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January 18, 2013

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

**Re: Docket No. FDA–2012–N–1154; Framework for Pharmacy Compounding:
State and Federal Roles, Notice of Public meeting; request for comments**

AHI is the national trade association representing manufacturers of animal health products – the pharmaceuticals, vaccines and feed additives used in modern food production, and the medicines that keep livestock and pets healthy. We appreciate the opportunity to submit these comments to **Docket FDA–2012–N–1154, Framework for Pharmacy Compounding: State and Federal Roles, Notice of Public meeting; request for comments.**

AHI member companies further the discovery, development, and approval of medicines that maintain and promote animal health in a research-driven industry. AHI works to ensure science-based review of animal drug products and supports continuing research and development in the area of animal health. AHI's members have a strong interest in preserving the scientifically rigorous Congressionally-mandated regime for FDA review and approval of animal drugs and ensuring that it is not circumvented or frustrated by the sale of unapproved and potentially hazardous products manufactured by individuals or firms engaged in bulk compounding. AHI believes that FDA has clear statutory authority to protect animal and public health by exercising its enforcement authority to prohibit the manufacture and sale of bulk compounded animal drugs.

Before we respond to the specific questions posed in this notice AHI would like to emphasize that the legislative and regulatory history for animal drugs is quite different from that for human medicines as discussed below. Because of these differences, we believe that FDA does not, and should not, have authority to establish a category of “non-traditional” compounding for animal drugs. There are two mechanisms for veterinarians to legally use, dispense, or prescribe

medicines. One is the use of FDA approved animal drugs in accordance with approved labeling, or, the use of animal or human drugs in an extra label manner in accordance with the Animal Medicinal Drug Use Clarification Act (AMDUCA). Within the provisions of AMDUCA, veterinary compounding is limited to an extra label use which entails the manipulation of FDA approved drug products by a licensed pharmacist or veterinarian such as the adding of flavorings to increase palatability, or converting tablets into an oral suspension for easier administration. These manipulations are for the express purpose of addressing the specific needs of individual animal patients.

Use of unapproved drugs such as those compounded from bulk pharmaceutical ingredients is illegal and in violation of the Act. Only through FDA regulatory discretion or inability to take enforcement actions do bulk compounded products for animal use continue to be produced and sold in interstate commerce. AHI supports a rigorous drug approval process and believes veterinary compounding from products approved for human or animal use under a veterinarian-client-patient relationship has a clear place in the appropriate treatment of animals. AHI also understands there is a limited role for FDA to exercise regulatory discretion to allow very circumscribed compounding from bulk drug substances in medically appropriate cases, under the order of veterinarian where there is no approved product with the same active ingredient or the use is not in a major species. However, AHI could never support a third process called “non-traditional” bulk compounding as a means of circumventing the safety and efficacy requirements of the Act. Congress did not include animal drugs in 21 U.S.C. § 353a therefore bulk drug compounding for animal use is not recognized as a legitimate process and therefore animal drugs should not be included in such proposals.

In 1994, Congress passed the Animal Medicinal Drug Use Clarification Act (AMDUCA), Pub. L. No. 103-396, 108 Stat. 4153, which amended the FDCA to address apparent restrictions in the animal drug provisions on the practice of veterinary medicine, including compounding, by providing a limited exception to the regulatory framework for the use of approved animal and human drugs. AMDUCA authorizes veterinary compounding under very limited circumstances. 21 U.S.C. § 360b(a)(4) provides in part that an approved drug that is used in a way that has not been approved by FDA shall not be deemed unsafe pursuant to the FDCA or be required to provide directions for using that drug off-label:

if such use or intended use—

- (i) is by or on the lawful written or oral order of a licensed veterinarian within the context of a veterinarian-client-patient relationship, as defined by the Secretary; and
- (ii) is in compliance with regulations promulgated by the Secretary that establish the conditions for such different use or intended use.

The regulations promulgated by the Secretary under clause (ii) may prohibit particular uses of an animal drug and shall not permit such different use of an animal drug if the labeling of another animal drug that contains the same active ingredient and which is in the same dosage form. AMDUCA was intended to reflect the reality that compounding may be medically necessary in the context of veterinary practice where there may be no drugs approved for a particular use. But AMDUCA responded to this reality in a carefully calibrated and limited way.

In providing a limited exception to the FDCA for veterinary compounding, Congress did not authorize bulk compounding. On the contrary, Congress left in place the pre-existing regulatory regime in all other relevant respects. *See Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 395 (5th Cir. 2008) (internal citation omitted) (“Where Congress creates specific exceptions to a broadly applicable provision, the ‘proper inference . . . is that Congress considered the issue of exceptions and, in the end, limited the statute to the ones set forth.’”).

Under the authority originally granted by the FDCA and in accordance with AMDUCA, FDA promulgated regulations that specifically address compounding of drugs. 21 C.F.R. § 530.13; 61 Fed. Reg. 57732 (Nov. 7, 1996). In accordance with AMDUCA’s manifest purpose to restrict compounding to compounding under veterinarian-initiated orders confined to individualized patient/client medical needs, the FDA regulation provides that the AMDUCA exception is limited to the use of “approved human or animal drugs,” “on the order of a veterinarian” and not “compounding from bulk drugs.” The regulation thus provides that:

This part applies to compounding of a product from approved animal or human drugs by a veterinarian or a pharmacist on the order of a veterinarian within the

practice of veterinary medicine. *Nothing in this part shall be construed as permitting compounding from bulk drugs. Id.* (emphasis added).

In line with the principle clearly set forth in AMDUCA that the exception to the FDA drug approval framework for compounded drugs for use in animals is a narrow one, the FDA regulation provides further limits, including:

- that the drug must be compounded by a licensed pharmacist or veterinarian within the scope of its professional practice only in the quantity needed (e.g., not for nationwide retail sale.);
- there must be procedures and processes in place that ensure the safety and effectiveness of the compounded product; and
- the pharmacist or veterinarian must compound the animal drug in accordance with all relevant state laws.

In short, FDA’s implementing regulation, 21 C.F.R. § 530.13, is consistent with, and necessary to implement Congress’ decision to authorize compounding only when determined to be necessary by a licensed veterinarian within a specific “veterinarian-client-patient” relationship and an approved drug is not available, not to authorize bulk compounding and nationwide solicitation and sales. AHI believes that FDA struck a sensible and workable balance in the Compliance Policy Guide.

With this history in mind we would like to respond to the three questions posed in this Federal Register publication and addressed by State representatives at the public meeting on December 19, 2012:

GIVEN EXISTING AUTHORITIES AND RESOURCES, ARE THE STATES CURRENTLY ABLE TO PROVIDE THE NEEDED OVERSIGHT OF PHARMACY COMPOUNDING AND CONSUMER PROTECTION?

AHI believes that states have adequate authorities and resources to regulate the practice of veterinary pharmacy compounding of animal drugs as defined by FDA in regulations promulgated under AMDUCA. However, the current illegal practice of large scale compounding of animal drugs from bulk active ingredients is beyond the capability of states to regulate as these are violations of the FD&C Act and should be regulated as prohibited practices by the FDA.

WHAT SHOULD THE FEDERAL ROLE BE IN REGULATING HIGHER RISK PHARMACY COMPOUNDING SUCH AS COMPOUNDING HIGH-VOLUMES OF DRUGS FOR INTERSTATE DISTRIBUTION? IS THERE A WAY TO RE-BALANCE FEDERAL AND STATE PARTICIPATION IN THE REGULATION OF PHARMACY COMPOUNDING THAT WOULD BETTER PROTECT THE PUBLIC HEALTH? WHAT STRATEGIES SHOULD BE DEVELOPED TO FURTHER STRENGTHEN FEDERAL/STATE COMMUNICATIONS?

Because of the unique legislative and regulatory history with animal drugs, AHI believes that “*higher risk pharmacy compounding such as compounding high-volumes of drugs for interstate distribution*” must be completely prohibited for animal drugs at the federal level. FDA allowance of the manufacturing and sale of large volumes of bulk compounded animal drugs that do not meet all of the requirements for safety, efficacy, and quality is in no way authorized under the Act, is not in the best interest of animal health, and will only serve as a significant disincentive for ethical manufacturers to spend the time and resources necessary to gain FDA approval. The dollar sales of most animal medicines are magnitudes below that of human drugs. But pre-approval regulatory requirements are essentially the same or even greater in some cases and like human pharmaceutical manufacturers, animal drug sponsors also incur significant user fee costs. Unlike human health there is no government or employer supported insurance programs that supplement the cost of veterinary medicines with virtually all costs borne by the animal owner. Therefore, the economic impact on approved animal drug sponsors by permitting “non-traditional” large scale compounding would likely be far greater than for human drugs. Additionally, the ability of manufacturers to fend off such illicit competition through enforcement of private intellectual property rights is often less for manufacturers of animal health products, due to the reality that new active ingredients often become available for animal health uses with significantly less patent protection remaining.

**DO YOU SEE A ROLE FOR THE STATES IN ENFORCING A FEDERAL STANDARD FOR “NON- TRADITIONAL” COMPOUNDING?
IF SO, WHAT ROLE? WHAT FACTORS WOULD AFFECT
A DECISION BY YOUR STATE TO TAKE ON SUCH RESPONSIBILITY?**

As stated previously AHI does not support FDA establishing any category of “non-traditional” compounding that would apply to animal drugs.

We appreciate the opportunity to comment on this critical topic and respectfully request that the agency carefully consider our comments and how future regulatory or legislative changes relative to pharmacy compounding can affect the safety and efficacy of animal health products.

Sincerely,

A handwritten signature in black ink that reads "Richard A. Carnevale". The signature is written in a cursive style with a large, prominent initial 'R'.

Richard A. Carnevale, VMD