

Legal issues in the pharmaceutical management of bovine reproduction

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Abstract

The ability for the bovine practitioner to implement reproductive management programs is scientifically well-based and clinically proven. However, as is being encountered in many areas of food animal medicine, science is no longer the major determinant of how a veterinarian practices or how a producer manages. Extra-label drug use (ELDU) allowed under the Animal Medicinal Drug Use Clarification Act was not extended to drugs used for production purposes, such as reproduction. Therefore, ELDU of drugs for reproductive purposes is not technically allowed in the Code of Federal Regulations (CFR). Compounding of drugs from raw pharmaceutical agents, except for a few specifically listed antidotes, is a violation of the CFR. Further, the use of illegally compounded products in food animals is ill-advised not only due to the legal and liability issues, but also because of a potential consumer perception issue. A final point to consider is the consumer reaction when current bovine reproductive management programs are presented to the consuming public by anti-agriculture activists.

Keywords: AMDUCA, compounding, management, reproduction, extra-label

AMDUCA and ELDU in reproductive management protocols

The Animal Medicinal Drug Use Clarification Act¹ (AMDUCA) of 1994 and the implementing regulations² were limited to drugs used for therapeutic purposes only.

Numerous comments to the proposed rule supporting the extension of the regulations to drugs used for reproductive management were considered but denied in the final rule. It is important to note that AMDUCA applies only to Food and Drug Administration (FDA or the Agency) approved drugs. The current situation has resulted in any extra-label use of reproductive drugs being illegal. The U.S. FDA has adopted an unofficial position of regulatory discretion. Any official position would require the generation and publication of a Compliance Policy Guideline (CPG) and the FDA has not indicated that it would consider taking this action.

The FDA's reasoning behind placing low regulatory priority on the issue of using drugs approved for reproductive purposes in a manner other than on the label is that these drugs have been proven safe and effective, and the dose, route and species are not altered. For example, the drug most often used in an extra-label manner is gonadotropin releasing hormone (GnRH). GnRH is a decapeptide and poses virtually no risk of residues nor any target animal safety issues. For these reasons, the Agency has suggested that they currently will not pursue any actions directed at extra-label use of reproductive hormones. At the same time, the FDA has indicated that they would be glad to entertain and possibly facilitate the approval of additional label claims for GnRH products so that the need for ELDU would be minimized or eliminated.

One final point which should be made regarding ELDU of reproductive drugs is that of client informed consent. ELDU has been the basis for at least one major lawsuit against a veterinary practice. In today's litigious society, ensuring that clients are aware of the extra-label nature of any use is appropriate. Having an informed and consenting

client is ever more important when such ELDU is not in compliance with the Code of Federal Regulations.

Compounded drugs

Compounding medications from unapproved drugs or raw pharmaceutical agents is illegal. References to this can be found in the AMDUCA regulations¹ and in an FDA CPG.³ There are exceptions in which drugs can be compounded under this CPG, but these are limited to certain specified antidotes only. The most common drug compounded for use in reproductive management protocols is some form of estrogen. Estrogens have been proven effective in initiating follicular waves both in embryo transfer programs and in routine breeding management systems.

However, in this case science has surpassed the veterinarian's armamentarium of approved drugs and, while the use of compounded estrogens may be tempting due to effectiveness, the potential for regulatory action and consumer backlash makes the use of compounded estrogens ill-advised. Currently the FDA lists one estrogen (diethylstilbestrol) on the list of drugs prohibited for extra-label use in food animals. An estrogen (estradiol cypionate) which was registered in 1953 but never approved has been withdrawn from the market by the sponsor based upon an impending request for an official approval application.

Of all the drugs used in cattle, both label and extra-label, the single drug with the greatest "headline potential" is any form of estrogen. The average consumer's lack of familiarity with animal husbandry and modern agricultural production practices, make the consideration of consumer acceptance relevant to the discussion of both ELDU and the use of compounded drugs in food producing animals. This significant downside to

the use of a drug compounded from unapproved products (specific antidotes are exceptions) makes such drug use illogical and irresponsible.

Consumer/public perception

Animal agriculture has numerous detractors in the form of activists. The issues which are used to malign the animal agriculture industries to the consuming public include, but are not limited to, animal welfare and factory farms. Because less than 1% of the population of the U.S. is involved in agriculture, the activist groups find the consuming public easily misled about commonly accepted, well proven, welfare-friendly and accepted management practices. The portrayal of modern agriculture as factory farming or intensive farm animal production is negatively compared to the typical small farming operation of 50 and 60 years ago. With this as background, some of the current reproduction management protocols which utilize multiple injections of various products coupled with timed artificial insemination would represent easy targets for malicious misrepresentation to the uninformed public. The point of this thread is not to argue that the management protocols are indefensible, rather that the discussion will have to ultimately be directed at a consuming public unfamiliar with any aspect of animal agriculture. The science-based discussions held with colleagues regarding choice or efficacy of protocol will not apply when the production practices are discussed in a public forum. The impacts that these programs have on animal productivity, operational sustainability and the production of a safe, abundant and affordable food supply will be the key communication points.

Summary

Extra-label use of drugs in reproductive management programs is not allowed under AMDUCA. Therefore, ELDU of drugs for reproductive purposes is not technically allowed in the CFR. Compounding of drugs from raw pharmaceutical agents, except for a few specifically listed antidotes, is a violation of the CFR. In addition, the use of illegally compounded products in food animals is ill-advised not only to the legal and liability issues, but also because of a potential consumer perception issue. A final point to consider is the consumer reaction when current bovine reproductive management programs are presented to the consuming public by anti-agriculture activists.

References

1. Animal Medicinal Drug Use Clarification Act of 1994, Pub. L. No. 103-396 (October 22, 1994).
2. Extralabel drug use in animals, 21 C.F.R. Sect. 530 (1996).
3. Compliance Policy Guide (CPG) section 608.400 entitled “Compounding of Drugs for Use in Animals”
(http://www.fda.gov/ora/compliance_ref/cpg/cpgvet/cpg608-400.html)