

Drug Piracy I: Legitimate Pharmacy Compounding, Pioneer and Generic Drugs and Registered Products, and Medical Devices? What are the Facts and how can this Affect My Practice?

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Introduction

Veterinarians are often unclear on the differentiation and the clinical ramifications of the use of pioneer and generic drugs and registered products, medical devices, and pharmacy-compounded products. In addition, what are the laws that revolve around these issues?

Definitions

Drug Piracy

Drug piracy is the mimicry of Food and Drug Administration (FDA) approved drugs. The pirated formulations are sold under the guise that one can expect the same quality; clinical safety and efficacy compared to FDA approved products. It is impossible for a drug pirate (often who disguise themselves as a compounding pharmacist) to formulate a product with the same quality, purity and stability of an FDA approved product, and assure efficacy and safety. Licensed pharmacists know they can't produce products of the same quality as FDA approved formulations. They are educated to this fact. Examples of drug piracy include attempts to mimic Gastrogard™, Ketofen™, Banamine™, Hylartin-V%, Rimadyl™, Enalapril™ Metacam™. This practice is initiated by ignorance, avarice or both on the part of the pirate, and supported by either ignorance, avarice or both of veterinarians.

Also added to the spectrum of activities of some drug pirates is the promotion of untested drugs and untested routes of administration, as if they have data to support this information (e.g., topical drug administration of antibiotics for systemic disease).

Drug compounding

There are two kinds of drug compounding.

1. Drug compounding may involve the alteration of FDA approved products. An example would be mixing Acepromazine™ and Rompun™ in the same syringe

at the patient's side. There is a provision in the law for this practice under the the Federal Food Drug and Cosmetic Act, Animal Medical Drug Use Clarification Act (AMDUCA). Alteration of FDA approved products is not of concern in this article.

2. The more important form of compounding with regard to this article is the compounding of bulk chemicals to form a new product. The focus of this article is drug compounding from bulk products to create a new formulation.³

Bulk Products

Bulk products are basically chemicals in drums, boxes, bags and bottles. In the case of most drug bulk products used for drug piracy in veterinary medicine, the products are often smuggled into the United States and come from India, Pakistan and China. The quality of these products is always in question. There is no guarantee of the products' strength, content and purity (e.g., How much active hyaluronic acid of a known molecular weight is in the powder? Is there hyaluronic acid in the powder? What else is in the powder?).

Legitimate Pharmacy Compounding

Pharmacy compounding is the legitimate activity of drug formulation to produce a product for medical management. Formulation is performed by a licensed pharmacist when no other FDA approved choice is available (e.g., dipyrone injectable or KBr). Prescription and labeling guidelines must be followed. Many compounding pharmacies produce excellent products, follow the law and Good Compounding Practices guidelines, and care about patients. Unfortunately, many drug pirates are licensed pharmacists, but producing a pirated drug is not legitimate pharmacy compounding.

Pioneer and Generic Drugs and Registered Products

Pioneer, generic and registered drugs all have FDA

approval. All of these are manufactured under Good Manufacturing Practices (GMP) legislation and guidelines. Pioneer drugs are the original product under which drug sponsors collected efficacy and safety data for FDA approval. Generic drugs are drugs that are allowed to be marketed based on essentially matching pharmacokinetics to the pioneer and the determination that the constituents of the product provide no safety risk. As with pioneer products, generic products require FDA approval. Registered products are intravenous fluids, vitamins, etc, with no claim, but are allowed to be marketed by FDA and still undergo GMP manufacturing criteria.

A common misconception by veterinarians, and often indicated by drug pirates, is that pirated drugs are generics. That is completely wrong!

Pirated drugs have no claim to drug quality, purity and stability. The bulk product is often made in laboratories in China, India and Pakistan. No bulk drug intended for use in veterinary species is allowed to be imported into the United States. Therefore, all bulk chemicals used in drug piracy have been imported illegally. Is this a homeland security issue?

Medical Devices

There are no veterinary device regulations. In other words, radiology equipment, extracorporeal shock wave equipment, ultrasound equipment, etc. specifically marketed for veterinary use has no governmental oversight, unless there is some relationship to food or public safety. Why is this important to understand? Products like MAP5™ (sodium hyaluronate, Bioniche Animal Health) registered as a device for its use as a cryopreservative; Chondroprotec™, (glycosaminoglycan, Neogen Corp.) and Hycoat™ both registered as devices for wound dressing, are not regulated by the FDA for use in animals. There is no provision in the law to use a device (these products) as a drug. Hence, when you use them, you are outside the law. The marketing of these products in veterinary medicine is likely a means to avert the law and adversely affects future drug development. The products have not been efficacy and safety tested for use in horses or any other species. If you get in trouble with these products, in their use in veterinary species, the sponsor has no responsibility to you. They are also not produced under drug GMPs. They do not meet the standards.

Background: Laws

Why do we have laws that insure the quality of drug products? In 1936, Masengill Company attempted to create a Sulfanilamide suspension for use in children. Unfortunately and without knowledge, the pharmacists

used a solvent that was tainted with 72% diethylene glycol. There were 105 human deaths associated with this incident. The Food and Drug Act (later adding cosmetics) was codified in 1938 to assure drug efficacy, safety, quality, strength and purity. It was well recognized that these attributes could not be guaranteed under normal drug compounding with bulk products. This is why I often discuss drug piracy as the “Devolution of veterinary medicine to the turn of the last century.” So that you do not think that is an issue of the past, a similar “Masengill-like” incident occurred in Haiti in 1995 and 1996 and led to 87 deaths.⁴ The DEG contamination was due to a tainted exipient from China.

The law provides no provision for compounding drugs for animals from bulk drugs. That means drug piracy is against the law. In addition, it may sound contrary, but there is no provision for legitimate compounding pharmacies using bulk drugs. The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) (21 CFR § 530.13(b)) allows for alteration and combination of FDA approved formulations. The Center for Veterinary Medicine Compliance Policy Guideline (Compounding of Drugs for Use in Animals, 608.400 (www.fda.gov/ora/compliance_ref/cpg/cpgvet/cpg608-400.html)) indicates that the government is interested in stopping practices “outside the bounds of traditional pharmacy practice (e.g., compounding that is clearly intended to circumvent the drug approval process...)”

This means it is illegal to compound from bulk chemicals for non-food animals. However, FDA is unlikely to pursue this practice if there is an essential medical need and there is no other FDA approved drug available for treatment of the patient. Bulk chemical (drug) use for food animals is not tolerated under any circumstance (see Figure 1).

That means formulation and use of drugs compounded from bulk products is ----- use of an adulterated, misbranded and mislabeled product. How would you like to be on the wrong side of that statement in a case involving an infected joint that you injected with a compounded preparation!

Liability Issues

See article 7 under exclusions in your Professional Liability Insurance policy.

“This certificate does not apply: ...7. to liability arising out of the intentional performance of a fraudulent or criminal act...” Using a pirated product is the use of a misbranded, mislabeled and adulterated product by law. I have had a few people indicate to me that they can use the “standard of practice” to overcome this issue. Standard of practice only relates to issues not stated as outside the law. If a whole group of people are speeding, that does not mean speeding is legal.

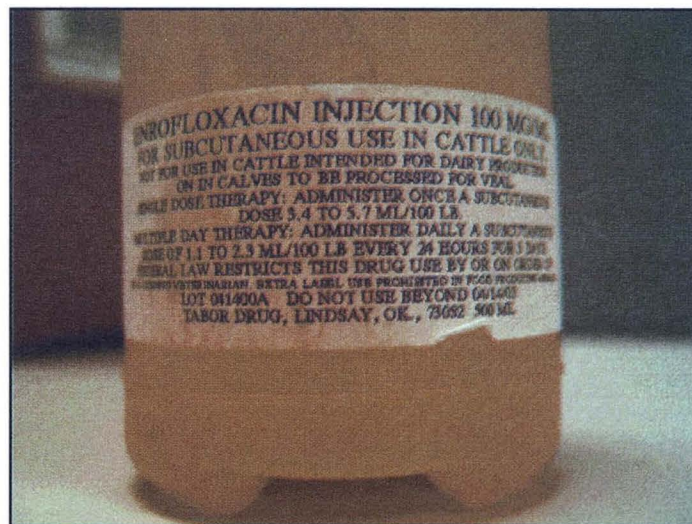
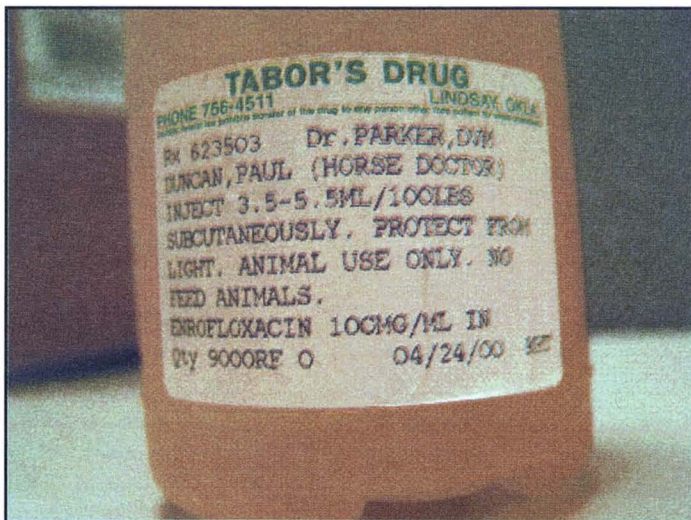


Figure 1. Pirated “enrofloxacin” created from smuggled into the country “enrofloxacin”, specifically made to treat food animals.

What is the Nature of Drug Piracy?

I continue to ask this question and as yet have identified only two possibilities.

1. The knowledgeable pirate

This pirate knows that FDA approved products are better for the patient and the legal, ethical, and scientific basis for this finding. The only conclusion, then, is that this pirate has no care for veterinary patients, clients, our profession or your practice.

2. The ignorant pirate

This pirate actually believes the things he/she mixes are just as good as approved products produced under GMP and regulated by the FDA. This pirate believes the bulk sources they use in unfriendly countries are equivalent to sources used in legal pharmaceuticals within the United States. The only conclusion that can be reached is that this pirate has no skills in compounding pharmacy and has no understanding of pharmaceutical science.

In conclusion, drug pirates are either unknowledgeable or care nothing about veterinary medicine. Your clients are paying for either the pirates' lack of knowledge or for their unethical behavior.

How do You Choose a Good Compounding Pharmacy?

Let me make this clear: legitimate compounding pharmacy is not drug piracy. In fact, the American College of Veterinary Pharmacists¹ indicated they are appalled by this activity and are being inadvertently and adversely affected by the practice. Legitimate pharmacy drug compounding is based on the extent of knowledge

and ethical behavior of the pharmacist. It is nearly impossible to identify the extent of a pharmacist's knowledge in compounding, and whether the pharmacist you are considering is an ethical individual. However, since drug piracy is an indication of lack of ethical behavior, or lack of knowledge, then at a minimum good compounding pharmacists do not drug pirate.

Scenario: What, Hopefully, You Don't Know About Pirated Drug Products

Nice profit margin! You purchase Drug A from a licensed distributor (e.g., MWI, Burns, Nelson, Columbus, etc.) for \$X.00. Drug A is an FDA approved drug (e.g., Gastrogard™, Rimadyl™, or a true generic for xylazine). You find out that you can purchase something from a “compounding pharmacy” that claims it has the same active ingredient of drug A, but it is 20% of your cost (compounding pharmacy is quoted because this is not the practice of pharmacy, although the pirates call themselves compounding pharmacists). You can pass the savings onto your client. However, many of you charge your client the same amount as you would have for the FDA approved drug. This adds up to a markup of 500%, or more in many cases. How can this be a problem!?!?

Well, let's hope that you didn't know that:

1. ...since an approved product is available, you sold your client a product that is substandard by definition.

2. ...since the pirated product is not produced under GMP regulations and guidelines, you have no assurance that the product in the bottle is what the pirate says it is. In fact, analyses to date indicate that the range of content of the active ingredient is 0 to 176% of the bottle label. Unfortunately, we have no data on non-pi-

rated drugs produced by good compounding pharmacies. However, since these individuals are more likely to understand their art and practice ethically, we can assume that these products are of much higher quality.

3. ...you have no assurance of a pirated drugs efficacy and safety attributes, especially compared to an FDA approved drug. You don't know what drug you have given. That speaks for itself.

4. ...by legal (Food Drug and Cosmetic Act) definition the pirated product is misbranded, adulterated and mislabeled. Keep that in mind when thinking of legal liability. Also keep in mind that since use of these drugs is illegal, you risk liability coverage when you use them in veterinary patients. See PLIT item 7 under "exclusions for coverage" in your policy.

5. ...pirated drugs are NOT generic drugs. Generic drugs are FDA approved, and hence undergo the same stringent FDA requirements for manufacturing as original FDA approved drugs. Many drug pirates (who misrepresent themselves as compounding pharmacists) portray the stuff they make as generic products. They are not.

6. ...since you added a markup to the product (which identifies the provider "compounding pharmacy" as a renegade drug manufacturer) you may be responsible for a "pharmacy" closure. Pharmacies are not licensed drug distributors, nor drug manufacturers. Ethical pharmacies provide drug formulation for spe-

cial needs and when no other similar-route active ingredient is available. They are not a source for better drug margins.

Why would one hope you did not know the six points listed above? There are only two choices: drug pirates are either ignorant of their craft, or they understand what they are doing and are preying on you and your clients. They are violating the public trust. However, with respect to you the veterinarian, if you did not have the above information, and you sold your client the pirated product, you were just ignorant of the facts. Blame it on your education. This article provides you with information that hopefully will improve the quality of your practice. However, after reading this article, or if you were previously aware of any of the six points above, and still chose to sell the pirated product to your client then you have violated, or will violate the public trust and could easily be labeled as

References

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