

# Compounding controversy

Are renegades ruining the industry for legitimate compounders?

by Denise Steffanus

COMPOUNDED drugs benefit veterinary medicine when they are formulated properly and used for appropriate medical purposes. No one involved on either side of the ongoing controversy over compounding denies their importance in a veterinarian's armamentarium. The legality of their manufacture and distribution, and how carefully and ethically they are produced, are the issues.

The biggest issue is piracy—producing a knockoff of a commercially available, United States Food and Drug Administration-approved product. Because they are produced illegally, these products have no quality control or safety testing, and in many instances, the raw materials needed to make them are proprietary to the drug manufacturer that developed the FDA-approved product. So renegade compounders must substitute whatever material they can find, wherever in the world they can get it, to make these knockoffs, which often do not work or can be outright dangerous.

Knockoffs are cheaper for the consumer to buy than medications produced by drug manufacturers, which must factor in the cost of research, development, and quality manufacturing processes to recoup their investments so they can continue to manufacture the drugs. Renegade compounders, who do not have to shoulder these costs, can garner a huge profit from these knockoffs while still undercutting the price for the commercially available product.

The simplest way to determine if a compounding pharmacy is operating within ethical and scientific boundaries is to ask the pharmacist to compound a knockoff, such as counterfeit GastroGard ulcer medication.

If that pharmacy agrees, it is an unethical compounder.

## What is compounding?

Compounding is any manipulation of a drug approved for use by the FDA beyond that stipulated on the label. For example, if a veterinarian needs a paste form of a specific FDA-approved antibiotic for use in an individual animal but that antibiotic is not available in a paste, a pharmacist who fills that prescription by mixing crushed tablets containing that antibiotic with a paste is formulating a compounded drug. (The terms "compounded drug" and "generic drug" are not interchangeable. A generic drug must acquire FDA approval.)

Compounding commonly involves:

- Combining two or more FDA-approved injectable drugs so the horse needs just one needle stick;
- Adding flavoring to an FDA-approved drug; or
- Altering the method of administration of an FDA-approved drug (as for the paste antibiotic mentioned above).

Compounding pharmacies are expressly forbidden from producing a knockoff drug. This regulation is designed to protect the interests of pharmaceutical manufacturers that spend millions of dollars and years of work developing and testing new animal drugs in compliance with FDA regulations. Without this protection, drug manufacturers would have no incentive to develop new drugs. But the regulation also protects consumers whose animals may be harmed by knockoff medications that do not meet safety, efficacy, and manufacturing standards.

In 2007, several horses in Louisiana became ill and two were euthanized after they received massive overdoses of the bronchodilator clenbuterol hydrochloride contained in

a knockoff version of Ventipulmin that was 70 times the strength of the Boehringer Ingelheim Vetmedica product.

Countless other casualties may occur when treatment fails because the practitioner has used a knockoff medication that does not work.

"That's the biggest problem with this issue," said Joe Bertone, D.V.M., professor of equine medicine at Western University and a former veterinary medical officer for the FDA. "It's not the death off the needle; it's not the joint that blows up because somebody injected a compounded medication into it. The much more serious and subversive problem is the horse that is ill or lame and gets treatment and dies or fails to respond. The excuse is that the patient was just too sick or the lameness just didn't respond. The poor-quality compounded drug, or the drug that has never been tested to work, doesn't get the blame. Several articles and papers have shown that compounded drug knockoffs are often of poor and/or of inconsistent quality and may not have in them what the labels say they have in them."

## Bulk ingredients

A major point of contention is compounding of medications from bulk ingredients, or raw materials, which the International Academy of Compounding Pharmacists vehemently defends but which is expressly forbidden by FDA regulations. The FDA asserts that compounding from bulk ingredients constitutes the formulation of a "new animal drug" without fulfilling the FDA's stringent protocols for approval and quality assurance. Legally, these drugs are considered mislabeled, misbranded, and adulterated.

Contrary to popular belief, bulk ingredients do not necessarily mean mass quantities, such as drums or vats. A bulk ingredient purchased for use in compounding may be a very small quantity, such as 100



Denise Steffanus photo

## COMPOUNDING FACILITIES

A pharmacy should be clean and orderly, assure proper handling and storage of materials, and establish standard operating procedures for equipment, personnel, and documentation

grams, said Gregg Pederson, R.Ph., president of Pharmacy Resources Inc. in Denver. Pederson explained that many times, it is necessary for a pharmacist to use the raw material when compounding a medication to assure the safety of the product.

"If you were going to make an injectable product that had methocarbamol in it, as an example," he said, "there probably is a source out there where you could buy Robaxin tablets and they would contain methocarbamol, but they would also have fillers, starch, and a number of other things in them. How would you make that into an injectable product? It's not possible. So, instead, you go to an FDA-approved chemical supplier that supplies very pure chemicals, and you buy the [methocarbamol] from them and make it into an injectable product. You just don't buy it from some mom and pop or somebody where you don't know where the product comes from."

"Whether it comes in a little bottle or a big container, the fact is that

it has an origin that you can support and a Certificate of Analysis. It's not just some powder that somebody sends me. I'm a reputable pharmacy."

The American Veterinary Medical Association supports the FDA's ban on the use of bulk ingredients.

"These bulk ingredients often originate from developing countries that may lack a well-regulated chemical industry," an FDA statement on the issue said. "These bulk ingredients may not be of the same quality as the bulk ingredients that the FDA requires a true drug manufacturer to use. Finally, these bulk ingredients may come from countries where there are concerns about the real threat of bioterrorism."

Bertone said drugs coming into the country under little or no oversight should be a serious concern for the Department of Homeland Security because it would be simple for a terrorist organization to taint the drugs, possibly with a deadly virus.

"It is a real means for getting something serious across the border," Bertone said. "If foot-and-mouth disease broke out through tainted drugs, it is well recognized that it would bring down the U.S. economy."

Bertone added that only about 2% of the drugs and bulk ingredients that come into this country are inspected by the FDA or the U.S. Customs and Border Protection.

Further complicating the issue of use of bulk ingredients is a 2006 ruling by the United States District Court in Texas that found the use of bulk ingredients in formulating medications for non-food animals does not constitute illegal compounding. The case is under appeal, but in the meantime, compounders and the FDA are arguing about the ruling's applicability to compounders outside Texas. †

**Next: How compounders respond to their critics.**



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## Selecting a compounder

VETERINARIANS are urged to use the following criteria when selecting a compounding pharmacy:

- Ask the pharmacy if it will make you a knockoff of a commercially available, United States Food and Drug Administration-approved medication. If so, do not use that pharmacy;
- Know the pharmacist and his or her background in pharmacy and in the veterinary industry;
- Choose a pharmacy that has a reputation for quality and that has been active in the veterinary industry long enough to be time-tested;
- Talk to other veterinarians who have established such relationships; and
- If possible, visit the pharmacy and establish a one-on-one relationship with the pharmacist and support personnel.—Denise Steffanus