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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

**Re: Comments on Advanced Notice of Proposed Rulemaking;
Federal Measures to Mitigate BSE Risks;
Docket No. 2004N-0264**

On behalf of the Center for Science in the Public Interest (CSPI), we appreciate the opportunity to submit written comments on the advanced notice of proposed rulemaking (ANPRM) relating to federal measures to mitigate BSE risks in the United States. CSPI is a nonprofit health advocacy and education organization focused on food safety, nutrition and alcohol issues. CSPI is supported principally by the 890,000 subscribers to its *Nutrition Action Healthletter* and by foundation grants. We accept no government or industry funding.

In 1997, FDA adopted a rule prohibiting the use of mammalian protein, with some exceptions, in animal feeds given to cattle and other ruminants.¹ In a report issued after the first BSE-positive cow was discovered in the United States, an International Review Team (IRT) made specific recommendations on how to strengthen the feed restrictions. These include: 1)

¹ 21 C.F.R. § 589.2000.

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banning all specified risk materials (SRM) from all animal feed, including pet food; 2) prohibiting the use of all meat and bone meal (MBM), including avian, in ruminant feed; and 3) assuring that measures to prevent cross-contamination are strongly enforced.²

Acting Commissioner Dr. Lester Crawford, in testimony before the Senate Committee on Agriculture, Nutrition, and Forestry, has emphasized that FDA's 1997 animal feed regulation "forms the basis of the Agency's efforts to prevent the spread of BSE through animal feed."³ Yet, rather than adopting the IRT recommendations as an interim final rule, FDA has issued only an ANPRM, seeking comment to determine the "best course of action" in light of the IRT recommendations.⁴ FDA must act now to correct the weaknesses in the current rule.

I. FDA SHOULD NOT FURTHER DELAY REGULATORY ACTION

On January 26, 2004, FDA announced in a News Release that it would publish an interim final rule "designed to lower even further the risk that cattle will be purposefully or inadvertently fed prohibited protein."⁵ In that news announcement, FDA stated that the interim final rule would implement four specific changes to the existing feed rule, including banning the use of poultry litter and plate waste as a feed ingredient for ruminants, and further minimize the possibility of cross-contamination of ruminant and non-ruminant animal feed by requiring dedicated equipment, facilities or production lines.

² International Review Team, *Report on Measures Relating to Bovine Spongiform Encephalopathy (BSE) in the United States* (Feb. 2, 2004) [hereafter *IRT Report*].

³ Statement by Lester M. Crawford, Deputy Commissioner of Food and Drugs, Department of Health and Human Services before The Committee on Agriculture, Nutrition, and Forestry, United States Senate (Jan. 27, 2004).

⁴ 69 Fed. Reg. 42,287, 42,293 (July 14, 2004).

⁵ HHS, News Release, Expanded "Mad Cow" Safeguards Announced to Strengthen Existing Firewalls Against BSE Transmission" (Jan. 26, 2004).

In the recent ANPRM, FDA references its January 26, 2004 announcement and states that the IRT recommendations provide a different set of measures for reducing the risks associated with animal feed. According to the FDA, “the broader measures recommended by the IRT, if implemented, could make some of the previously announced measures unnecessary.”⁶ On that basis, the agency issued an ANPRM, rather than an interim final rule, as it was poised to do on January 26, concluding that it needs additional information to determine the best course of action in light of the IRT recommendations. FDA had no legal or policy justification for choosing to delay action further.

Generally, if an agency proposes a rule and then decides to take some action that is considerably different from or not the logical outgrowth of its original proposal, it must, as a legal matter, re-propose the rule. In this case, however, FDA only issued a press release mentioning some intended measures. Therefore, FDA has no legal justification for issuing an ANPRM rather than promulgating an interim final rule.

More significantly, most of the measures set forth in the ANPRM have been under consideration by FDA for several years and have been the subject of extended public discussion and comment. Over the past seven years, the FDA has held many discussions and meetings with stakeholders and the public on the animal feed safety system,⁷ sought public comment on whether it should amend the feed ban,⁸ and previously issued an advanced notice of proposed rulemaking.⁹ More specifically, FDA has sought public comment on whether Specified Risk

⁶ 69 Fed. Reg. at 42,293.

⁷ 66 Fed. Reg. 50,929 (Oct. 5, 2001).

⁸ 67 Fed. Reg. 67,572 (Nov. 6, 2002)

⁹ 68 Fed. Reg. 44,344 (July 28, 2003).

Materials should be excluded from all rendered material,¹⁰ whether the present ban on the use of certain mammalian proteins in ruminant feed should be broadened,¹¹ whether the agency should require dedicated facilities for the production of animal feed containing prohibited material to prevent cross-contamination,¹² whether poultry litter and other recycled poultry waste should be added to the list of prohibited material in animal feed,¹³ and whether additional measures are necessary to guard against BSE in the United States.¹⁴

The 2001 Harvard Risk Assessment has described the feed ban as the “linchpin” of protection against the spread of BSE if in the United States.¹⁵ Despite the fact that FDA has been studying feed-related issues for the past seven years, and that “mad cow” disease has now been discovered in the United States, the agency has yet to take any action to strengthen the feed ban. The FDA not only has failed to take any action bolstering the feed ban, it has backtracked, announcing that it needs more information and intends to engage in more discussion.

In January 2004, when FDA announced its “interim final rule” to strengthen the animal feed rule, then-Commissioner Mark McClellan stated that “[w]ith today’s actions, FDA will be doing more than ever before to protect the public against BSE by eliminating additional potential

¹⁰ 67 Fed. Reg. at 67,572

¹¹ 66 Fed. Reg. at 50,930; 67 Fed. Reg. at 67,573 (whether the plate waste exemption should be eliminated).

¹² 66 Fed. Reg. at 50,930; 67 Fed. Reg. at 67,573.

¹³ 66 Fed. Reg. at 50,930; 67 Fed. Reg. at 67,573.

¹⁴ 66 Fed. Reg. at 50,930; 68 Fed. Reg. at 44,345 (asking for comments concerning weaknesses in current regulatory programs for feed safety).

¹⁵ Harvard Center for Risk Analysis, Harvard School of Public Health and Center for Computational Epidemiology, College of Veterinary Medicine, Tuskegee University, *Evaluation of the Potential for Bovine Spongiform Encephalopathy in the United States* (Nov. 26, 2001) [hereafter *Harvard Risk Assessment*].

sources of BSE exposure.”¹⁶ If FDA is to meet its responsibility to protect the public health, it should act promptly to take final action implementing tighter feed restrictions.

II. SRMS SHOULD BE REMOVED FROM ALL ANIMAL FEED

One of the recommendations of the IRT is that all Specified Risk Materials should be excluded from all animal feed, including pet food.¹⁷ The FDA should adopt this recommendation since animal feed is the principal vector for transmission of BSE.

A. SRMs are the Source of Highest Infectivity

According to the UN’s Food and Agriculture Organization, SRMs, including the brain, spinal cord, eyes, tonsils, and parts of the intestines account for over 95% of BSE infectivity.¹⁸ The IRT report also cited one study demonstrating the transmission of BSE with 10 mg of infectious brain tissue.¹⁹ A July 2001 review of the origin of BSE in the United Kingdom concluded that meat and bone meal (MBM) made from offal of BSE-infected cattle was so infective that accidental contamination of cattle feed with pig or poultry feed containing MBM was a significant factor which continued to spread BSE after the UK ban on the use of MBM in cattle feed.²⁰

¹⁶ HHS, New Release, *Expanded “Mad Cow” Safeguards Announced to Strengthen Existing Firewalls Against BSE Transmission* (Jan. 26, 2004).

¹⁷ *IRT Report*, at p. 8

¹⁸ FAO, *Mad cow disease: FAO recommends precautions* (8 February 2001), at p. 2, available at <http://www.fao.org/news/2001/010202-e.htm>.

¹⁹ *IRT Report*, at p. 5.

²⁰ Gabriel Horn, *et al.*, Independent Review Committee, *Review of the Origin of BSE*, commissioned by the UK Minister of Agriculture and the Secretary of State for Health, published by the Department for Environment, Food & Rural Affairs (July 5, 2001).

The typical incubation period for BSE is estimated to be from two to eight years.²¹ While it is generally believed that the total infective load of the BSE agent in cattle changes over time and is lower in cattle in the early stages of incubation than those approaching the end of the incubation period, the pathogenesis of the disease in cattle is not clearly understood. Moreover, the post-mortem tests currently in use only identify the presence of the BSE agent near the end of the incubation period and do not identify pre-clinical cases at earlier stages of incubation. Thus, even animals that test negative could be harboring infectious prions.

The lack of scientific certainty was recently underscored when a team of Italian scientists announced the discovery of the existence of another form of mad cow disease, known as bovine amyloidotic spongiform encephalopathy (BASE). According to one expert, this discovery “opens the possibility of a second strain of the agent in circulation – and that’s probably not good news.”²²

The lack of certainty should be a reason *for* implementing a ban on all SRMs in all animal feed - not a reason for further delay in taking such action. The 2001 Harvard Risk Assessment recognized that implementation of a ban on SRMs from the human and animal food chains has a “dramatic effect” on potential human exposure or the spread to cattle, reducing the predicted number of BSE cases in cattle by 80% and the potential human exposure by 95%.²³ For these reasons, FDA should prohibit all SRMs from all animal feed to assure that the most potentially infective material is kept out of the feed chain.

²¹ 69 Fed. Reg. 1861, 1863 (Jan. 12, 2004).

²² Donald G. McNeil, Jr., “Research in Italy Turns Up a New Form of Mad Cow Disease,” *The New York Times* (Feb. 17, 2004), at A.7.

²³ *2001 Harvard Risk Assessment*, at pp. iv & 96.

B. The Cattle Age for SRMs Should Be Lowered

In its Interim Final Rule on the Use of Materials Derived from Cattle in Human Food and Cosmetics, FDA defines SRMs to be the brain, skull, eyes, trigeminal ganglia, spinal cord, vertebral column and dorsal root ganglia of cattle 30 months and older, and the tonsils and distal ileum of the small intestine of all cattle regardless of age.²⁴ According to FDA, “[r]esearch to date indicates that 30 months is the appropriate threshold for removal of these materials unless surveillance indicates that there is a high prevalence of BSE in the U.S. cattle population”²⁵

In fact, the IRT recommended that the brain and spinal cord of all cattle over 12 months be designated as SRM “unless aggressive surveillance proves the BSE risk in the USA to be minimal according to the OIE standards.”²⁶ Current U.S. surveillance is not aggressive. USDA’s Animal and Plant Health Inspection Service (APHIS) has implemented a voluntary program which tests only a small portion of potentially infected cattle and which will not establish the true prevalence of BSE in this country.

According to the IRT, adoption of a 12-month age cut-off “represents a recognition of the fact that some cattle under 30 months of age may be slaughtered with infectivity present” in high risk tissues such as the brain and spinal cord.²⁷ Indeed, in both Japan and the United Kingdom, cattle as young as 21 months have tested positive for BSE agent. Accordingly, a rule banning SRMs from all animal feed would provide greater assurance that no high risk materials from cattle 12 months or older is allowed in cattle feed.

²⁴ 69 Fed. Reg. 42,255 (July 14, 2004).

²⁵ 69 Fed. Reg. at 42,296.

²⁶ *IRT Report*, at p. 5.

²⁷ *IRT Report*, at p. 5.

Finally, we note that in its Interim Final Rule on Use of Materials Derived from Cattle in Human Food and Cosmetics, FDA has defined “prohibited cattle material” and SRMs separately.²⁸ “Prohibited cattle material” includes SRMs, as well as material from nonambulatory disabled cattle, material from cattle not inspected and passed, or mechanically separated beef. SRMs are defined more narrowly to include the infectious parts of cattle 30 months and older, as well as the tonsils and distal ileum of the small intestine of all cattle.

Under these definitions, a ban on SRMs in animal feed would *not* encompass brain and spinal cord from nonambulatory disabled cattle under 30 months and material from cattle not inspected and passed that are under the age limit. As a result, a ban on SRMs in all animal feed could allow materials from the potentially highest risk animals – downers and cattle showing central nervous system symptoms – into animal feed.

III. FDA SHOULD PROHIBIT POULTRY LITTER AND ANIMAL PROTEIN IN RUMINANT FEED

FDA is considering whether it should expand the prohibitions in the current feed rule to exclude all mammalian and poultry protein from ruminant feed and prohibit the practice of incorporating poultry litter into ruminant feed. Poultry litter, particularly broiler litter, is used as a feed ingredient for cattle because of its nutritional value and its economical cost.²⁹ Broiler litter consists of bedding (wood shavings, rice hulls, peanut hulls, etc.), manure, and feed spilled by the birds to the floor of the house. Spilled feed can contain prohibited mammalian proteins in the form of meat and bone meal since MBM may be fed to poultry, as well as pigs and horses.

²⁸ Proposed rule section 189.5.

²⁹ D.S. Doctorian and G.W. Evers, *Using Broiler Litter as a Protein and Mineral Supplement for Beef Cows*, Texas A& M University Agricultural Research & Extension Service (Rev. July 15, 1997), available at <<http://overton.tamu.edu/forage-livestock.1996/litutil.html>>.

Indeed, the poultry and swine industries are the predominant consumers of meat and bone meal.³⁰ Because the prohibited protein could pass through the birds' digestive tracts, the BSE agent, if present, could be recycled to cattle through poultry waste or poultry carcasses that are in the litter.³¹

Although there is no reliable evidence that poultry are susceptible to developing symptoms of prion diseases,³² recent studies indicate "that the absence of clinical symptoms does not necessarily exclude transmission of prion disease across a species barrier" and suggest that subclinical or long preclinical carrier states exist in apparently resistant species.³³ For example, one study has found that hamster prions thought to be nonpathogenic for conventional mice could cause "prion replication to high levels in such mice but without causing clinical disease" in the mice.³⁴ The prions from these mice were shown to cause a TSE in hamsters. Thus, "BSE passaged in species other than cattle also may be pathogenic to humans" or to cattle.³⁵

In addition, there is evidence that the host range of a prion disease can be altered on

³⁰ R.D. Miles and J.P. Jacob, *Using Meat and Bone Meal in Poultry Diets*, University of Florida Cooperative Extension Service Factsheet PS-28 (Aug. 1998), p. 2.

³¹ While proper processing can destroy more common pathogens harbored by the litter, there is no evidence that this same processing would destroy the BSE agent if it were present in the litter. The most common method for killing pathogens in litter is a process called "deep stacking" which generally results in the heating of a stack of litter to between 140 and 160 degrees Fahrenheit. See North Carolina Cooperative Extension Service, *Deep Stacking Broiler Litter as a Feed for Beef Cattle*, Publication Number AG-515-2 (Apr. 1995), available at <<http://www.ces.ncsu.edu/drought/dro-49.html>>. Heating to this temperature will not, however, destroy prions.

³² R.J. Cawthorne, *Failure to confirm a TSE in chickens*, 141 *Veterinary Record* 203 (Aug. 1997); European Commission, Scientific Steering Committee, *Report on the Risk Born by Recycling Animal By-Products as Feed with Regard to Propagating TSE's in Non-ruminant Farmed Animals* (Adopted Sept. 1999).

³³ A. Hill and J. Collins, *Species-Barrier-Independent Prion Replication in Apparently Resistant Species*, 110 *APMIS*, 44-53 (Jan. 2002).

³⁴ A. Hill, *et al.*, *Species-Barrier-Independent Prion Replication in Apparently Resistant Species*, 97 *Proceedings of the National Academy of Sciences* 10248-10253 (Aug. 2000) [hereafter PNAS article].

³⁵ PNAS article.

passage through certain species. Mule deer Chronic Wasting Disease (CWD) is ordinarily not transmissible to Syrian golden hamsters. However, when ferrets were inoculated with CWD and then Syrian golden hamsters were inoculated with the ferret-passaged CWD, the Syrian golden hamsters developed a prion disease.³⁶ Accordingly, the possibility of transmission of the infectious agent that causes BSE or another TSE from asymptomatic poultry as well as other animals to an unknown range of species cannot be ruled out.

In its 2002 report on the animal feed ban, the Government Accountability Office found that “[r]ecent research on the ability of animals to be “silent” carriers of TSEs from another species raises questions about the advisability of including in feed for cattle, or other ruminants, proteins from animals such as pigs and horses.”³⁷ Although infectious prions have not been found in the feces of cattle or other animals, there is evidence that prions can be present in urine. Researchers in Israel found a component of the prion in the urine of hamsters, cattle, and humans suffering from TSEs.³⁸ In addition, contaminated saliva, urine, or feces are often cited as possible mechanisms for the transmission of CWD among deer and elk.³⁹ According to the University of Minnesota, the “pattern of transmission and association of prions with lymph tissue in the mouth and intestinal tract has led to the hypothesis that the CWD agent may find its way

³⁶ J.C. Bartz, et al., *The Host Range of Chronic Wasting Disease is Altered on Passage in Ferrets*, 251 *Virology* 297-301 (1998).

³⁷ GAO, *Mad Cow Disease: Improvements in the Animal Feed Ban and Other Regulatory Areas Would Strengthen U.S. Prevention Efforts*, GAO-02-183 (Jan. 2002), at p. 10.

³⁸ Gideon M. Shaked, et al., *A Protease Resistant PrP Isoform is Present in Urine of Animals and Humans Affected with Prion Diseases*, *Journal of Biological Chemistry* (June 21, 2001).

³⁹ Michigan Department of Natural Resources, *Chronic Wasting Disease*, Brochure (Aug. 6, 2002); University of Minnesota Extension Service, *Chronic Wasting Disease: Frequently Asked Questions* (Nov. 5, 2002); Alberta Agriculture, Food and Rural Development, *Chronic Wasting Disease (CWD) of Elk and Deer* (Rev. Dec. 2002).

through saliva, feces and urine onto grasses and other food. Deer eating contaminated food may contract the disease.⁴⁰ Likewise, if poultry consume infectious prions through contaminated feed, the possibility that their waste products might contain these prions cannot be ruled out.⁴¹

Because science still has not resolved the debate on whether the prion responsible for BSE and variant Creutzfeld-Jacob Disease can pass from cattle to poultry to cattle to humans and whether other animals can be silent carriers of TSEs, the FDA should take the most precautionary approach and ban animal protein and poultry litter from cattle feed.

IV. FDA SHOULD REQUIRE MEASURES TO PREVENT CROSS-CONTAMINATION

Under the 1997 feed rule, facilities handling both prohibited and non-prohibited material must control cross-contamination by either maintaining separate equipment or facilities, or using clean out procedures or other means adequate to prevent carry over of prohibited material into feed for ruminant animals.

Previously, FDA has considered whether to require dedicated equipment and facilities for the production of prohibited materials. However, in the ANPRM, FDA states its belief that if SRMs are prohibited in all animal feed, dedicated facilities and equipment may no longer be necessary to reduce the risk associated with cross-contamination.⁴²

Even with a ban on SRMs in animal feed, dedicated facilities, equipment, storage and

⁴⁰ Center for Animal Health and Food Safety, University of Minnesota, *Key Information About Chronic Wasting Disease (CWD)* (rev. Mar. 5, 2002).

⁴¹ The Scientific Steering Committee of the European Commission has concluded that the possibility of active replication of prions in birds is remote, but that necrophagous “birds are nevertheless able to ingest BSE infectious material and to spread the ingested infectious material through dissemination of faeces because it is unlikely that the pathological prion protein would be destroyed in the digestive tract.” European Commission, Scientific Steering Committee, *Opinion on Necrophagous Birds as Possible Transmitters of TSE/BSE* (adopted Nov. 2002).

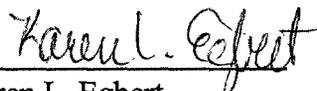
⁴² 69 Fed. Reg. at 42,297.

transportation are still necessary to prevent potential cross-contamination. Although facilities would be prohibited from using SRMs in animal feed, human food, or cosmetics, they still may receive specified risk materials from cattle for inedible rendering. To avoid any possibility of cross-contamination, such materials should therefore be processed, handled, stored and transported in dedicated facilities and using dedicated equipment. A requirement for dedicated facilities should also be accompanied by increased inspection by FDA and state officials.

CONCLUSION

FDA has delayed long enough in taking action to strengthen the feed ban. Now that a BSE-positive cow has been discovered in the United States, stronger precautionary measures are needed to prevent animal feed potentially contaminated with infective tissue from ever posing a serious public health threat. FDA should move quickly to tighten the existing rules.

Respectfully submitted,



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