PAST, PRESENT AND FUTURE OF THRESHOLDS

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ABSTRACT

The concept of threshold values in equine drug testing was introduced by the British Jockey Club in the mid-1980s to address the problem of the dietary source of salicylic acid. At the time, this concept was extremely controversial and it was only through extensive discussion on both a national and international basis that threshold values were introduced into the Rules of Racing. Article 6 of the International Agreement on Breeding and Racing allowed the introduction in the late 1980s of threshold values for arsenic, nandrolone, salicylic acid and theobromine. Article 6 states that threshold values may only be introduced for endogenous substances and substances of dietary origin. Subsequently, threshold values have been introduced for dimethyl sulphoxide, hydrocortisone and total CO_2.

Research is in progress to establish a threshold value for the endogenous hormone testosterone and also to investigate alternative approaches, other than the absolute threshold, to address the problem of administration of hydrocortisone or adrenocorticotropic hormone.

The concept of threshold values for therapeutic substances was introduced in the early 1990s and is now a reality. The California Horse Racing Board has established authorised acceptable levels for 8 therapeutic substances and the Canadian Authorities have introduced a threshold value for procaine. Approaches to addressing the issue of detecting trace levels of therapeutic substances were discussed in depth at a meeting organised in Kentucky in 1994 by Professor Tom Tobin[1].

Extending the threshold value concept to therapeutic substances increases the commitment to quantitative analysis for laboratories, with the need for quantification at low levels. Where it is mandatory for confirmatory analysis to be carried out in a nominated laboratory other than the primary laboratory, inter-laboratory variation may become an issue.

In the future, interesting challenges may evolve with regard to substances of dietary origin and protein hormones and related products from the bio-technology industry are also issues to be addressed. Thus, there is no doubt that the threshold value concept will continue to present challenges to the analyst and the industry.

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[1] *Testing for Therapeutic Medications, Environmental and Dietary Substances in Racing Horses* (1994) Proceedings of a Workshop held at the Maxwell H Gluck Research Center, University of Kentucky. Editors: T. Tobin, G. P. Mundy, S. P. Stanley, R. A. Sams and D. Crone.

RESPONSE TO A SURVEY AMONG INTERNATIONAL RACING AUTHORITIES ON THERAPEUTIC MEDICATIONS, ENVIRONMENTAL AND DIETARY SUBSTANCES IN RACEHORSES

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ABSTRACT

This report addresses the way in which countries are dealing with therapeutic substances following the Lexington workshop 'Testing for Therapeutic Medications, Environmental and Dietary Substances in Racing Horses' held in August 1994. A survey was conducted by The Jockey Club of London, The Hong Kong Jockey Club, The Kentucky Racing Commission and The Maxwell H. Gluck Equine Research Center.

The survey was distributed to 55 racing authority analysts worldwide and 21 responded, all of whom were from primary laboratories for flat or jump racing. Four replies were received from Europe, 6 from North America, 2 from South America and 9 from Asia.

Detailed analysis showed that 76% had implemented, or intended to implement, the amended international list of prohibited substances. Fifty-five percent had published or planned to publish thresholds for non-endogenous, non-dietary substances. Twenty-nine percent had or planned for defined but unpublished thresholds for such substances. Thirty percent had undefined and unpublished discretionary thresholds. Fifty percent had deliberately rejected or planned to reject unnecessarily sensitive analytical methods for specific substances. Ninety percent did not have a professional review step that could determine whether trace findings were significant. Sixty-seven percent invariably disqualified a horse in breach of the medication rules. Thirty-five percent had or planned to offer elective testing. Fifty-five percent had or intended to provide detection/withdrawal times. Forty-two percent gave forewarning of new tests. Twenty-seven percent had or planned to introduce a notification-of-treatment regulation. Finally, in none of the surveyed jurisdictions could regulatory veterinarians authorise race day treatment for any condition.

CHANGES IN NORTH AMERICA

In the United States, the first outcome of the workshop was in November 1994, when Louisiana outlined its programme of adjusted-sensitivity testing and graduated penalties at a meeting of the Association of Racing Commissioners International - Quality Assurance Program (ARCI-QAP). In December 1994, a recommendation for adjusted-sensitivity testing[1] based on this model was adopted by the American Association of Equine Practitioners. In February 1995, the Kentucky Racing Commission passed a resolution noting that its policies were in agreement with the AAEP recommendation. In May 1995, the full board of the ARCI addressed the issue of trace findings of therapeutic substances having no pharmacological effect on the performance of the animal in a race; and recommended policies whereby all chemical findings in official test samples undergo a veterinary review process, by the commission veterinarian or appropriate veterinary consultant, prior to initiating any regulatory action.

Shortly before the May ARCI meeting, the California Horse Racing Board moved to introduce urinary thresholds for acepromazine (25 ng/ml), mepivacaine (10 ng/ml), promazine (25 ng/ml), albuterol (1 ng/ml), atropine (10 ng/ml),

[1] *Louisiana does not use ELISA tests for ARCI Class 4 or 5 agents and limits the volume of urine used for confirmatory procedures on these agents to 5 ml.*

benzocaine (50 ng/ml), procaine (10 ng/ml) and salicylates (750 µg/ml), all of which are now incorporated into the California rule. Additionally, the Maxwell H. Gluck Equine Research Center of the University of Kentucky offered the first short course in the area of equine medication control, entitled 'The Commission Veterinarian/Equine Medical Director: A Short Course' in Lexington in November 1995.

INTERNATIONAL CHANGES

Significant international changes also followed the workshop. These were aimed at reducing the problem of identification of inconsequential 'positives' for therapeutic substances. Anti-infectious substances were deleted as a category from Article 6 of the International Agreement on Breeding and Racing, following an earlier decision to remove anti-parasitic substances.

THE HONG KONG/KENTUCKY SURVEY

In January 1996, a survey was conducted by The Hong Kong Jockey Club and The Maxwell H. Gluck Equine Research Center to monitor specific changes resulting from the Lexington workshop. Copies of the survey were distributed worldwide to 55 racing authority analysts. The objective of the survey was to 'identify the racing authority's approaches for dealing with non-endogenous, non-dietary therapeutic medications (as distinct from substances produced naturally within the horse or found in normal feed)'. The analysts who participated in the survey 'analyse samples routinely (as distinct from just offering a confirmatory service) for flat or jump racing (as distinct from harness racing, Arab-racing, Quarterhorse racing, endurance racing, point-to-points, or racing with animals other than horses)'. A copy of the survey is attached as an Appendix 1 to this paper.

Of the 55 analysts approached, 21 responded; 4 replies were received from Europe (19%), 6 from North America (29%), 2 from South America (9%) and 9 from Asia (43%). These analysts represent the following authorities: Ministry of Agricultures and Rural Affairs, Jockey Club of Turkey; The Hong Kong Jockey Club; Bangalore Turf Club Ltd; Comisión de Carreras Jockey Club Argentino; Federación Equestre Argentina; Victoria Racing Club; South Australian Jockey Club; Tasmanian Thoroughbred Racing Council; New Zealand Racing Conference; State of New Hampshire Pari-Mutuel Commission, USA; Canadian Pari-Mutuel Agency; Macau Jockey Club; Japan Racing Association, Regional Public Racing (23 racing authorities); Italian Jockey Club; Australian Jockey Club (NSW); Western Australian Turf Club; Darwin Turf Club; Alice Springs Turf Club; Michigan Office of the Racing Commissioner, USA; Michigan Department of Agriculture, Financial Services Division (Expositions and Racing Section); Jamaica Racing Commission; Club Hipico Santiago; Hipodromo Chile; Sporting Club; Club Hipico Concepción; Louisiana State Racing Commission, USA; Racing Industry and Sport Administration, Puerto Rico; Direktorium für Vollblutzucht und Rennen, Germany; Associated Clubs of the Malayan Racing Association (viz: Penang Turf Club, Perak Turf Club, Selangor Turf Club, and Singapore Turf Club; Jockey Club, Czech Republic; The Jockey Club, Great Britain.

The survey presented 16 questions, each having 3 mutually exclusive answers: a) In place already; b) Should be in place shortly; c) Neither planned nor in place. Survey participants were requested to leave the answer blank rather than give an uncertain response. The format also allowed each respondent to make comments or clarify answers.

Question 1: The international approach

The first and second questions referred to rules that are not blanket bans covering all therapeutic substances. The first question asked whether or not all medications are prohibited that fall within the list of prohibited substances approved by the International Federation of Horseracing Authorities. This list was amended in 1995 by removing anti-infectious substances as a category from prohibition. The survey asked respondents to give the position of the racing authority that was being represented 'with the amended list (or a definition effectively the same)'. The responses were: in place already (52%); should be in place shortly (24%); and neither planned nor in place (24%). The participants who had already accepted the list represented Turkey, Bangalore, Argentina, Victoria, New South Wales [NSW], New Zealand, Chile, Louisiana, Puerto Rico, Malaysia/Singapore and Great Britain. The participants who planned to accept the list included Hong Kong, Macau, Italy, Germany and the Czech Republic. The participants who did not plan to accept it were New Hampshire, Canada, Japan, Michigan and Jamaica. One representative commented that their jurisdiction 'requires the medication to be capable of affecting speed, stamina, courage or conduct'. One participant commented 'except furosemide and phenylbutazone'. Reviewing the responses to Question 1, the authors of the survey concluded that 76% had implemented (or intended to implement) the amended international list of prohibited substances.

Question 2: Other definitions that do not prohibit all therapeutic medications

This question asked respondents whether or not their racing authority used a definition of a prohibited substance that 'differs substantively from the international definition but likewise excludes some or all therapeutic substances that by their nature present no threat to the integrity of racing'. Of 19 responses, 21% indicated that such a definition was already in place, 11% planned to implement one, and 68% had no such plan. The participants who stated 'in place already' included Turkey, Bangalore, Argentina and Canada. Participants from Chile and Puerto Rico planned to create such definitions. The participants from Hong Kong, Victoria, NSW, New Zealand, New Hampshire, Macau, Italy, Michigan, Jamaica, Louisiana, Germany, Malaysia/Singapore and Great Britain did not plan to create such definitions. No participants made comments, but the participants representing Hong Kong, New Zealand and NSW submitted regulations of racing from their jurisdictions.

Reviewing the responses to Question 2, the authors concluded that this question should be ignored as some responders answered affirmatively for both Questions 1 and 2.

Question 3: Published thresholds

Questions 3 to 6 covered analytical limits agreed by the racing authority. Question 3 asked if regulation numerical limits for non-endogenous, non-dietary substances in plasma or urine 'are announced by the racing authority'. Of the 20 responses, 35% said limits are announced, 20% said announcements of regulation numerical limits in plasma or urine will be part of their procedure at a later date, and 45% indicated that the announcement of limits in plasma or urine is neither in place nor planned to be in place. The racing authorities who had already announced numerical limits were from Bangalore, Canada, Macau, Italy, Michigan, Louisiana and Malaysia/Singapore. Those who responded that announcements would be in place shortly included Turkey, Chile, Puerto Rico and the Czech Republic. Those who responded that their jurisdictions did not plan to make such announcements were from Hong Kong, Argentina, Victoria, NSW, New Zealand, New Hampshire, Japan, Germany and Great Britain.

The authors concluded that 55% had published or planned to publish thresholds for substances in addition to those in Article 6.

When asked to 'specify any non-endogenous, non-dietary therapeutic medications for which this approach is used (or is planned to be used shortly),' one participant specified 'Penicillin G Procaine (Procaine)'. One participant commented 'there are none, as threshold limits are set only for endogenous substances'. One participant specified 'Phenylbutazone (5.0 µg/ml in serum)', and commented 'ORC only'. This state's 'Expositions and Racing have no published thresholds'. One participant specified 'Phenylbutazone 5 µg/ml plasma'. One representative did not participate in this question, but did comment 'It is at the discussion stage' specifying 'Furosemide' and 'Phenylbutazone' and one participant specified the numerical limit for 'Furosemide 100 ng/ml in plasma', indicating that the announcement of numerical limits will soon be part of their policy.

Question 4: Defined but unpublished thresholds

Question 4 asked if 'the laboratory uses numerical limits agreed by the racing authority as in Question 3 except that they remain unpublished'. The question was then clarified by adding that in this case 'while technically a trace is still a prohibited substance, in practice a substance is a prohibited substance only if the unpublished threshold is exceeded'. Twenty-four percent of the participants said that this was their jurisdictions' practice. They were from Hong Kong, Canada, Japan, Michigan and Louisiana. Chile said that this is planned to be part of their policy shortly. Turkey, Bangalore, Argentina, Victoria, NSW, New Hampshire, Macau, Italy, Jamaica, Puerto Rico, Germany, Malaysia/Singapore and Great Britain did not plan to implement this practice (71% of the respondents).

The authors concluded that 29% had or planned for defined but unpublished thresholds.

Question 4 on 'defined but unpublished thresholds' also asked the participants to specify (unless private) 'any non-endogenous, non-dietary therapeutic medications for which this approach is used (or is planned to be used shortly)'. One representative replied 'Procaine: 0.75 mg/ml in urine (to safeguard the Club against procaine lingering over 3 weeks when administered as procaine penicillin by official veterinarians, as per Question 15)'. The representative went on to say 'although not therapeutic substances, in-house thresholds have also been agreed for these contaminants of fodder and feed additives (which the Club supplies to trainers): caffeine: 0.01 µg/ml in plasma or 0.03 µg/ml in urine; morphine: 0.1 µg/ml (free and conjugated) in urine'. One representative commented that the matter was

'private'. One racing association representative specified 'Ethanol'. One Office of Racing Commissioners specified 'Trimethoprim (500 ng/ml in urine)'. And one Jockey Club representative commented 'none'.

Question 5: Undefined and unpublished discretionary thresholds

Question 5 asked if 'the analyst is given the authority to decide independently the level (and other factors) at which a substance becomes a prohibited substance'. Thirty percent (Turkey, Argentina, New Hampshire, Macau, Louisiana and Germany) indicated that the analyst does have such independent authority, whereas 70% of the represented jurisdictions have this procedure neither in place nor planned. The representatives who made up this 70% included Hong Kong, Bangalore, Victoria, NSW, New Zealand, Canada, Japan, Italy, Michigan, Jamaica, Chile, Puerto Rico, Malaysia/Singapore and Great Britain. The representative from Louisiana reported "done with the advice of the commission. It is not wholly independent'.

The authors concluded that 30% had undefined and unpublished discretionary thresholds.

Question 6: Thresholds imposed by limiting analytical sensitivity

Question 6 asked if the jurisdictions being represented utilised the approach that 'involves deliberate rejection of unnecessarily sensitive analytical methods for specific substances, again in agreement with the racing authority'. An example for clarification was given: 'ELISA may have been rejected as the screening method for isoxsuprine on the grounds (at least in part) that it is too sensitive; alternatively, if ELISA is used for reasons of efficiency, either the sensitivity of the test is reduced or isoxsuprine must also be detectable by TLC (say) before it is a prohibited substance'. Victoria, NSW, New Hampshire, Canada, Macau, Japan, Michigan, Chile and Louisiana have initiated this type of approach. Hong Kong noted that the approach should be in place shortly, However, 50% of the responding jurisdictions reported that this approach is neither in place nor planned (Turkey, Bangalore, Argentina, New Zealand, Italy, Jamaica, Puerto Rico, Germany, Malaysia/Singapore and Great Britain).

The authors concluded that 50% had deliberately rejected or planned to reject unnecessarily sensitive analytical methods for specific substances.

Question 6 also asked participants to specify (unless private) 'any non-endogenous non-dietary therapeutic medications for which this approach is used (or planned to be used shortly)'. One representative replied, 'Phenylbutazone and some other NSAIDs (rejecting selected ion monitoring for screening), and isoxsuprine (rejecting enzyme linked immunosorbent assay [ELISA])'. Another analyst commented, 'NSAIDs, Clenbuterol, Anti-infectives, and Diuretics'. The Canadian representative and the representative from the Australian Jockey Club (NSW) commented by saying 'private'. One Jockey Club representative specified 'Isoxsuprine'. One participant commented, 'ARCI class 4 and 5 drugs must be detectable at TLC levels unless the drugs are known to be below TLC sensitivity less than 24 h after administration (ie Dexamethasone)'. And one analyst replied 'no ELISA for drugs in classes 4-5 of Louisiana list', and also stated that there is 'limited extraction of sample (volume) for confirmation'.

Question 7: Panel review/medical director that can decide whether trace findings are significant

Questions 7 to 9 covered disciplinary procedures. Question 7 asked if 'an independent administrative/ professional review step exists between a laboratory report of the presence of a substance and the convening of a medication enquiry'. The representatives were asked to reply neither planned nor in place 'unless a purpose of the review step can be to decide whether a finding should be ignored for the sole reason that the amount is pharmacologically insignificant'. Bangalore and Louisiana (10%) indicated that their jurisdictions already have an independent administrative/ professional review step that decides the pharmacological significance of a finding. All other representatives (90%) neither have this in place nor plan to create such a panel review/ medical director position.

The authors concluded that 90% did not have a review step that could decide whether trace findings are significant.

Question 8: Leniency to rare offenders

Question 8 asked for the jurisdictions' policies toward the suggested approach of a 'sliding scale of penalties...for certain medication offences' in which 'the penalty on the trainer is slight or non-existent the first time within a specified period (and may not be coupled with disqualifying the horse), but increases with subsequent offences. (This approach is distinct from the general practice of dealing more harshly with habitual offenders: it

applies only to certain substances, a scale is laid down, and the first and possibly second offences are not treated as serious)'. Turkey, Italy, Louisiana and Germany (21%) have this policy already in place and Chile noted that it should be in place shortly. Jurisdictions that did not plan to implement this policy (74%) include Hong Kong, Bangalore, Argentina, Victoria, NSW, New Zealand, New Hampshire, Canada, Macau, Michigan, Jamaica, Puerto Rico, Malaysia/ Singapore and Great Britain.

When asked to 'specify any therapeutic medications for which this approach is used (or is planned to be used shortly)', 3 jurisdictions responded. The first commented 'all'. The second said 'a penalty is applied since the first offence, and increases with subsequent offences'. This representative continued: 'the disciplinary committee seeks explanations from the veterinary consultant on the therapeutic substances which have been administered. Where a doping substance has been detected, in any case, the disqualification of the horse is ordered and the trainer is fined'. The third representative commented 'category 4 and 5; however, while severe penalties are given for 1–3, there is also a penalty scale for these categories'.

The authors concluded that this question should be ignored as some responders seem to have misinterpreted the question.

Question 9: Discretionary action against the horse

Question 9 asked the participants if 'the enquiry board exercises discretion over whether to disqualify a horse in breach of the medication rules '(other than as described in Question 8)'. The representatives were asked to reply neither planned nor in place 'if the horse is invariably disqualified (or is invariably disqualified except for an aberration), even though the Rules of Racing say may'. Responses from Turkey, New Zealand, Macau, Michigan, Jamaica and Germany (33%) stated that the policy was already in place. The remaining participants (67%) marked that the policy was neither in place nor planned.

The authors concluded that 67% invariably disqualified a horse in breach of the medication rules.

Representatives were also asked to 'specify any drug classes for which this approach is used (or planned to be used shortly). If all, write all'. Four jurisdiction representatives commented 'all'. One representative commented by saying 'disqualification would be automatic for non-therapeutic drugs, eg narcotics'.

Question 10: Elective testing

Guidance for practising veterinarians and trainers was the topic of Questions 10, 11 and 12. Question 10 referred to elective testing. The question asked whether a trainer can request and pay for 'a horse to be tested for a specific therapeutic medication before declaring it to run. The laboratory report deals only with the substance in question'. Twenty-nine percent of responses stated that elective testing was in place already, (Victoria, NSW, New Zealand, Macau and Germany). Great Britain plans to adopt this policy in the future, but 65% neither have this policy in place nor plan for it.

The authors concluded that 35% had or plan to have elective testing.

Question 11: Detection times/clearance times

Question 11 asked whether 'detection times are provided as a guide for practising veterinarians and trainers'. In response Turkey, Victoria, NSW, New Zealand, Canada, Macau, Chile and Malaysia/ Singapore (44%) said that detection times were already provided as a guide to veterinarians and trainers, while Germany and Great Britain (11%) plan to provide them in the future. However, 44% noted that this policy was not in place nor planned. The participant from New Zealand commented 'unofficial', and 'provided by Veterinary Association'.

The authors concluded that 55% had (or intended to provide) detection/withdrawal times.

Question 12: Forewarning of new tests

Question 12 asked if 'practising veterinarians and trainers are given adequate notice before a new test with improved sensitivity for a therapeutic medication is introduced (and in jurisdictions that supply detection times, the revised detection time is provided)'. In response, 42% of the participants said that their jurisdictions give notice of new tests to veterinarians and trainers (Turkey, Victoria, NSW, New Zealand, Canada, Macau, Chile and Louisiana). The remaining participants (58%) answered that this procedure was neither in place nor planned to be implemented. The analyst from Canada commented 'selectively'; Great Britain indicated that 'updates on detection periods will be provided'.

The authors concluded that 42% gave forewarning of new tests.

Question 13: Time rules

Regulations protecting against inadvertent breaches was the topic of Questions 13 to 16. Question 13

dealt with 'time rules' and asked whether 'the rules specify periods prior to post within which the horse must not be treated with certain groups (or with any group) of prohibited substances.' Turkey, Hong Kong, New Hampshire, Macau, Japan, Michigan, Louisiana and Malaysia/ Singapore (47%), said that periods prior to post are specified in their jurisdictions. The analyst from Puerto Rico indicated that specification of periods will become policy shortly. However, 47% of the analysts responded that their jurisdictions neither had in place nor planned to specify periods prior to post.

The authors concluded that this question should be ignored as some responders answered this question in the affirmative, seemingly because they had a rule for Lasix of up to 4 h before the race.

Question 14: Notification of treatment

Question 14 asked if the trainer is required to notify the stewards of any treatment administered to a horse in a defined period prior to post' and 'if as a result the stewards withdraw the horse, the trainer suffers no further disability'. Macau, Italy and Louisiana (20%) have this procedure already in place. Chile said that this policy will be in place shortly. However, 73% of the participants marked that their jurisdictions neither had in place nor planned to initiate this practice.

The authors concluded that 27% had or plan to have a notification-of-treatment regulation.

Question 15: Officially provided treatment

Question 15 asked if 'routine veterinary services are provided by veterinarians employed by the racing authority'. Turkey, Hong Kong, Bangalore, Macau, Japan, Italy, Chile, Louisiana and Malaysia/ Singapore (53%) reported that this procedure is already in place. Victoria, NSW, New Zealand, Canada, Michigan, Jamaica and Great Britain (47%) indicated that policies for routine veterinary services provided by the racing authority were neither in place nor planned. In some jurisdictions that provide such services, their use is optional whereas in others it is compulsory, and where they were provided respondents were asked to show whether they were optional or compulsory. Chile, Louisiana and Malaysian/Singapore jurisdictions marked optional, whereas Hong Kong, Macau, Italy and Great Britain marked compulsory.

The authors concluded that this question should be ignored as not all responses were logical.

Question 16: Controlled race day treatment for minor conditions

The last question of the survey asked if 'regulatory veterinarians can give written approval for specific treatment of a minor condition on a race day (or can treat it themselves)'. The question went on to explain that the presence of a so-authorised substance would not be regarded as a medication case. In response, all 18 participants that answered said that this procedure was not the policy of their jurisdiction nor was it planned.

The authors concluded that nowhere could regulatory veterinarians sanction race day treatment for any condition.

Other

The analysts were asked to 'specify other approaches planned or in place'. Only one response was given, from Turkey, saying 'According to the legislation of horse races and doping-control regulation of Turkey, in the case of the treatment with therapeutic medication, race of the horse has been prohibited for one week'.

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1) Testing for Therapeutic Medications, Environmental and Dietary Substances in Racing Horses. Proceedings of the Workshop held at The Maxwell H. Gluck Equine Research Center, University of Kentucky, Lexington, August 1994.

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APPENDIX 1

ADMINISTRATIVE APPROACHES TO NON-ENDOGENOUS NON-DIETARY THERAPEUTIC MEDICATIONS THAT CAN BE DETECTED TOO WELL

FLAT AND JUMP RACING

Your name (in capitals or type) .....

Do you analyse samples routinely (as distinct from just offering a confirmatory service) for flat or jump racing (as distinct from harness racing, Arab racing, Quarterhorse racing, endurance racing, point-to-points, or racing with animals other than horses)? Yes/No
If your answer is No, ignore the rest of this form but still return it.

Which racing authority (or authorities) do you analyse such samples for? Give the full name (or names). If more than one, photocopy this form and submit separate replies unless the responses are identical.

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On the following pages, identify the racing authority's approaches for dealing with non-endogenous non-dietary therapeutic medications (as distinct from medicinal substances produced naturally within the horse or found in normal feed):

- Some may be in place already, in which case tick 'In place already'.
- Racing administrators may have agreed to others, but implementation awaits data, agreement of detail or formal approval of a change in the Rules of Racing; in this case tick 'Should be in place shortly'.
- For approaches that administrators have not agreed to, tick 'Neither planned nor in place'.

If you are unable to determine the correct response for the racing authority, make no tick rather than a misleading one. No approach precludes the use of some other approaches.

Feel free to add comments.

	In place already	Should be in place shortly	Neither planned nor in place
A. RULES THAT ARE NOT BLANKET BANS COVERING ALL THERAPEUTIC SUBSTANCES			
1. The international approach All medications are prohibited that fall within the list of prohibited substances approved by the International Federation of Horseracing Authorities. This list was amended in 1995 by removing anti-infectious substances as a category from prohibition. Tick to show the position with the amended list (or a definition effectively the same).	☐	☐	☐
2. Other definitions that do not prohibit all therapeutic medications The definition of a prohibited substance differs substantively from the international definition but likewise excludes some or all therapeutic substances that by their nature present no threat to the integrity of racing.	☐	☐	☐
APPEND A COPY OF YOUR DEFINITION WHATEVER YOUR RESPONSES TO 1 AND 2 (SHOWING ANY CHANGES AWAITING FORMAL APPROVAL)			
B. ANALYTICAL LIMITS AGREED BY THE RACING AUTHORITY			
3. Published thresholds Regulatory numerical limits in plasma or urine are announced by the racing authority. Specify any non-endogenous non-dietary therapeutic medications for which this approach is used (or is planned to be used shortly).	☐	☐	☐
4. Defined but unpublished thresholds The laboratory uses numerical limits, agreed by the racing authority as in Approach 3, but in this case they remain unpublished. While technically a trace is still a prohibited substance, in practice a substance is a prohibited substance only if the unpublished threshold is exceeded. Specify (unless private, in which case write 'Private') any non-endogenous non-dietary therapeutic medications for which this approach is used (or is planned to be used shortly).	☐	☐	☐

	In place already	Should be in place shortly	Neither planned nor in place
5. Undefined and unpublished discretionary thresholds The analyst is given the authority to decide independently the level (and other factors) at which a substance becomes a prohibited substance.	☐	☐	☐
6. Thresholds imposed by limiting analytical sensitivity This approach involves deliberate rejection of unnecessarily sensitive analytical methods for specific substances, again in agreement with the racing authority. For example, ELISA may have been rejected as the screening method for isoxsuprine on the grounds (at least in part) that it is too sensitive; alternatively, if ELISA is used for reasons of efficiency, either the sensitivity of the test is reduced or isoxsuprine must also be detectable by TLC (say) before it is a prohibited substance.	☐	☐	☐
Specify (unless private, in which case write 'Private') any non-endogenous non-dietary therapeutic medications for which this approach is used (or is planned to be used shortly).			
C. DISCIPLINARY PROCEDURES			
7. Panel review/Medical director that can decide whether trace findings are significant An independent administrative/professional review step exists between a laboratory report of the presence of a substance and the convening of a medication enquiry. Tick the last box unless a purpose of the review step can be to decide whether a finding should be ignored for the sole reason that the amount is pharmacologically insignificant.	☐	☐	☐
8. Leniency to rare offenders A sliding scale of penalties is laid down for certain medication offences: the penalty on the trainer is slight or non-existent the first time within a specified period (and may not be coupled with disqualifying the horse) but increases with subsequent offences. (This approach is distinct from the general practice of dealing more harshly with habitual offenders: it applies only to certain substances, a scale is laid down, and the first and possibly second offences are not treated as serious.)	☐	☐	☐
Specify any therapeutic medications for which this approach is used (or is planned to be used shortly)			
9. Discretionary action against the horse The enquiry board exercises discretion over whether to disqualify a horse in breach of the medication rules (other than as described in Approach 8). Tick the last box if the horse is invariably disqualified (or is invariably disqualified except for an aberration), even though the Rules of Racing say 'may'.	☐	☐	☐

	In place already	Should be in place shortly	Neither planned nor in place
Specify any drug classes for which this approach is used (or is planned to be used shortly). If all, write 'All'.			
.....			
.....			
.....			
D. GUIDANCE FOR PRACTISING VETERINARIANS AND TRAINERS			
10. Elective testing The trainer requests and pays for a horse to be tested for a specific therapeutic medication, before declaring it to run. The laboratory report deals only with the substance in question.	☐	☐	☐
11. Detection times/Clearance times Detection times are provided as a guide for practising veterinarians and trainers.	☐	☐	☐
12. Forewarning of new tests Practising veterinarians and trainers are given adequate notice before a new test with improved sensitivity for a therapeutic medication is introduced (and in jurisdictions that supply detection times, the revised detection time is provided).	☐	☐	☐
E. REGULATORY PROTECTION AGAINST INADVERTENT BREACHES			
13. Time rules The rules specify periods prior to post within which the horse must not be treated with certain groups (or with any group) of prohibited substances.	☐	☐	☐
14. Notification of treatment The trainer notifies the stewards of any treatment administered to a horse in a defined period prior to post. If as a result the stewards withdraw the horse, the trainer suffers no further disability.	☐	☐	☐
15. Officially provided treatment Routine veterinary services are provided by veterinarians employed by the racing authority.	☐	☐	☐
Use of these services is optional in some jurisdictions, compulsory in others. If this approach is used, tick which:			
OPTIONAL ☐			
COMPULSORY ☐			
16. Controlled raceday treatment for minor conditions Regulatory veterinarians can give written approval for specific treatment of a minor condition on a raceday (or can treat it themselves). The presence of a so-authorized substance is not regarded as a medication case.	☐	☐	☐
F. OTHER			
Specify other approaches, planned or in place.			
.....			
.....			

Signature ..... Date .....

THE DETERMINATION OF A THRESHOLD VALUE FOR TESTOSTERONE: APPROACHES TO THE PROBLEM

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ABSTRACT

The Laboratoire de la Fédération Nationale des Sociétés de Courses (France), the Racing Laboratory of the Hong Kong Jockey Club (Hong Kong) and the Horseracing Forensic Laboratory (UK) undertook a collaborative study to investigate strategies to provide definitive thresholds for testosterone in the gelding and the mare/filly. Quantitative methods for several endogenous steroids have been developed and normal levels established for post competetion urine samples. Administration studies for testosterone esters were carried out at the 3 laboratories and samples were exchanged for analysis to determine urinary concentrations of testosterone and other steroids. This paper presents the collective data from the 3 laboratories.

INTRODUCTION

Testosterone is the principal endogenous androgenic-anabolic steroid in horses and man. It is used in veterinary medicine as an androgen in the treatment of deficient libido in males, in suppression of oestrus in females and as an anabolic steroid for therapeutic purposes. However, as an anabolic and androgenic agent, it can also be abused. In human athletics, testosterone is the substance most frequently reported in steroid misuse and it is controlled by monitoring the testosterone to epitestosterone (T:E) ratio (Catlin *et al.* 1996). Introduced by Donike *et al.* (1983), the ratio of the glucuronides of testosterone to epitestosterone has been accepted by the International Olympic Committee and most international sport organisations which consider a T:E value of >6 to indicate that testosterone may have been administered (Anon 1982, 1992). In man, the major metabolites of testosterone are the 17-oxo steroids androsterone and etiocholanolone, excreted primarily as the glucuronic acid conjugates. The metabolism differs markedly in the horse where the major metabolites are testosterone sulphate and the glucuronic acid and sulphate conjugates of the reduced metabolites, namely isomeric androstane-3,17-diols (Dumasia and Houghton 1981).

Two preliminary approaches to establishing threshold values have been proposed recently to monitor misuse of testosterone preparations in the horse: 1) the testosterone to prasterone (T:P) ratio for geldings and fillies proposed by Houghton (1995); 2) the T:E ratio for fillies proposed by Bonnaire *et al.* (1995). Prasterone (also known as dehydroepiandrosterone) is produced by the adrenal gland and is a precursor rather than a metabolite of testosterone. It is therefore a suitable candidate as an endogenous reference steroid. Low concentrations of epitestosterone have been detected in normal urine samples from geldings and fillies. Epitestosterone has not been identified as an *in vivo* metabolite of testosterone and thus it too is a suitable reference steroid for the ratio approach. No definitive data are available concerning the adrenal origin of epitestosterone in the horse although its presence in the follicular fluid of the cycling mare has been reported (Short 1960; Silberzahn *et al.* 1983).

The entire male horse produces large amounts of testosterone. Castration removes this primary source but, using immunoassay techniques, low levels of testosterone have been reported in geldings, presumably arising from an adrenal source (Crone and Choi 1984). The gelding has a low urinary androgen profile with average testosterone and related metabolite concentrations <10 ng/ml. The cryptorchid is an animal in which one or both testes do not descend into the scrotum. Removal of the scrotal testis from a unilateral cryptorchid produces a horse which, on physical examination, appears to be a gelding. In such cases,