

## **Medication Guidelines: Whose Responsibility?**

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### **Introduction**

The Rules of most sporting jurisdictions — in particular those jurisdictions where the positive identification of any of a wide range of substances may be evidence of an offence against the Rules — place significant constraints on pre-race medication of horses. Even in those sports where certain levels of such substances may be permitted, there is significant restriction on their pre-event use.

These Rules in their ultimate application are designed to ensure as far as possible that events are true comparisons of horses' relative abilities, and this presumes that competitors are fit and healthy; that there is no possibility of performances being modified by the presence within the horse at the time of competition of any substance that may or may not have known performance-affecting capability. To achieve these ends many authorities have adopted policies that allow for no detectable residues of sometimes quite a wide range of substances.

Although jurisdictions may and do vary in the extent to which these principles are applied, the question still remains. Where can veterinarians and horsemen obtain information that will enable them to treat horses for legitimate complaints and ailments without running the risk of an inadvertent contravention of the relevant rules?

This matter was discussed at some length at the Fifth International Conference held in Toronto in 1983, when some details<sup>1</sup> of studies performed at Agriculture

Canada's Equine Drug Evaluation Centre were presented. Various views were put forth, but no firm recommendations were made.

It was noted, however, that the numbers of horses used were small, and dosage regimes were limited. Although testing methods employed were those in vogue in Canada at the time, the results were presented as guidelines only, and should not be construed as absolute for every horse to which one or other of the various drugs studied was administered. Further reports<sup>2,3</sup> from Agriculture Canada in 1985 and 1987 have complemented the 1981 report.

There has been a tendency among some racing authorities to distance themselves from the problems associated with the "mine field" of pre-race medication of horses, and the matter is being constantly confused by the availability of new therapeutic substances and, more importantly, continuing advances in technology that are leading to the detection (positive identification) of more substances for sometimes greatly extended periods after administration.

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### **Australian Situation**

The objective of this presentation is to recount Australian experiences in this matter, and to report on measures that have been introduced as a result of this experience. It is a problem that is common to all authorities, and it is hoped that from this Conference will come a statement of preferred policy to be adopted.

#### *Rules of Racing*

In common with many other countries Australian

racing authorities in 1964, in response to problems that had arisen with the application of long-existing Rules to the post-war pharmacological and technological revolutions, undertook an extensive review of the relevant Rules of Racing. Among the Rules introduced at the time was a Rule requiring trainers to notify the Stewards any treatment that horses had received in the seven days prior to racing.

#### "Notice of Treatment

117A. (a) Treatment to a horse for any condition by a Veterinary Surgeon, trainer, or any other person within seven days prior to a race in which it is to start shall be reported in writing by the trainer to the Stewards as soon as practicable after treatment and in any event not later than one (1) hour before the advertised starting time of the race in which the horse is engaged.

(b) 'Treatment for any condition' in Clause (a) includes treatment by mouth, by application or by any other means."

The purpose of this Rule was two-fold: to identify pre-race any horse that, because of some ailment, might not be fit to race (the horse reported could be inspected by the course veterinarian and its state of health assessed) and to ensure as far as possible that a positive test would not result from the reported treatment where a drug was involved in this treatment. If, in the opinion of the Stewards, there was a likelihood that such would happen, the treated horse was withdrawn, and the horse and its connections usually suffered no further disability.

#### Guidelines

Correct assessment of the significance of a treatment required knowledge of the limits of detectability of the therapeutic agents involved. At the time, the literature contained little information on this aspect, and under the sponsorship of the racing authorities studies were undertaken using small numbers of horses — some in training, but mostly horses at rest — to establish limits of detectability using routine analytical procedures then in vogue for a variety of dosing regimes for the more commonly-used therapeutic agents.

This information was considered necessary for the most

effective consideration of pre-race reports of treatment, and was supplied to all authorities and to course veterinarians who were members of the Association of Official Veterinarians (and Analysts). Most of these individuals were private practitioners who were engaged on a daily basis by race clubs.

Other private practitioners who did not hold racecourse appointments considered that they were professionally disadvantaged, and ultimately the information was supplied to the Australian Equine Veterinary Association for dissemination to equine practitioners in general. Whereas the lines of communication existed to keep veterinarians informed, it was not considered desirable, as the vast majority of substances were scheduled drugs, to advise trainers in general in spite of an unfortunate feature of Australian racing, namely, the apparent ready availability of certain scheduled substances. Many trainers have access to these drugs, and treat their horses without veterinary supervision.

Attempts were made to up-date the information as new "drugs" appeared and as new methods of detection were introduced into routine screening procedures. The fluid nature of these guidelines is demonstrated from the following consideration of amendments that were made from the time to time in recent years to recommended pre-race withholding periods shown in hours pre-race for certain substances:

Phenylbutazone	96 (1964) 144 (1973)
Isoxsuprine	96 (1981) 120 (1982)
Caffeine	72 (1966) 96 (1974) 144 (1975)
Clenbuterol	72 (1966) 120 (1984)
Cortico-steroids	72 (1966) 144 (1984)

In fact, it was with only a small number of substances that there has not been some extension of the recommended pre-race withholding periods since any information was first published in 1964.

In spite of disclaimers and repeated advice that the information was based on a small number of tests

involving only a small number of horses, there was a regrettable tendency, even among veterinarians and Stewards, to regard the information as absolute, not subject to change and pertaining to every circumstance of use — size of dose, number of doses, method of administration, age and sex of horse, and use of other substances at the same time. Certain manufacturers of horse medicines incorporated dosing guideline information on product labels and, where withholding periods were extended, found it impossible to recall stock for label amendment. Veterinarians were kept informed of changes to guidelines, but not the "do-it-yourself" trainers. This was an attempt to discourage the unsupervised use of scheduled substances, and to encourage the more appropriate involvement of the veterinary profession in the treatment of equine ailments.

### *Application of Rule 117A*

Some indication of the degree of compliance of trainers with the requirements of AR.117A was obtained from analytical findings on winning horses reported as treated and sampled post-race. In a six-month period in 1987 there were 14 reports of the use of certain vitamin/mineral preparations in winning horses, and 43 reports of the use of sulphonamides in such horses. At this stage sulphonamides were not regarded as prohibited substances for the purposes of the Rules.

As far as suspending agents contained in the vitamin/mineral preparations were concerned, the Analyst reported the presence of the substances in 13 or 14 horses reported as treated. Forty-three (43) horses were treated with sulphonamides, and one or other of these substances was demonstrated in 30 of the treated horses. Failure to demonstrate a substance in urine must be considered due to the time of dosing, the size and number of doses, or some other factor.

In the same period the Analyst demonstrated the unreported presence of one or other of these substances in 6 horses, indicating a possible offence against the Rule.

These observations suggested that the majority of trainers complied with the requirements of the Rule.

While the Rule has since 1964 allowed some 20 horses that could have returned a positive post-race test

(usually to an N.S.A.I.D., a cortico-steroid or theobromine), to be withdrawn, on 4 occasions treatment was reported, the horse permitted to run, and a positive test resulted. Incomplete details of treatment that involved treatment beyond 7 days, and not requiring to be reported in 2 cases, and increased sensitivity of testing procedures in the other 2 cases were responsible. There have been 6 cases of "positives" resulting from treatments beyond 7 days and in each case protracted over-dosing was responsible.

In investigations of 14 of some 85 "positives" obtained since 1964, it was established that horses had been treated, and this treatment not reported, so that the trainer chose to ignore the protection offered by the Rule, and was found guilty on two counts.

For a variety of reasons the Rule has not fully realized its potential to eliminate positive tests, and some of the problems associated with the promulgation of guidelines became evident.

### *Nature of Treatments Reported*

The presence of the Rule and the relatively high degree of compliance with its requirements gave some indication of the nature of treatments applied to horses racing in metropolitan Victoria.

Although perhaps not totally relevant to a discussion on guidelines for pre-race drug use, it was of particular interest to analysts and to the Stewards, and to the small number of regulatory veterinarians in Australia as it gave some indication of the extent of use of certain substances, and changing patterns of this use.

Reports of treatment received at race meetings conducted in metropolitan Melbourne in the six months' period from 1st August, 1985 are shown below. This provides an insight into "racehorse" medicine as practiced here.

Number of race meetings:	69
Number of starters:	7,297
Number of times reported:	
Vitamins, electrolytes, etc. —	
"routine" therapy:	1,755 (24% of starters)
Antibiotic/anti-bacterial therapy:	144 (2%)
N.S.A.I.D. therapy:	18 (0.25%)

Cortico-steroid therapy: 81 (1.1%)  
Miscellaneous therapy: 170 (2.3%)  
(Topical applications, patent medicines, etc.)  
N.B. Some horses received more than one form of therapy.

If the information provided in the reports was correct, and if most of the treatments were reported, it did seem that AR.117A was achieving one of its ends, i.e., ensuring that horses were presented fit and healthy for racing with no drug residues detectable in their systems. Some trainers were under the mistaken belief that no drug treatments can be given within 7 days prior to racing so that, if a horse required such treatment, then it did not become a declared runner. On three occasions in the period under review, declared horses were withdrawn by their trainers on race eve or race morning because some acute ailment had necessitated treatment that could have returned a positive. The scratching fees in these instances were waived on production of an appropriate veterinary certificate.

### *Other Considerations*

One of the benefits of the requirement of notification of treatment was that a significant amount of pharmaco-kinetic information could be obtained using racehorses in training. Pre-race blood testing of all horses reported treated with certain substances and post-race testing of winning horses reported treated has enabled much useful information to be assembled.

As far as a post-race urine testing is concerned, in the period 27/9/86 to 1/10/87 forty reports in winning horses of the use of single dose long-acting cortico-steroid at six days pre-race gave no positive findings post-race on routine screening. Similar results were obtained in 23 horses dosed with clenbuterol up to five days prior to racing. No accurate details of dosing were available. Phenylbutazone could not be detected on HPLC six days after dosing, usually with single doses, in 24 horses blood tested pre-race and in five of those horses that subsequently ran and were post-race urine tested, using TLC.

## **Discussion**

The reason for this rather lengthy consideration on this aspect of our Rules is that because of this Rule

medication guidelines were introduced initially, i.e. to enable Stewards and official veterinarians to assess accurately reports of treatment, and only incidentally to provide veterinarians with guidelines for pre-race medication.

While these requirements did seem to be indicated, in the light of our experience, they could not be totally met, and for the following reasons it was decided to repeal the Rule on 30.11.87:

- (i) The inability of guidelines to cover every circumstance of medication;
- (ii) the tendency to regard the guidelines as absolute;
- (iii) the mistaken impression that any medication was permitted more than 7 days prior to racing even if such medication resulted in a positive test;
- (iv) continuing advances in technology leading to increased limits of detectability;
- (v) the availability of new therapeutic agents that had not been studied;
- (vi) the difficulty of promptly promulgating amendments and additions to the guidelines; and
- (vii) the need to re-affirm the requirement of the Rules for the trainer to present a horse for racing free of certain substances.

The advantages of the Rule were acknowledged, but these were more than counter-balanced by the disadvantages.

The decision having been taken to delete the Rule, the need for the production of guidelines has disappeared, although analysts and regulatory veterinarians may still have the need for pharmaco-kinetic information to give reliable advice to Stewards.

This decision has been keenly felt by members of the veterinary profession in particular, but the Australian Equine Veterinary Association has conceded that it is inappropriate for a controlling body to be the source

of such information. The Australian Equine Veterinary Association has undertaken to produce an information document for the use of its members that will, it is expected, consist of a review of the available literature and hitherto unpublished experimental data accumulated as a result of excretion studies performed by the Australian racing chemistry laboratories.

The situation in other countries and the policies adopted there are worthy of consideration. The praiseworthy efforts of Agriculture Canada with its publications<sup>1,2,3</sup> listing the results of a limited number of administration studies, and making no comments except to note that the observations may not be repeated in every horse have already been noted.

In Australia perhaps we went too far in our application and interpretation of AR.117A. With the wisdom of hindsight, it is obvious that we tried to do too much, and did not fully comprehend the ramifications of our policy and legislation. There is a need in the general literature for more review articles of the types already published<sup>4,5</sup> but one questions whether the information contained therein might become shortly dated.

The efforts of the Royal College in keeping on file for its members an up-dated record of administration studies is to be commended, but it is notable that the literature often tends to be concerned with methodology for detection rather than pharmaco-kinetics of drugs. Some drugs have received close "attention", but none more than phenylbutazone.

The FEI policy with respect to phenylbutazone stimulated drug company-sponsored research<sup>6</sup> to establish dosage regimes that would not exceed the permitted levels, while in the United States an extensive series of Commission-supported studies undertaken on the pharmaco-kinetics of phenylbutazone<sup>7,8</sup> has established plasma concentrations following a wide range of dosing schedules. Recent studies on the bio-availability of phenylbutazone<sup>9,10</sup> have contributed to the wealth of knowledge with respect to this particular drug. One report<sup>11</sup>, mainly concerned with methodology, has reported urine and blood levels of phenylbutazone and oxyphenbutazone many orders of magnitude higher than those reported by other analysts using comparable dose rates in horses, and this report has the potential to further confuse the issue.

The involvement of drug companies in the establishment of guidelines for pre-race medication should be encouraged, and the position at law not only of the drug company but also the practising veterinary surgeon in the event of a positive test and possible financial loss needs to be clearly defined.

It seems that the only realistic policy that can be adopted is to establish a mechanism whereby further research on the pharmaco-kinetics of therapeutic agents is encouraged, and the results of such research made available to the profession, either by teaching institutes, drug companies or professional associations. It would seem inappropriate for the racing authority to be directly involved, and to be perceived to authorize publication.

Irrespective of what policy is adopted, any publication must reiterate the advice that it is impossible to provide guidelines that will apply to every circumstance of drug administration. Every adoption of common Rules and the implementation of common methods of testing could not provide a solution to this perplexing problem.

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