

Kensey Nash Corporation (KNC) manufactures and supplies bovine sourced Type I collagen for the medical device industry. Our products are incorporated into cardiovascular and orthopedic devices that enhance patient care. We believe it is necessary to comment on this guidance document because of the requirements regarding collagen or other animal-derived material have the potential to impact other medical devices within and outside the US. Statements made in this guidance may be interpreted as overly strict and in conflict with the current USDA practices for risk assessment and control of BSE occurrence in the US. To date, the US has found two documented cases of BSE and under this guidance; the US would not be considered a “BSE-free” country.

In this draft guidance document, the FDA specifies unreasonable standards for animal tissue used in medical devices, which will negatively impact the medical device industry and allow outside Competent Authorities to use this guidance as a basis for rejection of medical devices utilizing animal tissue sourced from the US. An example of another country’s acceptance of FDA documents has recently been seen with the Chinese State Food and Drug Administrations’ (SFDA) usage of the FDA (outdated) 1998 Guidance Document, “Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices”).

KNC recognizes that the FDA must protect and enhance the public health; yet balance the benefits of utilizing animal tissue in medical devices with the potential risks of BSE. KNC recommends allowing alternative methods to fulfill the FDA requirements without increasing the risk to patients.

Objectionable Document Statements:

Section 6, Material and Performance Characteristics subsection (A), Material Specification, Collagen or Animal Derived Material:

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

- 1. description of how the individual animal’s (or when appropriate, the herd’s) health was maintained and monitored (e.g., whether or not the herd was closed, composition of food)*

KNC Response/Recommendation:

KNC is not aware that the FDA or other US agency has defined the term ‘closed’ herd. We believe the agency should define the term ‘closed’ or reference a document, such as EN12442-2, where it is defined.

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

KNC Response/Recommendation:

KNC assumes that the requirement for ‘certification’ is an ‘official’ certification from an authorized government agency. KNC has faced the challenge of obtaining “certification” for other regulatory bodies (requirement of EN12442-2) and has found that the USDA will not certify that hides are “fit for human consumption” (reference March 9, 2005 FSIS memorandum prohibiting the USDA inspector/veterinarian sign off of non-edible animal products during

slaughter). We believe that asking for this certification is overly burdensome and not justified when US government agencies refuse to provide certification for bovine hides from animals already certified as ‘fit for human consumption’ slaughtered in a USDA facility.

If this is not the intent of the requirement, then FDA should define or clarify what is meant by ‘certification’ (eg, self-certification).

Additionally, we believe that this requirement, in general, is overly restrictive and does not provide alternative risk-based methods for manufacturers to comply with FDA’s requirements.

Based on the reference to the USDA’s specific country listing, this statement could be literally interpreted, especially by those agencies outside the US, that the material source country must be **‘from a country (totally) free of (BSE)’**. This statement implies that medical device materials made from animal tissues could not be taken from US animals. Considering that both the USDA and USFDA have themselves determined that the United States has two documented cases of BSE, the US would not be considered a “BSE free country”. We believe a risk-based approach to animal sourcing is the preferred method of assuring safety. KNC obtains all animal tissue from US sources and relies on extensive sourcing procedures to assure that bovine hides come from BSE free herds.

Examples of risk-based methods of control include the following:

- self-certification that the animals are sourced from a ‘closed’ herd,
- self-certification that the device material is derived from animal tissue defined as having no detectable levels of infectivity, e.g., bovine hide or tendons as well as where potential cross-contamination is controlled,
- self-certification that the manufacturer is in conformance with international BSE control and sourcing standards, such as EN12442: 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 of viruses and transmissible agents (EN12442-3).

KNC recommends that the guidance document’s certification of BSE-free source country statement should be replaced with the following alternative wording:

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<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 tendons), 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>
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3. *standard vaccinations given to the animal (herd) (we recommend focusing on live modified viruses)*

KNC Response/Recommendation:

KNC requests clarification on this requirement. Animal vaccination records are obtainable from our hide suppliers, however managing changes to the farmers' veterinary care would be overly burdensome and changes may be difficult to update (eg, would this require new 510(k) or Master File updates?). We recommend that manufactures be responsible for assuring appropriate veterinary care but the requirement for documenting the vaccines in a pre-market submission be removed.

4. *tests performed to determine that material is acceptable for further processing or pooling with material from other animals.*

KNC Response/Recommendation:

Kensey Nash requests that the agency clarify this requirement and/or give a specific example of the type of processing or pooling with which they are concerned.