Comparative Pharmacokinetics of Two Oral Formulations of Dantrolene in the Horse

Heather K. DiMaio Knych, DVM, PhD; Rick M. Arthur, DVM; Anne Taylor, BS; Benjamin C. Moeller, PhD; and Scott D. Stanley, PhD

After oral administration, maximal plasma concentrations were comparable for both dantrolene capsules and the compounded paste formulation tested here. Based on pharmacokinetics, a 48- and 168-h withdrawal guideline for plasma and urine, respectively, should be adopted for oral administration. Authors’ addresses: K.L. Maddy Equine Analytical Chemistry Laboratory, School of Veterinary Medicine, University of California, Davis, California 95616 (Knych, Taylor, Moeller, Stanley); and School of Veterinary Medicine, University of California, Davis, California 95616 (Arthur); e-mail: hkknych@ucdavis.edu. © 2010 AAEP.

1. Introduction
Dantrolene is classified as a class 4 (Penalty Class C) foreign substance by the Association of Racing Commissioners International (ARCI), and whereas its use before racing is not permitted, it is commonly used therapeutically before strenuous training to prevent exertional rhabdomyolysis. The primary goal of this study was to describe plasma concentrations with respect to time after oral administration of two formulations as a means of recommending an appropriate withdrawal time before competition.

2. Materials and Methods
A randomized, balanced two-way crossover design was used wherein eight horses received a single oral dose of either capsules or paste. Blood samples were collected at time 0 and at various times up to 96 h after drug administration. Plasma samples were analyzed using liquid chromatography–mass spectrometry (LC-MS) and data were analyzed using non-compartmental and compartmental analysis.

3. Results and Discussion
Peak plasma concentrations were 28.9 ± 21.6 and 37.8 ± 12.8 ng/ml for capsules and paste, respectively, and occurred at 3.8 h for both formulations. Dantrolene and its major metabolite were both cleared from plasma by 48 h and urine by 168 h after administration. Based on pharmacokinetics, oral dantrolene should be used cautiously in regulated competition when urine samples are used as the primary means of drug control.