

Summary

On November 18, 2019 the Food and Drug Administration issued draft Guidance for Industry #256 regarding the use of bulk drug substances to compounding animal preparations. The draft guidance describes the specific circumstances under which the agency, using enforcement discretion, will allow the use of bulk drug substances. If properly implemented and enforced, this guidance will protect animal and human health by curtailing the practice of some large pharmacies acting like drug manufacturers and marketing compounded products as less expensive alternatives to FDA-approved drugs. This guidance should be finalized as soon as possible and vigorously enforced.

Background

In 1994 Congress passed the Animal Medicinal Drug Use Clarification Act (AMDUCA) providing for legal compounding of animal preparations when the compounder manipulates an approved human or animal drug upon a prescription by a veterinarian to meet the medical need of a specific patient. Such compounding is considered “extra-label drug use,” is legal and is unaffected by the new draft guidance.

Compounding animal preparations from bulk drug substances, rather than approved drugs, is illegal. This fact is stated in the regulations implementing AMDUCA, has been consistently upheld by three federal appeals courts, and is explained again in draft GFI #256.

A compliance policy guide (CPG) issued by FDA in 1996 described the agency’s intent to use enforcement discretion to allow for a limited amount of animal drug compounding from bulk substances in instances where there is no approved human or animal drug with the specific active ingredient needed to meet a patient need. That CPG was withdrawn by the agency in 2015 when a draft guidance document was issued. That draft guidance, withdrawn by FDA in 2017, is replaced by GFI #256.

The Problem

In recent years, some compounding pharmacies have acted like drug manufacturers under the guise of compounding. Using bulk drug substances, they have compounded animal preparations in large quantities and advertised them as less expensive alternatives to approved drugs. They have compounded drugs that are copies of or near copies of FDA-approved drug products.

This illegal activity endangers patient health and undermines the FDA approval process. Animal drugs compounded from bulk substances do not carry the proof of safety and efficacy that approved drugs do. In 2009 21 polo horses in Florida died as a result of a compounding mistake. In 2014 four horses died as a result of an erroneously formulated compound. And in July 2019 FDA announced that horses in regionally diverse part of the country died or were euthanized as a result of the use of compounded drugs. Published research and FDA inspection reports have documented inconsistencies in potency and amounts of active ingredient in compounded products as well as lack of sterility testing of these products.

In addition to endangering the health of animals treated, this compounding undermines the FDA drug approval process. In order to get a drug approved by FDA, drug manufacturers must prove the drug is safe for its intended use, that it effectively addresses the target disease and that the company can consistently manufacture the drug in large quantities. This is a process that takes millions of dollars and several years. When compounders can copy the product without the same investment in proving safety and efficacy, the incentive for companies to engage in new discovery is severely diminished. Given the large number of animal species and the relatively small number of approved drugs, there is a need for more research, development and discovery of safe and effective drugs that veterinarians can rely on to treat a wide variety of animal conditions.

FDA Guidance

This draft guidance provides a long-needed bright line description of exactly what compounding from bulk will be permitted by enforcement discretion. Implementation and enforcement of this guidance is intended to allow veterinarians and pharmacists to meet medical needs of patients while not allowing compounders to endanger animal health by acting like unregulated drug manufacturers or disincentivizing manufacturers from developing safe and effect new animal drugs.

This guidance applies only to compounding animal preparations from bulk drug substances. In all situations it requires:

- Compounding be done under the supervision of a veterinarian or pharmacist in a state licensed pharmacy or federal facility;
- Reporting of adverse event by the pharmacy or veterinarians;
- Labeling of the preparation as a compounded drug

When the compounding from a bulk drug substance is being done for a specific patient, it cannot be a copy of an FDA approved drug, and if it contains an active ingredient similar to an FDA-approved drug the veterinarian must show the compound makes a clinical difference in the identified patient.

If the compounding from a bulk drug substance is being done without a patient-specific prescription, it can only be done using an active ingredient on the public bulk substances list maintained by FDA.

Conclusion

The animal health industry supports legal compounding as described in AMDUCA and supports the use of bulk drug substances for compounding preparations in those situations where no active ingredient needed to address patient conditions is found in an approved product. Specific guidance to describe these situations where FDA will permit compounding from bulk substances – which is otherwise illegal – is a critical need. The issuance of this draft guidance is an important step forward. There is a 90-day comment period, after which we urge FDA to issue final guidance as soon as possible. Congress can help protect human and animal health by supporting final guidance and providing adequate resources to allow FDA to enforce this policy guidance.