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

Re: Substances Prohibited from Use in Animal Food or Feed, Proposed Rule, Docket
No. 2002N-0273

February 14, 2006

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) is providing comment to the proposed rules issued by the Food and Drug Administration (FDA) Center for Veterinary Medicine (CVM) entitled Substances Prohibited From Use in Animal Food or Feed; Proposed Rule, 21 CFR Part 589; 70 Federal Register 58570 (October 6, 2005). PhRMA applauds the FDA's continued actions to protect the cattle population of the United States from BSE (bovine spongiform encephalopathy) and, as discussed further below, strongly supports additional safeguards in addition to those proposed in amended 21 CFR Part 589.

PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, healthier and more productive lives. Investing more than \$30 billion annually in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures.

Animal-derived materials are ubiquitous in our lives and have many important uses. They are often used in pharmaceutical manufacturing and are sourced according to

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guidelines issued by regulatory authorities and the specifications outlined by the quality systems of the pharmaceutical company. The BSE status of the country where the animal lived and an assessment of the controls in place to prevent the spread of the disease, if it should occur, are important considerations in sourcing bovine-derived materials. While a country may have animals diagnosed with BSE, evaluation of the measures put in place to halt the spread of the disease is as crucial as identification of the disease itself. PhRMA continues to support an internationally harmonized, science-based approach to determining appropriate safeguards against BSE. PhRMA believes that FDA efforts to communicate these science-based concepts to our trading partners worldwide are critical. It is just as important to institute sound science-based policies in order to stop the spread of disease.

Consideration of the safeguards enacted in the various countries where ruminant-derived raw materials are sourced provides the underpinning for regulatory guidance. The cattle population of the United States must continue to be an acceptable source of bovine-derived raw materials for human food and pharmaceutical manufacturing. As such, continual re-evaluation of existing safeguards against BSE must occur based on new information and advances in science. Due to confirmation that BSE is indeed present in North America, rapid implementation of enhanced safeguards for cattle and animal feed is required.

We continue to be concerned about the amount of time it has taken the Center for Veterinary Medicine (CVM) to institute any changes to the 1997 feed ban; a lot has happened since 1997, not the least of which is the identification of a BSE cow native to the United States (June 2004). As we have urged for many years, the 1997 feed ban must be enhanced based on new information, including the experimental results that

show as little as 0.001 gram of infected tissue fed orally to cattle may result in BSE infection of cattle¹.

PhRMA supports actions of the Food and Drug Administration Center for Veterinary Medicine (FDA CVM) to extend certain provisions in the 1997 Ruminant to Ruminant feed ban to all animal feed. As noted in the 1997 ruminant feed final rule (§ 589.2000) and described in the October 6, 2005 Federal Register notice,² the use of mammalian-derived proteins is currently prohibited in ruminant feed, with the exception of certain proteins believed not to pose a risk of BSE transmission. These exceptions to the definition of "protein derived from mammalian tissues" include: blood and blood products; gelatin; inspected meat products which have been cooked and offered for human food and further heat processed for feed (such as plate waste and used cellulosic food casings), referred to herein as "plate waste"; milk products (milk and milk protein); and any product whose only mammalian protein consists entirely of porcine or equine protein. The 1997 ruminant feed final rule does not prohibit ruminant animals from being fed processed animal proteins derived from non-mammalian species (e.g., avian or aquatic animals). The 1997 ruminant feed final rule permits the manufacture of non-ruminant feed containing prohibited mammalian protein and ruminant feed on the same premises, provided that separate equipment is used in the production of ruminant feed or that documented adequate clean-out procedures are used between production batches.

PhRMA has commented numerous times on the inadequacy of the 1997 feed ban (our latest comments were provided to Federal Register Docket 2004N-0264 and dated August 12, 2004). We stated that the current exemptions in the feed ban must be

¹ <http://www.defra.gov.uk/animalh/bse/science-research/pathog.html#dose>

² Federal Register, Docket 2002N-0273, Vol. 70, No. 193 58570-58601. Part III, Department of Health and Human Services, FDA 21CFR589 Substances Prohibited from Use in Animal Food or Feed; Proposed Rule

critically examined in light of the identification of BSE positive animals in Canada, Washington, and subsequently in Texas. Over the last few years, PhRMA has urged that serious consideration be given to prohibiting all specified risk material (SRM) in rendered product used for non-ruminant feed due to the potential for "on farm" cross-contamination with feed designated for ruminants. We have strongly recommended implementation of measures to ensure that SRM is excluded from all animal feed. In addition, PhRMA urged the complete removal of the exception for ruminant blood and the exemptions for plate waste and poultry litter from the ruminant feed ban. As such, we strongly support the current FDA position to eliminate SRM from all animal feed and urge its immediate implementation. This safeguard must be implemented rapidly. Regrettably, FDA proposes to eliminate only the brain and spinal cord from cattle 30 months of age or older, not the complete list of SRMs currently designated for human food. Given the absence of a species barrier when non-ruminant feed is fed (inadvertently or deliberately) to ruminants, we urge the FDA to reconsider its position and eliminate the complete list of SRM from all animal feed.

We are steadfast in our position urging the removal of the exemption for plate waste and poultry litter. This position is based on the lack of species barrier and the inclusion of tissues with potentially high levels of infectivity present in plate waste and poultry litter. Allowing the exception for plate waste provides a direct route for feeding ruminants to ruminants because plate waste may contain uneaten food items such as T-bone steak waste, including bone innervated with dorsal root ganglia (DRG). The absence of a species barrier when feeding ruminants to ruminants would facilitate the transmission of infectivity by the demonstrated high titer DRG, if infectivity were present. We have evaluated the rationale provide by FDA CVM for not banning plate waste (in summary: SRMs are prohibited in human food therefore plate waste will not contain SRMs and can be fed back to cattle). This rationale does not take into account the lack of a species barrier when feeding cattle plate waste containing beef. The lack

of a species barrier, coupled with the definition of SRMs limited to cows over 30 months of age, combined with the knowledge that there is circulating BSE agent (albeit at exceedingly low levels) in North America, are strong reasons to completely ban the feeding of plate waste to bovines. In addition, the FDA states in the proposed rules that they do not have an estimate of the amount of plate waste added to bovine feed, but the available anecdotal information states that the amount is not significant. If there is only a limited amount of plate waste being processed to bovine feed, given the lack of species barrier, it appears logical to prohibit the use of plate waste completely. PhRMA does not agree that eliminating all plate waste from bovine feed is an 'unnecessary measure' and we strongly urge CVM to reevaluate its position.

Both specified risk materials (SRM) and plate waste are currently allowed in poultry feed. We recommend that both SRM and plate waste be removed from poultry feed so that poultry litter can be used as a bovine nitrogen source. If these materials are not removed from poultry feed, then we recommend that poultry litter be banned from the diet of cattle.

The proposed rule contains a provision to utilize certain dead cattle in animal feed. Allowing deadstock (dead, down, disabled, diseased) into the animal food chain if the brain and spinal cords have been removed does not take into account that these animals are the most likely to harbor infectivity as symptoms of BSE disease confound the segregation of these animals. The total amount of infectivity does not reside in the brain and spinal cord and removal of these tissues does not make the remainder of the carcass acceptable to process into animal feed. According to risk assessment models, adult cattle deadstock are the population harboring the majority of the potential

infectivity if BSE were circulating in a population³. Elimination of the deadstock from the animal food chain is critical to prevent the spread of disease.

The other exemptions in the 1997 feed ban such as blood and milk/milk products are less problematic as long as milk and blood are sourced to prevent cross-contamination with high infectivity tissues. We agree with the FDA's approach to these two tissues if the potential for cross-contamination is minimized.

In summary, we recognize the tremendous efforts CVM has expended on defining a strategy for enhanced feed controls in the United States to help stop the spread of BSE. The thoughtful evaluation of all comments as a result of the publication of the Advance Notice of Public Rule Making (July 14, 2004) reflects an Agency attempting to balance the risks of continuing current feeding practices with the practical considerations of various industries. We appreciate a risk based approach but have misgivings about the level of safeguards contained in the proposed rule.

To reiterate, our main concerns center on the following three issues – the narrow definition of the SRM to be excluded from non-ruminant feed, instead of a complete ban as for ruminant feed; the continued allowance of plate waste and poultry litter in ruminant feed and finally, the provision to allow certain deadstock cattle into the animal food chain.

PhRMA appreciates the opportunity to comment on the proposed changes to the ruminant feed ban and the implementation of controls on non-ruminant feed. PhRMA member companies manufacture human medicines using a wide variety of materials. We continue to source animal derived raw materials according to regulations of FDA

³ 2001 Harvard Risk Assessment and amendments

and the quality systems of the company. The United States must continue to be recognized as an acceptable source of these animal derived raw materials both domestically and by our international trading partners. Using sound science to influence regulatory approaches to animal husbandry is the key to preventing the spread of BSE in the United States. FDA and USDA have already done a lot to protect the United States but more must be done as reflected in our comments herein. Please contact me if you have any questions or would like to arrange a meeting to discuss our comments.

Sincerely,



Marie A. Vodicka, PhD