Compounded pharmaceutics can be essential to equine veterinary practice. The veterinarian must be aware of the quality considerations in these products. Certain questions should be asked before a compounding pharmacy is chosen. Veterinarians bear responsibility for the use of compounded medications, whether or not the compounding pharmacy uses state compounding guidelines. Author's address: 3815 Baker Valley Rd., Frederick, MD 21704. © 1997 AAEP.

1. Introduction
Essential to rational therapeutic drug use is knowledge of the quality, strength (concentration), purity, and availability of the molecule in the formulation we intend to administer. Further, the veterinarian’s responsibility is to practice medicine scientifically and ethically. If we believe that these statements are valid, then we can appreciate that various levels of scientific or empirical evidence regarding the nature of a particular drug formulation provide us with various levels of assurance that patients will respond favorably to the administration of a drug. In this respect, when a compounded drug is prescribed, veterinarians should have complete knowledge of the compounding pharmacy selected for this process, because the veterinarian bears responsibility for the use of these formulations. In addition, veterinarians must decide when quality is outweighed by cost. In other words, they must decide when a clinical decision to use a compounded medication is worth the risk of ineffectiveness or adverse drug events in the patient and to the client.

2. Responsibility for the Use of Compounded Drugs
It is judicious for veterinary practitioners to assume that they are ultimately responsible for the use of a compounded product. This more clearly defines the seriousness of using compounded formulations. Clearly, it behooves the veterinary practitioner to be sure that the compounding pharmacy is following appropriate compounding and pharmacy guidelines.

3. Clinical Evidence and the Use of Compounded Drugs
The highest assurance for safe and effective use of a drug comes when the available drug formulation (dosage form, excipients, concentration, etc.) was associated with a desirable response, without adverse effects, as evidenced in controlled clinical trials that evaluated safety and efficacy. When well-controlled clinical studies are lacking we must use more tenuous supportive information, which includes pharmacokinetic data and data collected from other species, case series, or anecdotal reports. As the specificity and unbiased nature of the supporting data weaken, our confidence in the drug’s effect...
should diminish. We must keep the value of the available evidence for safety and efficacy in mind when applying any therapeutic medication. As equine veterinarians, we are fairly familiar, and to some degree comfortable, with the use of drugs in the absence of clinical scientific evidence. The literature is replete with case series, case reports, pharmacokinetic, in vitro data (microbiology), and so on. This information is, at best, loosely indicative of a drug formulation’s effectiveness. Controlled prospective clinical studies evaluating drug effects in horses are rare. With all of this uncertainty, the least we must know is that we are actually administering the drug we intend to administer.

Inherent for drug formulations approved by the Food and Drug Administration (FDA) is their quality (content, stability, and strength). FDA-approved formulations have high quality of manufacturing controls and support a high level of confidence regarding the drug product content. The dilemma of equine veterinary medicine is that practitioners find themselves attending to conditions for which there are little clinical data to support therapeutic choices, such as pituitary adenoma, and for which no approved formulation exists, or for which approved formulations, for other uses or species, are impractical to administer. In these situations, equine veterinarians often use compounded medications.

4. Regulation of Compounding Practices

Do not assume that the quality of a compounded medication for use in companion animals (which include horses) is being controlled by the federal or state government. It is a common misconception that the FDA actively regulates the content and quality of compounded products for veterinary use. It is judicious to assume that compounded formulation content is dependent on the ethical and quality characteristics of the compounding pharmacy.

Compounding practices, in general, are outlined by the attending jurisdiction, which for the most part are the state pharmacy boards. However, do not depend on state boards to police the compounding of veterinary drugs for companion animals. State pharmacy boards tend to be reactionary, which means they respond to complaints. If you believe that a pharmacy is performing in an unethical manner (e.g., compounding for lay persons, not providing the drug in the prescribed concentration, etc.), then your first line of action should be to file a report to your state pharmacy board. However, remember that even with compounding pharmacies with high quality standards, there is little scientific information for the pharmacologic characteristics of compounded formulations.

Drugs are administered with the hope of achieving a desirable effect. Veterinarians find themselves in situations in which the only choice for treatment is a compounded medication. However, the use of compounded medications is bounded ethically by several stipulations that include, but are not limited to, the development of a veterinarian–client–patient relationship, prescription drug-dispensing restrictions, and use in the treatment of disease or to improve the welfare of the animal. In addition, there should be no FDA-approved product in a suitable dosage form to treat the condition (e.g., a need for an intravenous formulation, when only tablets are approved).1

Basic to achieving a positive effect when administering drugs is knowing that the drug is administered in the desired strength and that the drug is available to the patient. If practitioners choose to compound, or to prescribe compounded medications, they accept the responsibility for formulation effectiveness, safety, and composition. Approved drugs are consistently formulated to specification. Assurance of a formulation’s composition or its availability to the patient is less certain when veterinarians prescribe compounded medications. Therefore, the veterinarian must collect specific information to aid in the identification and choice of a quality compounding pharmacy.

5. Economics

A. Cost Versus the Use of FDA-Approved Formulations

Most state pharmacy board guidelines do not allow for the compounding of a drug that is available in an FDA-approved similar dosage form (e.g., compounding of flunixin meglumine for intravenous or oral use when the approved forms are marketed). Compounding of formulations that are the subject of a New Animal Drugs Approval (NADA, FDA veterinary approval) is inappropriate. Compounding pharmacies that provide this service should be suspect in their activities. However, the cost of some formulations that are the subject of a New Drug Approval (NDA, drugs for use in persons) may preclude the use of these drugs for veterinary practice. This area is as yet unresolved. The question is, when does cost preclude quality? Remember, you as a veterinarian will bear the responsibility for this action. Clearly the owner should be apprised of this choice.

B. Cost and Choosing a Compounding Pharmacy

Cost should not be calculated into the choice of a compounding pharmacy. Once the quality of competing firms is established, then the cost may be taken into account. Quality is paramount.

C. Cost and Increasing Profit

I cannot condone any drug compounding in which the purpose is to increase a practitioner’s profit margin. In my opinion, this activity is inappropriate, unscientific, and unethical.

6. Information Concerning the Compounding Pharmacy

The issues listed below are not issues directly related to quality drug compounding, but they relate to the conduct of the practice of pharmacy medicine. As a
practitioner, I am concerned that if a compounding pharmacy does not follow state pharmacy guidelines relative to the practice of pharmacy medicine, how can I be sure it is following state pharmacy guidelines in relation to compounding practice for veterinary species? For specific compounding guidelines, contact your state pharmacy board.

A. Does the Firm Use Advertisements Beyond a Statement of the Services Offered?

Most state pharmacy boards do not allow pharmacies to develop price lists or other advertisements beyond an indication of the willingness to provide compounding services. Firms that provide these lists and advertisements should be suspect in their activities.

B. Does the Compounding Pharmacy Ship Products Interstate?

Shipping compounded drugs interstate is appropriate if the drug is prescribed by a veterinarian. However, many state pharmacy boards require that a pharmacy that ships drug to another state must be registered in the state of destination. Again, a compounding pharmacy that neglects to adhere to this requirement should be suspect.

C. Does the Firm Compound Therapeutic Medications for Laymen Without a Prescription?

If the answer is yes to this question, then I would suspect the actions of these compounding pharmacies. Invariably, this action is not approved by pharmacy boards or guidelines, which specifically state that compounding of drugs should only occur by request of medical professionals and by prescription only. This activity has been deemed unethical by most state pharmacy boards.

7. Information Concerning the Compounding Pharmacy

The issues discussed below are specific questions concerning compounding practice.

A. Is a Licensed Pharmacist on Staff?

Having a licensed pharmacist on staff who supervises the compounding process is essential for quality drug compounding and, depending on the jurisdiction, is legally required. Pharmacists have the training and legal and ethical responsibility to follow good compounding practices as prescribed by the practice of pharmacy and as outlined by the attending jurisdictions (the state pharmacy boards). Pharmacists have the training to understand the issues of quality, strength, purity, bioavailability, and stability essential to the rational use of drugs. Some compounds do not have pharmacists on staff, or there is at best a loose association between the compounding firm and a pharmacist. To avoid this situation, veterinarians should identify the pharmacist and verify the name and state license number. The state board will have information concerning that pharmacist and any actions against them.

B. If Bulk Product is Used to Produce the Compounded Formulation, Are These Raw Materials of High Quality?

In some situations, the use of bulk products provides for greater safety than the use of approved dosage forms in compounding. A clear example is the use of an oral tablet versus a bulk product to produce an injectable solution, or when excipients or other ingredients in the approved formulation are potentially detrimental to the species in which the compounded drug is to be used.

Clearly, the raw materials must be of high quality for the final product to be of high quality. Good manufacturing practices ensure that the product contained in an FDA-approved formulation has the quality attributes identified by its label and certificate of analysis. Good manufacturing practices provide for the controls necessary to ensure that the resultant product has and retains the intended identity, quality, strength, and purity. A certificate of analysis should be forwarded with each shipment of product to the compounding pharmacy. Quality compounding pharmacies will not hesitate to provide certificates of analyses for the bulk drug they use with your ordered formulation. Some compounding pharmacies do not verify the quality of their raw materials and simply find the least-expensive source regardless of the manufacturing controls. At a minimum one should ask the compounder if the wholesaler of the bulk drug is licensed, or registered, with the state pharmacy board. In addition, and minimally, the bulk product should be a United State Pharmacopeia/National Formulary (USP/NF) listed product.

It is important to note that using bulk raw materials to compound drugs intended for use in food animals or for use in horses intended for human consumption is not appropriate, except in rare instances. This relates directly to the lack of assessment of the safety of these products in terms of food residues. Where horses are companion animals and are not used for food, the use of bulk products for compounding is of no food-safety concern for humans.

C. What Type of Quality Testing is Performed?

Ideally, each batch of the final packaged, compounded product should be quality tested. Unfortunately, this is impractical in many situations. Nevertheless, if a compounded formulation is produced on a regular basis for a large group of animals, some form of test batch analysis should be expected. Even when USP/NF bulk drugs of known strength and quality are used, loss of active ingredient or formulation errors may occur during compounding. An analysis of the compounded drug should be performed after the compounding process is complete. Quality compounding pharmacies will test commonly prescribed recipes for their own quality control. I recommend that if a compounded drug is
used on a regular basis, the veterinarian collect a sample to be sent for analysis to a certified laboratory. Some state racing laboratories can assist you in this aspect. This will act as your own quality control and may give you some information concerning the product’s shelf life.

D. Are Stability Data Available?

The nature of equine practice leads us to stress the stability of compounded products. We tend to work outdoors, which is not a temperature-controlled environment. Chemists cannot predict, with great confidence, the stability of formulated products without data from controlled stability studies. Therefore, it is judicious to identify if and under what conditions stability testing has been performed. Quality compounding firms may collect such data. I recommend that veterinarians keep adequate samples for analysis, especially if the product is prescribed with some frequency. The expiration date should be set at the time a prescription should be entirely used. Regardless of the testing available, the compounding pharmacy should give some advice on storage of the formulation.

8. Other Considerations

Equine veterinarians must not take the prescription of compounded drugs lightly. Approved drugs give us the highest assurance of quality, strength, purity and stability, as well as the best opportunity for accurate dosing. Dramatic changes in drug disposition (i.e., bioavailability) may occur with minor changes in compounding technique, even while using the same recipe. In addition, approved formulations undergo rigorous tests under various environments to define the limits of storage conditions. This assures us that under conditions of use the approved drugs are reasonably stable.

9. Conclusions

Veterinarians rarely have the ability to establish drug stability, physical and chemical compatibility, and pharmacodynamic action of the drugs they use. Ethically, we must take responsibility for the use of compounded drugs. To do so, we must collect information on the practices of individual compounding firms. In addition, we must depend on licensed pharmacists to provide us with well-compounded drug formulations. It behooves us, our clients, and our patients to become informed of the quality of product produced by firms we choose to compound our needed formulations.

References