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The regulation of drugs and medicines in horse racing in the United States. The Association of Racing Commissioners International Uniform Classification of Foreign Substances Guidelines

C.R. SHORT
R.A. SAMS*
L.R. SOMA† &
T. TOBIN‡

*Department of Veterinary Physiology, Pharmacology and Toxicology, School of Veterinary Medicine, Louisiana State University, Baton Rouge, LA 70803; *Analytical Toxicology Laboratory, College of Veterinary Medicine, The Ohio State University, Columbus, OH 43201; †Department of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, Kennett Square, PA 19348; ‡Department of Veterinary Science, Gluck Equine Research Center, University of Kentucky, Lexington, KY 40506, USA*

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C. R. Short, Department of Veterinary Physiology, Pharmacology and Toxicology, School of Veterinary Medicine, Louisiana State University, Baton Rouge, LA 70803, USA.

INTRODUCTION

Horse racing is an ancient sport which almost certainly extends back to 1500 BC or further in the Middle East, Egypt and areas of modern day Russia (Evans *et al.*, 1977; Edwards, 1991). The first recorded ridden race was at the Greek Olympiad in 624 BC. The development of the Thoroughbred in 17th and 18th century England, along with the Standardbred in France and the United States early in the 19th century, formed the basis for modern racing. British flat and steeplechase racing was exported to the colonies; harness racing developed in the U.S. and Europe and is particularly popular in Scandinavia, Russia, the U.S., New Zealand, Australia and a few other countries.

If for no other reason than the competitiveness of mankind, one can be certain that chemical substances designed to improve prospects of winning have found their way to racehorses for decades, if not centuries. These 'treatments' generally take one of two forms: (1) the administration of medications as therapeutic agents to relieve musculoskeletal inflammation or some other health related problem; or (2) the intentional use of stimulants, depressants or other agents with the direct purpose of affecting performances of a horse. The latter is of particular concern in racing as it attempts to alter the natural ability of a horse and fitness to race by surreptitious means, by using chemicals that can stimulate or depress a variety of physiological systems. The effect may be subtle, such as a change in temperament, mood, aggressiveness or awareness, or it could be more readily apparent by obvious stimulation of the central nervous system. The purpose is not always to produce a winner by stimulation, but often to produce a winner with small doses of tranquillizer or sedative that calm an excited ('washy') horse. The ultimate purpose may also be to defraud the betting public by retarding the performance of a race favourite, a practice referred to as 'nobbling' in British racing circles (see Tobin, 1981). A particularly bothersome side effect is that such pharmacological manipulation may cause the horse to injure itself and its rider, as well as others in the race.

The English Jockey Club, founded *c.* 1752, formulated very simple rules regarding 'doping', such that 'any person who administers or allows to be administered or connives at the administration to a horse of a substance, other than a normal nutrient, which could alter its racing performance at the time of racing, shall be guilty of a breach of the rules and may be declared a disqualified person or otherwise penalized by the stewards of the Jockey Club in accordance with their powers'. This all encompassing rule, commonly referred to as the 'hay, oats and water' rule, has been the guiding principle for much of the racing world for the past century or more. As pointed out by Tobin (1981), however, this is honoured as much in the breach as in the observance in the U.S., as some states have developed medication rules which define prohibited substances as narcotics, local anaesthetics and tranquillizers which could stimulate or depress the circulatory, respiratory or central nervous systems of a horse, thereby affecting its performance. This leaves considerable license for the use of steroidal and non-steroidal anti-inflammatory agents, muscle relaxants, diuretics, antihis-

tamines and other substances used to maintain the running soundness of horses. The rules in other states have varied from 'hay, oats and water' to some middle ground acceptable to the participants and commissions.

A reconsideration of the definition of 'prohibited substance' in the U.S. has come about in part through advances in chemistry, both pharmaceutical and analytical, over the past 50 years. In the 1940's there were really very few drugs that could be detected and confirmed with certainty. Melting point analysis was a mainstay of identification. This was followed by microcrystalline analysis, an art form with greater application, but which was useful only in the hands of a few skilled professionals (Moss, 1992). The rediscovery of chromatography followed in the 1950's, and this led in two directions: (1) to the gas chromatograph and (2) the useful application of thin layer chromatography in the 1960's. These techniques allowed the detection of drugs (and their metabolites), such as amphetamines, administered in much smaller doses (tens of mg) than many of the commonly used medications, such as phenylbutazone, administered at a dose of 2 g or more. As pharmacology progressed to quantitative structure, i.e. activity analysis of isolated receptors in the 1970's, pharmacologists and pharmaceutical chemists began to design drugs with higher affinities, and greater specificity. The result has been enhanced potency with fewer side effects, and the potential to produce measurable effects in the single digit mg (total dose) range or lower. Many of these substances found their way to the racetrack in the 1980's, and the chase was on to detect substances such as the fentanyls, etorphine, and more recently detomidine, which produce effects at total doses in the sub-milligram range. The resourceful chemist has turned to a variety of immunoassays for initial screening specific agents, with confirmation by gas or liquid chromatography/mass spectrometry. This technology has helped to control the use of some very potent drugs which have no legitimate use on the racetrack. The paradox, however, is that if applied to many of the therapeutic agents used in equine medicine, it can greatly extend the length of time that they can be detected post-dose. Thus, an issue for the 1990's and beyond is whether this technology should be applied to the detection of all foreign substances which could appear in equine biological fluids. If so, should thresholds (analytical, or no-effect thresholds) be developed for certain substances, but not others? If this is an acceptable concept, one must then determine which substances should have threshold limits. The question can be rephrased to ask 'should an equal value of dis-merit be assigned to all substances regardless of their ability to affect the outcome of a race, irrespective of the fact that their very nature indicates a purposeful intent to alter the outcome of a race?'

Disciplinary action

When the presence of a drug or its metabolites is confirmed in a post-race urine or blood sample, the stewards and commissioners must make a judgment on the seriousness of the infraction of the rules and set an appropriate penalty. Disciplinary action is taken against the trainer, who is almost always considered the sole insurer of the horse's fitness to race. The penalty levied usually takes the form of a fine and/or license suspension for a specified period of time, or permanent revocation of license. The owner is also penalized in that the purse may be re-distributed. The chemists findings are considered *prima facia* evidence. If confirmed by a second referee laboratory, this evidence and the testimony of stewards, security agents, veterinarians, jockeys, stable lads, and the trainer usually constitutes the evidence in a case. The commissioners or stewards deciding the penalty must then act on the evidence, part of which is the nature of the drug itself.

The Association of Racing Commissioners International

In the U.S., racing and pari-mutuel betting are regulated at the state rather than national level. Thus, the 38 states considered to be 'horse racing states' because they regulate racing, each have their own Rules of Racing. Where Thoroughbred and harness racing are present in the same state, separate Rules of Racing may apply to each. The National Association of State Racing Commissioners (NASRC) was founded in 1934 in order to bring some uniformity in rules to racing in the U.S. In 1988, this organisation became the Association of Racing Commissioners International (ARCI). The ARCI does not serve as a regulatory body. Its members are (politically) appointed members of state commissions and its primary purpose is to make recommendations on uniform rules and policies for member states. It also serves as a national repository for rulings and racing industry statistics, and it publishes volumes on Racing Law. With the reorganization of 1988, the new ARCI took on the additional responsibility of establishing a monitoring system for testing laboratories. The Drug Testing and Quality Assurance Program (QAP) established a proficiency testing programme as well as a blind sample distribution programme in which member laboratories received unknown and unidentified samples from the racetracks. The intent of this programme was to set minimum standards of performance for member laboratories. The QAP was replaced by a similar operation entitled the Drug Testing Standards and Practices Program (DTSP) in 1995. The DTSP has placed emphasis on the development of new analytical procedures for foreign substances which are difficult to detect.

The ARCI Model Rules of Flat Racing

The ARCI has recently developed a set of guidelines which commissioners can use in whole or as templates for enacting legislation or developing or modifying their Rules of Racing. This set of recommendations, entitled the 'Model Rules of Flat Racing', contains 10 chapters which cover subjects ranging from licensing to pari-mutuel wagering (ARCI, Model Rules of Flat Racing, 1997). These Model Rules are updated as necessary. Veterinary Practices, Equine Health, and Medication are the subjects of Chapter 8. Among the topics covered in this chapter are the Uniform Classification Guidelines, penalty recommendations, medication restrictions, and the permitted use of phenylbutasone and furosemide. The latter two substances will be the subjects of further reviews. The development and implementa-

tion of the Uniform Classification Guidelines is the subject of the present review.

ARCI McKinsey Report Operations Implementation Task Force

With financial assistance from The Jockey Club, the ARCI underwrote a study of medication surveillance practices in horse racing in the U.S. by McKinsey and Co., Inc., a leading management consulting firm. A national strategic plan entitled 'Building a World-Class Drug Detection System' was presented at the ARCI annual convention held in Cincinnati in June, 1991. The McKinsey Report's general recommendation was that the racing industry should have consistency across all states in rules, penalties and testing capabilities. Among the several conclusions of the study was the finding that penalties for infractions of medication rules varied widely among, and even within, jurisdictions for positive findings for given drugs or their metabolites.

The Chairman of the ARCI at that time, Mr Joe Smreker, appointed an Operations Implementation Task Force to review the McKinsey Report and make specific recommendations for implementation of uniform policy. The development of a national penalty scheme received high priority, and two committees were created to develop recommendations. The Drug Penalty and Sample Selection Sub-Committee of the QAP created a penalty scheme and a model rule which described the actions of stewards in response to the finding of a prohibited foreign substance by the racing laboratory. The penalties and actions of the stewards, in turn, relied on a drug classification scheme, which was developed by the Drug Classification Subcommittee. This Task Force, drawing on the entire resources of the ARCI, but especially the QAP Committee, and with review and input from organizations such as the Horsemen's Benevolent and Protective Association, the American Association of Equine Practitioners, the American Horse Council, the Thoroughbred Racing Protective Bureau, and others, produced within a period of approximately one year the first national drug classification system, recommended penalties for different drug classes, a model rule on drug classification and penalties, and several other model rules (e.g. split samples, sample selection, and absolute insurer) which were eventually incorporated into the complete Model Rules of Flat Racing.

The ARCI Uniform Classification Guidelines for Foreign Substances

The first drug classification scheme in use in the U.S. was adopted by the Louisiana State Racing Commission as a guideline in 1988 (Short *et al.*, 1990). This was a five-tiered system of drug categories based on pharmacological capacity for altering the outcome of a race and consideration of appropriateness of use in the racing horse. Those drug substances which have no recognized use in modern equine medicine, which stimulate or depress the central nervous system, and which have a history of abuse (in either humans or horses) were placed in Category I, while those medications used routinely in equine medicine and which were also judged to have the least potential for affecting performance were placed in Category V. This classification scheme supported a Penalty Guideline, which had as its most severe penalty (for repeated Category I violations) the lifetime suspension of license and a $10,000 fine, while on the other hand a first offense for a Category V violation received a $250 fine. The purse was to be redistributed for all violations.

The QAP Drug Classification Subcommittee, (in 1995 renamed the Veterinary Pharmacology Subcommittee of the Veterinary Advisory Committee, DTSF) revised the Louisiana Categories and Recommended Disciplinary Action scheme into an expanded system of five Classes of foreign substances with a similar set of Penalty Guidelines. The Uniform Classification Guidelines for Foreign Substances were first published by ARCI in 1992.

Rationale for development of a classification scheme

1 Medication use is allowed during training in the U.S. The Model Rules of Flat Racing recommend only that no drug substance should be administered during the 24 h before a race. This rule has been adopted by most states, though a few have longer withholding rules (e.g. 36, 48 or 60 h) and at least two states allow the use of some agents (such as certain non-steroidal anti-inflammatory drugs) with no specified withholding period. The time required for many medications, or their metabolites, to reach concentrations below the limits of detectability of screening methods for urine may exceed the mandated withholding period. It is not unexpected therefore that traces of some medications, either parent drug or metabolite, may be detected in urine samples taken immediately post-race.

The sensitivity of the method of detection used in screening samples will largely determine whether positive findings occur under the circumstances. As there are no uniform recommendations on testing methodologies in the U.S. at present, commissioners are, on occasion, presented with positive findings for low therapeutic concentrations of agents such as non-steroidal anti-inflammatory drugs, muscle relaxants and antihistamines. This evidence must be placed in perspective with regard to findings of performance altering drugs clearly administered to alter the outcome of a race, such as morphine or the amphetamines. Herein lies rationale for basing disciplinary action on a drug classification scheme that is based on both (1) the pharmacological potential for altering performance and (2) the acceptability of use of drugs as therapeutic agents in modern equine medicine.

2 Racing Commissioners in the U.S. are largely political appointees. While their expertise may lie in business, law, medicine or other professions, few have expertise in pharmacology applicable to horse racing. In addition, the average tenure of commissioners is approximately 6 years (Association of Racing Commissioners International, 1997), as it often coincides with gubernatorial elections. A drug classification scheme, along with the testimony of a qualified veterinary pharmacologist (where available), assists the commissioner in understanding the significance of the findings presented by the chemist. In addition it transcends the turnover of personnel and provides a measure of continuity to the operation of the commission.

3 The causes of infractions of the medication rules often reflect carelessness or inattention to dose or dosage form, perhaps

coupled with a degree of biological variability in drug disposition, reduced drug metabolism or elimination caused by chronic hepatic or renal disease, co-administration of other substances, misunderstanding of instructions, or other misadventures. Much more rarely, positive findings reflect the administration of substances which imply a high degree of intent to alter the outcome of a race. There are no acceptable rationales for finding etorphine, the fentanyls, amphetamines or mood-altering drugs approved only for human use, in the urine of racing horses. More understandable, however, is the occasional appearance of a low concentration of an antihistamine or a non-steroidal anti-inflammatory agent. Thus disciplinary action can, and should, be scaled according to the perceived gravity of the offense. A drug classification scheme is an obvious requirement for establishing a uniform penalty code.

Criteria for classification

1 The Rules of Racing

The ARCI Model Rules of Flat Racing do not specify that all foreign substances are prohibited. The only recommendations regarding which substances should or should not be allowed are (1) that phenylbutazone may be permitted up to 5 μg/mL in blood and (2) furosemide may be allowed for the control of exercise induced pulmonary haemorrhage (EIPH), with a specified dosing regimen.

The Uniform Classification Guidelines for Foreign Substances thus contain only substances which could have an effect, minimal as it may be in some cases, on the performance of a horse during a race. Substances for which there is no evidence of ability to affect performance are of no interest to regulatory matters and are not classified. Examples of substances that are specifically omitted include antibiotics, sulfonamides and other antimicrobials, anthelmintics and vitamins.

2 Pharmacology

The following considerations apply to the ability of a substance to alter performance:

(a) Is the substance clearly a stimulant or depressant of the nervous, cardiovascular or respiratory systems? Is it a narcotic or local anaesthetic? Is it analgesic? Does it relieve pain directly or as a secondary effect, i.e. *via* the reduction of inflammation?

(b) What is the dose necessary to produce an effect? At one extreme, a dose of 25 μg/animal (or less) of etorphine will act as a central nervous system stimulant. At the other extreme, there are therapeutic agents dosed in multiple-gram quantities. The question is one of potency for relative effect, and in a sense, intent. All of the substances considered to be the most offensive are very potent CNS stimulants, administered at very low doses. Most (but admittedly not all) of the substances considered to be least offensive are administered at higher doses, and as a general rule, are more easily detected. The knowledgeable trainer or veterinarian is aware of this and cannot be expected to willingly contravene the medication rules with therapeutic substances. The willing use of drugs to enhance or retard performance usually involves the use of substances administered in minute doses, or the administration of substances which are otherwise difficult to detect, or differentiate from endogenous substances.

(c) The maximal possible effect will vary greatly. High doses of one drug (e.g. dimethyl sulfoxide) may have considerably less effect, or essentially no effect, compared to a very small dose of another agent (e.g. fentanyl).

(d) A very localised action may be considerably different than a generalised effect. For example, local anaesthetics that are not available for injection are placed in a lower class than those that are (and could more easily be employed as nerve blocking agents). Likewise, H_2 receptor histamine antagonists used to reduce the incidence of gastric ulceration are placed in a lower category than H_1 receptor blockers which have generalized effects (and especially those which have somnolescent activity).

3 Patterns of use and acceptability of drugs as therapeutic agents

In contrast to the situation in many other countries, horses in the United States usually are stabled on the racecourse for the duration of a meet. Also, in contrast to European racing where a racing meet usually lasts 1 to 3 days, race meets in the United States normally last several weeks, or even months. There are thus recommendations in the Model Rules of Flat Racing that limit the possession and administration of drugs on the grounds of the racecourse.

Whether horses are stabled on or off the racecourse, trainers licensed by the Commission are considered, historically and by recommendation of the Model Rules, to be the sole insurer of the condition of the horse. Thus, if a drug finding is reported in a post-race blood or urine sample, the trainer is the person who faces disciplinary action. Others, such as the veterinarian, assistant trainer, and stable personnel may be brought into discussions at Steward inquiries and subsequently at Commission hearings, and they may also be found culpable.

The following considerations regarding the appropriateness of use by the trainer, or veterinarian, on or off the racecourse, apply to the classification of medications or other drug substances.

(a) Is the drug one which the trainer should have in his possession? If the trainer possesses a controlled substance (i.e. Drug Enforcement Agency (DEA) Schedule II drug) without a veterinarian's prescription or order, its finding on the trainer's person or in his stable would be a violation of Federal law. Though not a specific criterion, DEA Schedule II substances are usually found in Classes 1 and 2 of the ARCI Uniform Classification list.

(b) Is the drug a therapeutic agent that one would expect to be used in the horse? How far does one have to stretch the imagination to accept a legitimate use for the drug in the racehorse? Is it, on the other hand, approved, recommended, or commonly used as a therapeutic medication?

(c) Is there an historical or otherwise recognized incidence of uninformed or unintentional misadventure with a medicinal agent? For example, substances such as eugenol have appeared in post-race urine samples from the application of a brace applied topically after the race but before the sample was collected at the test barn. Caffeine containing nutritive preparations have also

caused positive findings. In both of these examples it was not clear from labelling that these agents were present. Likewise, the previously high incidence of procaine findings in post-race urine is almost certainly the result of procaine penicillin G administration rather than the use of procaine as a nerve blocking agent (Tobin *et al.*, 1977; Tobin, 1981; Stevenson *et al.*, 1992).

(d) Does the dosage form affect the drug's potential for misuse? For example, there are several local anaesthetics that are available only in formulations for topical administration. Their detection likely does not imply the same level of intent as lidocaine or other injectables that could be used as nerve blocking agents.

Prohibited substances

Class One: Stimulant and depressant drugs which have the highest potential to affect performance and which have no generally accepted medical use in the racing horse. Examples: Opiates, amphetamines, pemoline.

These are the drugs which are of greatest concern from the standpoint of pharmacological effect and intent to alter the outcome of a race. This class of drugs is the one that has the highest penalties and the longest restrictions from practice on the race track. They include opiates, opium derivatives, synthetic opioids and psychoactive drugs, amphetamines and amphetamine-like drugs, and related drugs such as apomorphine, nikethamide, masindol, pemoline and pentylenetetrazoles. Some of them are DEA Schedule II drugs-in particular, the opiates and their derivatives and the amphetamines. Some are not controlled substances, but they are nevertheless potent stimulants that we know have been used in racing, but which have no legitimate use in the racing horse. There are actually very few substances in this class. A complete list of agents in Class One can be found in Table 1.

Table 1. Complete list of agents in Class One

Alfentanil	Methadone
Amphetamine	Methamphetamine
Anileridine	Methaqualone
Apomorphine	Methylphenidate
Carfentanil	Metopon (methyldihydromorphinone)
Cocaine	Morphine
Dextromoramide	Nikethamide
Diamorphine	Oxycodone
Endorphins	Oxymorphone
Enkephalins	Pemoline
Ethylmorphine	Pentylenetetrazol
Etorphine	Phenazocine
Fentanyl	Phencyclidine (PCP)
Hydromorphone	Phendimetrazine
Hydroxyamphetamine	Phenmetrazine
Levorphanol	Picrotoxin
Masindol	Strychnine
Meperidine	Sufentanil
Mephentermine	
Metaraminol	

Class Two: Drugs which have a high potential to affect performance, but less of a potential than those in Class One. These drugs are not generally accepted as therapeutic agents in racing horses, except that therapeutic agents that have a high potential for abuse are included. Class Two contains the following classes of agents:

(a) Opiate partial agonists, or agonist-antagonists.

(b) Non-opiate psychotropic drugs. These drugs may have stimulant, depressant, analgesic or neuroleptic effects.

(c) Miscellaneous drugs which might have a stimulant effect on the central nervous system (CNS).

(d) Drugs with prominent CNS depressant action, including:

1 Barbiturates, anaesthetics and sedatives;

2 Volatile anaesthetics;

3 Phenothiazine tranquillizers and other phenothiazines with prominent sedative effects (except promazine and acepromazine);

4 Miscellaneous anaesthetics;

5 Benzodiazepines and other anxiolytic, sedative and hypnotic drugs.

(e) Antidepressant and antipsychotic drugs, with or without prominent CNS stimulatory or depressant effects, including:

(f) Muscle blocking drugs – those that have a direct neuromuscular blocking action;

(g) Local anaesthetics which have a reasonable potential for use as nerve blocking agents (except procaine).

These are drugs that are of concern because they may affect the outcome of a race. Most are not drugs which we would expect to find in a horse. Examples would include the psychotropic drugs used in humans, such as mood-elevating drugs and agents used to reduce anxiety. Others found here could be used as therapeutic agents, but would not be expected to be found in a racing horse, and could act as cardiovascular and respiratory system stimulants or depressants. All of the major tranquillizers are found in this class except for acepromazine and promazine. The latter two are found in Class Three because of their common use in the control of fractious animals and because of their use in minor surgical repairs. Injectable local anaesthetics are included in this class because of their high potential for abuse as nerve blocking agents.

Class Three: Drugs which may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class Two. Class Three contains the following classes of agents:

(a) Drugs affecting the autonomic nervous system which do not have prominent CNS effects, but which do have prominent cardiovascular or respiratory system effects. Bronchodilators are included in this class.

(b) Local anaesthetics which have minimal potential for use as nerve-blocking drugs, or have a high potential for detection in urine resulting from a method of use not related to the anaesthetic effect of the drug (procaine).

(c) Miscellaneous drugs with mild sedative action, such as the sleep inducing antihistamines.

(d) Primary vasodilating/hypotensive agents.

(e) Potent diuretics affecting renal function and body fluid composition.

In Class Three, one finds drugs which may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class Two. The bronchodilators which are used in training, sometimes to overcome bronchiolitis, which is very common among horses at most of the tracks in the United States, are in this class. Procaine was not listed with the other local anaesthetics in Class Two because of the frequency of misadventures, and this applies again to use patterns. Positive findings for procaine result primarily from procaine penicillin G administration, as it can be detected for at least 2 weeks after the administration of this antibiotic. The antihistamines with sedative properties are also in Class Three. Some of these agents are very potent sedatives, and are actually marketed as the active ingredients in sleep medications.

Class Four: Therapeutic medications which would be expected to have less potential to affect performance than those in Class Three. Class Four contains the following classes of agents:

(a) Non-opiate drugs which have a mild central analgesic effect.

(b) Drugs affecting the autonomic nervous system which do not have prominent CNS, cardiovascular, or respiratory effects, including:

1 Drugs used solely as topical vasoconstrictors or decongestants;

2 Drugs used as gastrointestinal antispasmodics;

3 Drugs used to void the urinary bladder;

4 Drugs with a major effect on CNS vasculature or smooth muscle of visceral organs.

(c) Antihistamines which do not have a significant CNS depressant effect, and include:

1 H_1 receptor blocking agents;

2 Other mechanisms.

(d) Mineralocorticoid drugs.

(e) Skeletal muscle relaxants.

(f) Anti-inflammatory drugs, which reduce pain as a consequence of their anti-inflammatory action, and include:

1 Non-Steroidal Anti-Inflammatory Drugs (NSAID's) (aspirin-like drugs);

2 Corticosteroids (glucocorticoids);

3 Miscellaneous anti-inflammatory agents.

(g) Anabolic and/or androgenic steroids and other drugs.

(h) Less potent diuretics.

(i) Cardiac glycosides and antiarrhythmics, including

1 Cardiac glycosides;

2 Antiarrhythmic agents (exclusive of lidocaine, bretylium, and propranolol);

3 Miscellaneous cardiotonic drugs.

(j) Topical Anaesthetics–agents not available in injectable formulations.

(k) Antidiarrhoeal agents; and

(l) Miscellaneous drugs including:

1 Expectorants with little or no other pharmacological action;

2 Stomachics; and

3 Mucolytic agents.

Many of the agents in Class Four are commonly used as therapeutics agents in horses during training.

Class Five: Drugs in this category are therapeutic medications and certain miscellaneous agents which could be expected to be of only minor interest.

Included specifically in this category are agents which have very localized action only, such as the anti-ulcer drugs, and certain antiallergic drugs. The anticoagulant drugs are also included.

Permitted medications: This classification scheme does not include phenylbutazone, a medication permitted up to a blood concentration of 5 μg/mL in the ARCI Model Rule Guidelines. The ARCI DTSP Committee has adopted penalty recommendations presented in Appendix A. The ARCI Model Rules of Racing also permit the use of furosemide for the prevention of exercise-induced pulmonary haemorrhage (EIPH). The total dose to be given (intravenously (i.v.)) should not exceed 250 mg/animal, nor be less than 150 mg, and it must be administered no sooner than 4 h prior to post-time. At the present time, the ARCI does not have a recommendation on monitoring furosemide, although several studies have been conducted with the aim of setting blood concentration limits. Several states have furosemide monitoring programmes in place, and have set upper limits for furosemide which are used in combination with lower limits of urine specific gravity in samples recovered post-race. As there is no accepted concentration limit, there is also no ARCI recommendation for a penalty scheme at present. The many issues concerning the use of furosemide are the topic of a subsequent review in this series.

Non-classified drugs: The classification system omits drugs which are considered to be of no interest to equine regulatory matters. For example, the Uniform Classification Guidelines specifically omit

(a) antibiotics

(b) sulfonamides

(c) antihelmintics

(d) vitamins

Finally, it should be noted that there are instances where there is a rather fine distinction between drugs in one Class and those in the next. This is a reflection of a nearly continuous spectrum of effects from the most innocuous drug on the list to the drug that is most offensive.

There are currently more than 700 substances listed in these Guidelines. The Veterinary Pharmacology Committee continues to review this list and to make recommendations for classification of new drugs as they appear. The current RCI penalty guidelines based on the Classification Guidelines are presented in Appendix A.

Implementation

There are no recent surveys of state statutes which can be used to assess the degree to which the recommendations in Chapter 8 of the Model Rules of Flat Racing, and the Uniform Classification of Foreign Substance Guidelines in particular, have been adopted. There is little doubt, however, that the classification system has been widely acknowledged and accepted by horse-

men, trainers, veterinarians and commissions. It is also used by analysts to establish laboratory priorities. Of course, as with any set of recommendations made to independent states or jurisdictions, modifications have been made or sections of the Model Rules have been revised to suit local needs and opinions. For example, California has developed a system that is largely based on the ARCI Guidelines but contains seven classes of drugs. Kentucky allows the use of several NSAIDs in addition to phenylbutasone. Some states allow more or less than 5 μg/mL of phenylbutasone, or more than 250 mg furosemide and in at least one case, less than 4 h pre-post administration. With regard to the latter two substances, many states have had phenylbutasone and furosemide rules similar or identical to the present recommendations for at least a decade because they conformed to recommendations of the NASRC in the early 1980's. In fact, these recommendations were largely a carry-over of previous guidelines, and were not a part of the recommendations developed by the Drug Classification Committee.

Comparison to regulations in other countries

Canada

In Canada, pari-mutuel wagering falls under the jurisdiction of Agriculture Canada, which implements the Pari-Mutuel Betting Supervision Regulations as part of their mandate. Agriculture Canada maintains a schedule of prohibited substances which would be expected to alter the performance of a horse. Approximately 130 of these substances are registered in Canada for use in veterinary medicine. In addition, all drugs not approved for use in veterinary medicine, all drugs within 240 days of receiving a Canadian Drug Identification Number, all drugs which could interfere with analysis of drugs on the list, and all drugs not approved for use in Canada, are prohibited.

Agriculture Canada, through the Drug Control Service of the Canadian Pari-Mutuel Agency, also conducts trials to determine the approximate length of time that certain drugs on the list can be detected in the blood and urine of horses. This research is conducted on Standardbred mares at the Agriculture Canada Equine Drug Evaluation Centre, and is presented in a booklet, in English and French, entitled 'Schedule of Drugs'. The data is presented as a computer generated graph of concentration vs. time after administration until the concentration reaches the detection limit for the method employed. This provides a reference for use by trainers and veterinarians on 75 scheduled drugs as of 1994, the publication date of the last issue.

The Canadian list includes two drugs for which there is a quantitation limit below which the drug can be detected but will not be reported as a positive:

(a) Procaine. Procaine can be detected in urine for more than 2 weeks, under some situations, following the administration of procaine penicillin G. The Canadian regulations provide that this antibiotic salt can be administered under a set of conditions that include: (1) the last administration must be at least 48 h before the scheduled post-time; (2) provincial officials and sample collection personnel are notified; (3) that a blood sample is collected; and (4) that a formal statement is made regarding the administration. Having satisfied these conditions, the sample will not be declared positive unless the concentration of procaine exceeds 0.025 μg/mL of blood.

(b) Salicylic acid. This substance occurs in some grasses and hays and therefore can appear at low concentrations in the blood or urine as a dietary contaminant. In the early 1980's, Agriculture Canada and its official racing laboratories conducted studies which resulted in an accepted concentration limit for salicylic acid of 6.5 μg/mL in blood and 750 μg/mL in urine. These were subsequently verified independently by the Horseracing Forensic Laboratory in Newmarket, UK, and accepted as international thresholds for salicylic acid.

The list of agents published in the 'Schedule of Drugs' is not divided into classes. Thus there is no official, or recommended, assignment of penalties. At least three of the Provinces, however, are known to refer to the ARCI Uniform Classification Guidelines for assistance in assessing penalties.

International Conference of Racing Authorities

The International Conference of Racing Authorities is an organization based in Paris which has promulgated recommendations that apply to many aspects of breeding, racing, international movement and disease control in horses. Four years ago, the Conference formally established a federation – the International Federation of Horseracing Authorities. The Federation holds a technical meeting annually, now referred to as the International Conference of Racing Authorities. The Conference has developed an International Agreement on Breeding and Racing to which most countries ascribe, in whole or in part. North American jurisdictions ascribe to some articles of the Agreement, though not to Article 6. Article 6 of this Agreement lists recommendations on doping control which are referable primarily to prohibition of drugs or medications which affect specific physiological systems of the horse. While there is no list of agents *per se*, the following are listed as prohibited substances:

(a) Substances acting on the nervous system
(b) Substances acting on the cardiovascular system
(c) Substances acting on the respiratory system
(d) Substances acting on the digestive system
(e) Substances acting on the urinary system
(f) Substances acting on the reproductive system
(g) Substances acting on the musculoskeletal system
(h) Substances acting on the blood system
(i) Substances acting on the immune system other than those in licensed vaccines
(j) Substances acting on the endocrine system: endocrine secretions and their synthetic counterparts.
(k) Antipyretics, analgesics and anti-inflammatory substances
(l) Cytotoxic substances

Antiparasitic and anti-infective drugs have recently been removed from the prohibited category, except in the case where an agent might be shown to affect one of the aforementioned systems. Several jurisdictions, such as Britain and Hong Kong, have deleted (k) and (l) from their rules also, as they are covered

in the systems listed in (a) through (j) The Agreement makes no provision for a classification scheme or a penalty system, which is not surprising considering the diversity of cultures and the independent nature of the many nations which are signatories to this Agreement. There are also no recommendations for specific pre-post periods during which foreign substances should not be administered, nor are any substances listed as permitted drugs. There is, however, a recommendation for threshold concentrations of certain substances which occur as endogenous (physiological) agents or as substances of nutritional origin. These include available carbon dioxide, hydrocortisone, dimethyl sulfoxide, nandrolone, salicylic acid, testosterone and total arsenic. As noted previously, this subject will receive more attention in a further review on thresholds.

For purposes of this review, representatives of the Association of Official Racing Chemists (AORC) or the International Group of Specialist Racing Veterinarians (IGSRV) representing 12 countries worldwide, were surveyed regarding the Rules of Racing under which they work. These countries or national jurisdictions included Australia, Brazil (Brasileiro), Chile, Dubai (UAE), France, Germany, Great Britain, Hong Kong, Jamaica, South Africa (includes Zimbabwe) and New Zealand. The following summary provides some comparison between the ARCI Model Rules of Flat Racing and those employed elsewhere.

1 The ARCI Uniform Classification of Foreign Substance Guidelines is referred to officially in only one of these national jurisdictions (Jamaica).

2 Nine of the 12 countries surveyed define a Prohibited Substance as one that affects specific physiological systems, as listed in the International Agreement on Breeding and Racing. However, as few as six (New Zealand) or seven (Australia) systems are mentioned in some racing statutes.

3 Three jurisdictions have developed some form of classification system. In Brazil, for example, the systems affected have been divided into three groups, with a fourth group containing such substances as drug vehicles, with a penalty (suspension periods and fines) assigned to each group.

4 Seven of these jurisdictions accept the International Agreement on Breeding and Racing recommendations for thresholds. An additional two accept thresholds for only one or two of the substances on the list. Unofficially, laboratories have set thresholds for several other substances that may occur as endogenous agents or be of nutritional origin.

5 In addition to Jamaica, only one other of these 12 jurisdictions sanctions 'permitted' drugs (Chile; phenylbutazone and furosemide).

6 The requirement for a specific pre-race period when no drugs or medications may be administered ranged from No Recommendation, to the time of registration for the race (Chile), to 48 h (South Africa), to 7 days, or for specific drugs, longer (Hong Kong), to 9 days (Korea).

7 Recommendations on penalty assessment are notably absent from the Rules in most of the jurisdictions surveyed. Penalties are, in general, decided after due consideration of the facts pertinent in the case. For example, France Galop rules specify a range of maximum fines. The rules for Chile specify suspension terms for first, second or third occurrences. As described above, penalties are assigned to four groups of drugs in Brazil.

Some of the jurisdictions surveyed are considering the implementation of a classification system. Article 6 of the International Agreement on Breeding and Racing will soon undergo revision, and may include provisions for classification systems in its new form.

SUMMARY

The primary reason for developing the ARCI Uniform Classification of Foreign Substances was to give stewards and other racing regulators guidelines to assist them in understanding the relative performance effects and general offensiveness to the Rules of Racing of various drugs and medications. As such, these guidelines have been very useful in the world of racing regulation – officially or unofficially – because this classification system, for the first time, places a relative number on the inappropriateness of any one of more than 750 agents appearing in forensic samples taken from racing horses.

The guidelines set up by this system established the first framework for dialogue among veterinary pharmacologists reviewing these drugs. Prior to development of the guidelines, pharmacologists had their own opinions about these agents and their effects on performance. The guidelines, however, established a framework for discussion, and there has been surprising unanimity about the classification of each of these agents.

Not only does this classification system provide a useful basis for dialogue among experts, it is also useful for regulators, horsemen and other laymen, most of whom have little training or experience with drugs and their effects on horses. The system is easily understandable and communicates the relative possibility of any classified substance to affect the performance of a horse. Consequently, the system has made it possible for laymen to understand the degree of impropriety of all drugs and medicines with which they may have contact.

Grouping a large number of drugs into specific classes has greatly facilitated discussion about regulations and penalties, and the classification system is related to proposed penalty guidelines which were developed in parallel. With regard to penalties for Class 1 agents, it is easy to assign and defend substantial penalties after examining the guideline statement describing the possible performance effects of this group of agents as well as the fact that they have no well recognized therapeutic role. Similarly, the relatively modest effects of class 4 and 5 agents, combined with the fact that these groups encompass a large number of well recognized therapeutic agents, helps in understanding the possible presence of trace levels of these agents in post-race samples.

In summary, the ARCI Uniform Classification of Foreign Substances Guidelines condenses data on drugs and medications and places them into a simple five class system. This system has made it possible to confidently discuss the regulatory implications of the identification of any one of the ≈ 750 classified substances potentially found in forensic samples from a

performance horse. As such it facilitates both the development and implementation of more understandable and equitable regulatory processes.

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APPENDIX A

Recommended Penalties and Model Rule

Penalty Recommendations (in the absence of mitigating circumstances):

Class 1 1–5 years suspension and at least $5,000 fine and loss of purse

Class 2 6 month–1 year suspension and $1,500–$2,500 fine and loss of purse

Class 3 60 days–6 months suspension and up to $1,500 fine and loss of the purse

Class 4 15–60 days suspension and up to $1,000 fine and loss of the purse

Class 5 0–15 days suspension with possible fine and/or loss of purse

Model Rule on Drug Classification and Penalties:

'Upon finding of a violation of these medication and prohibited substance rules, the Stewards shall consider the classification level of the violation as currently established by the Uniform Classification Guidelines of Foreign Substances as promulgated by the Association of Racing Commissioners International and impose penalties and disciplinary measures consistent with the recommendations contained therein. Provided, however, that in the event a majority of the Stewards determine that mitigating circumstances require imposition of a lesser penalty, they may impose the lesser penalty. In the event a majority of the Stewards wish to impose a greater penalty or a penalty in excess of the authority granted them, then, and in such event, they may impose the maximum penalty authorized and refer the matter to the Commission with specific recommendations for further action.'

Phenylbutazone

ARCI DTSP Committee recommendations for over-limit phenylbutazone concentrations occurring within a 12-month period:

First violation:

Concentrations above 5 μg/mL, but below 10 μg/mL in plasma or serum – a minimum fine of $250.

Concentrations above 10 μg/mL – a fine of up to $500.

Second violation:

Concentrations above 5 μg/mL but below 10 μg/mL in plasma or serum – a minimum fine of $500.

Concentrations above 10 μg/mL – a fine of up to $1,000.

Third or subsequent violations:

A fine of up to $1,000, suspension of up to 30 days, and possible loss of purse. In lieu of redistributing the purse, restriction of the trainer's future use of phenylbutazone for up to one (1) year.