bovine-derived materials, have had a negative, albeit unintentional, impact on our industry. In this regard, rules designed to protect the human food and animal feed chains, must be designed in such a way as to allow the medical technology industry access to the components necessary to manufacture medical devices. For example, IVDs do not have human or animal contact. Thus, general prohibitions on the use of or the ability to obtain bovine-derived materials have a crippling affect. Rather than prohibitions on material use or denaturing of material, appropriate labeling of materials as "intended for medical device manufacture" and "not for use in human or animal food" must be the method of choice.

SPECIFIC COMMENTS

While many of the questions posed by FDA and USDA do not have a direct bearing on the manufacture of medical devices, answers to several of the questions have the potential to impact the availability of appropriate bovine-derived components. It is these questions for which we provide comment. The questions are numbered to reflect the corresponding number in the advanced notice of proposed rulemaking.

28. What data or scientific information is available to evaluate the IRT recommendation described above, including that aspect of the recommendation concerning what portion of the intestine should be removed to prevent potentially infective material from entering the human food and animal feed chains?

While we support measures deemed necessary by the Food Safety and Inspection Service (FSIS) and FDA to ensure safe human and animal food chains, the agencies must implement such measures in a manner that does not impact other industries that rely on by-products of the small intestine. Specifically, in regards to in vitro diagnostic devices (IVDs) intended for human use, which have no patient, user, or animal contact, enzymes derived from the small intestine are an essential component. Any decision to remove the small intestine must not adversely impact the ability of IVD manufacturers to obtain, transport, import/export, or use by-products of the small intestine in the manufacturer of medical products.

In our experience, measures taken to assure human food and animal feed chain safety have had a negative, albeit unintentional, impact on our ability to source manufacturing materials for life-saving IVDs. Import bans have severely impacted our ability to source manufacturing materials.

The impact to our industry of requiring the removal of the entire small intestine from the human food and animal feed chains must be considered. Provisions allowing continued use of this material for non-food purposes must be implemented in a manner that does not place undue burden on the IVD industry. Requirements to denature material, such as the small intestine, would render it useless.

Further, efforts to ensure that the entire small intestine is not considered, designated, or referenced as specified risk material (SRM) is of utmost importance. The ability to attest that bovine-derived components are not sourced from SRMs is essential to global trade. Materials derived from other portions of the small intestine, such as the duodenum or jejunum must continue their status as non-SRM. We note FDA's interim final rule Use of Materials Derived From Cattle in Human Food and Cosmetics clearly articulates that the reason for removal of the entire small intestine is to ensure effective removal of the distal ileum, not that the small intestine is an SRM1.

Maintaining the current status of the small intestine, with the exception of the distal ileum, as non-SRM is also supported by scientific evidence. The agent has been documented to be found in certain lympho-reticular system tissues called the Peyer's patches, which are concentrated in the distal ileum of the small intestine2. Current research indicates that the infective agent is not found in other gastro- intestinal tissues other than the distal ileum3. Specifically, research has shown that the infective agent is not present in the duodenum and the jejunum portions of the small intestine even when the agent is found in the ileum4. Additionally, the infective agent for BSE has only been found in the distal ileum of cattle, which were inoculated with the BSE infective agent; due to the increased amount of infective agent the animals were exposed to; the agent has not been reported to be found in animals, which have succumbed to the disease naturally5.

29. If SRMs are prohibited from animal feed, what requirements (labeling, marking, denaturing) should be implemented to prevent cross-contamination between SRM-free rendered material and material rendered from SRMs?

We support the elimination of SRM from animal feed. SRMs should be segregated for use by other industries. As stated previously, enzymes sourced from the small intestine are a vital component of many IVDs. Denaturing the material would render it useless. FDA should not

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[1] 69 FR 42259 (July 14, 2004)
[2] Wells, G.A.H., Dawson, M., Hawkins, S.A.C., Green, R.B., Dexter, I., Francis, M. E., Simmons, M. M., Austin, A. R., Horigan, M. W., 1994: Infectivity in the ileum of cattle challenged orally with bovine spongiform encephalopathy. The Veterinary Record: 135, pages 40-41.
[3] Wells, G.A.H., Hawkins, S.A.C., Green, R.B., Austin, A. R., Dexter, I., Spencer, Y. I., Chaplin, M. J., Stack, M. J., Dawson, M., 1998: Preliminary observations on the pathogenesis of experimental bovine spongiform encephalopathy (BSE): an update. The Veterinary Record; 142 pages 103-106
[4] Terry, L. A., Marsh, S., Ryder, S. J. Hawkins, S. A. C., Wells, G. A. H., Spencer, Y. Il, 2003: Detection of disease specific PrP in the distal ileum of cattle exposed orally to the agent of bovine spongiform encephalopathy. The Veterinary Record: 152, pages 387-392.
[5] Wells et al., 1998; Terry et al., 2003

place prohibitions on use of the material or require denaturing of the material. Rather such material should be conspicuously labeled as "intended for medical device manufacture" and "not for use in human or animal food."

30. Is there scientific evidence to show that the use of bovine blood or blood products in feed poses a risk of BSE transmission in cattle and other ruminants?

We do not support the use of bovine blood or blood products ruminant feed. However, banning blood and blood products in animal feed must not unintentionally impact the ability of medical device manufacturers to obtain, use, transport, or import/export bovine blood and blood products intended for the manufacture of medical devices, including IVDs. Bovine blood and blood products are a critical component of IVDs. Decisions in regard to the use or handling of bovine blood and blood products must bear this in mind.

31. When and under what circumstances should the program transition from voluntary to mandatory?

To assure the overall safety of the animal-sourced materials, AdvaMed supports a mandatory animal identification system. A mandatory system will facilitate tracing of herd-mates and progeny of a BSE-infected animal, expediting the removal of potentially infected animals.

32. Should FDA include exemptions to any new requirements to take into account the future development of new technologies or test methods that would establish that feed does not present a risk of BSE to ruminants?

Yes, however international acceptance of such a broad exemption should be considered. Global trade would be hindered where an exemption does not receive national recognition.

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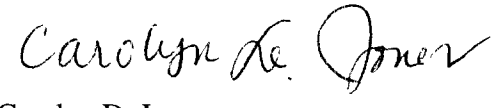
AdvaMed appreciates the opportunity to provide comments. If you have any questions, please do not hesitate to contact me.

Respectfully submitted,



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