TABLE OF CONTENTS

| P | A | G | E |
|---|---|---|---|
| | | ~ | _ |

| FOREWORD | 2 |
|-------------------------------------------------|----|
| INTRODUCTION | 3 |
| EXECUTIVE SUMMARY | 6 |
| I. SCREENING OF LABORATORY SAMPLES | 10 |
| II. RCI CLASS 1, 2 AND 3 DRUGS | 13 |
| III. REGULATORY THRESHOLDS | 15 |
| IV. ANTI-INFLAMMATORY MEDICATIONS | 17 |
| V. ANIMAL SELECTION | 19 |
| VI. RESEARCH AND METHOD DEVELOPMENT | 22 |
| VII. NUMBER OF SAMPLES TESTED AND DOLLARS SPENT | 23 |
| VIII. AGREEEMNTS BETWEEN LABS AND COMMISSIONS | 27 |
| IX. SUPERTEST FINDINGS | 28 |
| X. RECOMMENDATIONS | 34 |
| ACKNOWLEDGMENTS | 39 |
| APPENDIX A | 44 |
| APPENDIX B | 45 |
| APPENDIX C | 47 |
| APPENDIX D | 48 |
| APPENDIX E | 52 |
| APPENDIX F | 55 |

FOREWORD

The Task Force wishes to thank Cornell University's Equine Drug Testing Program and the University of California-Davis Equine Analytical Chemistry Laboratory for their commitment to this project, and to acknowledge the efforts of the respective laboratory directors, Dr. George Maylin and Dr. Scott Stanley, in this endeavor.

In addition, the Task Force wishes to acknowledge the following racetracks, which voluntarily underwrote the costs for testing samples selected from their facilities:

Golden Gate Fields

• Aqueduct

• Del Mar

- Arlington Park
- Bay Meadows
- Belmont Park
- Calder Race Course
- Churchill Downs
- Hollywood ParkHoosier Park

Ellis Park

• Finger Lakes

Fair Grounds

• Gulfstream Park

• Ho

•

•

We appreciate their support.

- Keeneland Association
- Oak Tree at Santa Anita
- Santa Anita Park
- Saratoga Race Course
- Turfway Park

Our thanks also to Dr. Richard Sams of the Analytical Toxicology Laboratory at Ohio State University and Thomas Lomangino of the Maryland Racing Commission Laboratory, who provided the independent analytical review of this report to ensure that the test results were scientifically valid, and to Dr. Melvin V. Koch for his counsel during the preparation of this report. Additionally, we would like to thank R.D. Hubbard for his efforts as one of the original co-chairs of the Task Force.

Finally, we wish to express our appreciation to the co-authors of this report, Jim Gallagher, executive director of the Drug Testing Task Force, and Dr. Scot Waterman DVM, the Task Force director of methods and procedures.

The members of the NTRA Racing Integrity and Drug Testing Task Force,

Jack K. Robbins VMD, co-chair

Rogers Beasley Buddy Bishop Esq. Gary Biszantz Edward S. Bonnie Esq. Don Dizney Ogden Mills Phipps, co-chair

Alan Foreman Esq. Gary Lavin VMD Paul Oreffice Bill Walmsley Esq.

> The Jockey Club Round Table Saratoga Springs, New York August 19, 2001

INTRODUCTION

The pari-mutuel racing industry is dependent on the confidence the betting public has in the integrity of racing. Because horseracing is funded via legal wagering, the stability, growth, and public acceptance of the sport is reliant on the industry's ability to demonstrate the highest level of integrity and to enforce its rules fairly. State racing commissions are statutorily authorized to promulgate and enforce the rules of racing.

Post-race drug testing is a component of this enforcement. This testing is conducted to ensure that performance-altering drugs are not administered and that permitted, therapeutic medications are given properly. If a finding falls outside the parameters set up by an individual jurisdiction, action may be taken against the trainer, who, under a variety of rules, is responsible for the condition of the horse on race-day.

Horses, like other athletes, sometimes suffer minor training injuries that necessitate the administration of accepted therapeutic medications. The rules of racing dictate acceptable levels and types of medications. Those rules vary from state to state, however, creating challenges and complexity for all licensees, i.e., what is permitted in one state may constitute a rule violation in another.

The Racing Integrity and Drug Testing Task Force

In 1998, the National Thoroughbred Racing Association (NTRA) formed the Racing Integrity and Drug Testing Task Force to review drug testing issues affecting Thoroughbred and Quarter Horse racing in the United States. The Task Force's mission is to work in a complementary manner with state racing commissions to improve drug testing procedures and standards and reinforce public confidence in the integrity of the sport.

The Task Force members are:

- Co-Chair Jack K. Robbins VMD, president of Oak Tree Racing Association and distinguished life member and former president of the American Association of Equine Practitioners;
- Co-Chair Ogden Mills Phipps, chairman of The Jockey Club, New York Racing Association Trustee and a National Thoroughbred Racing Association Board member;
- Rogers Beasley, director of racing at Keeneland;
- Buddy Bishop Esq., Stoll, Keenon and Park LLP, a leading firm in equine law based in Lexington, Kentucky;
- Gary Biszantz, chairman of the Thoroughbred Owners and Breeders Association and a racehorse owner;
- Edward S. Bonnie Esq., one of the country's foremost legal experts on drug testing, served in an advisory role in the production of the McKinsey report, "Building a World-Class Drug Detection System for the Racing Industry," a seminal study of equine drug testing;
- Don Dizney, owner of Double Diamond Farm in Ocala, Florida, and chairman of United Medical Corporation;
- Alan Foreman Esq., chairman and chief executive officer of the Thoroughbred Horsemen's Association and one of the country's foremost legal experts on drug testing;
- Gary Lavin VMD, distinguished life member and past president of the American Association of Equine Practitioners;
- Paul Oreffice, New York Racing Association Trustee and former chairman of Dow Chemical Company; and

• Bill Walmsley, spokesman for and past-president of the National Horsemen's Benevolent and Protective Association, current president of the Arkansas HBPA and a National Thoroughbred Racing Association Board member

The Executive Director of the Task Force is Jim Gallagher, who accepted the position in August 1999 after 22 years with the New York State Racing and Wagering Board in various policy-making positions. The Task Force Director of Methods and Procedures is Scot A. Waterman DVM, a graduate of the University of Illinois College of Veterinary Medicine and the University of Arizona Race Track Industry Program.

The Task Force Scientific Advisory Committee

The first act of the Task Force was to put together a Scientific Advisory Committee (see Appendix A) to assess current testing practices. The Committee was composed of a group of individuals who had extensive analytical chemistry experience and technical management backgrounds, but were outside of the racing community. The report made by this Committee, "Equine Drug Testing: An Assessment of Current Practices and Recommendations for Improvements," has served as a guide for the activities of the Task Force.

The Supertest Program

The first project undertaken by the Task Force has been the Supertest program. The purpose of the Supertest project is to determine what drugs are in use and to improve drug-testing standards through a national survey of samples. Although the original goal was to conduct this testing on samples from horses competing in graded stakes, the project grew to include races representative of each participating jurisdiction. This type of nationwide examination originally was suggested in "Building a World-Class Drug Detection System for the Racing Industry," commonly referred to as the McKinsey report.

In the Supertest program, aliquots from urine samples that tested negative for prohibited substances were submitted anonymously and subjected to a more comprehensive testing regimen than currently conducted by any individual jurisdiction. Twenty-eight of the 32 jurisdictions (88%) conducting racing in the United States participated by submitting samples representative of racing in their states (see Appendix B).

The collection of samples for Supertest analysis began in April 2000. The Task Force contracted with Cornell University's Equine Drug Testing Program and the University of California-Davis' Analytical Chemistry Laboratory to analyze selected samples. The complete standard operating procedure for the submission of samples is contained in this report as Appendix C.

The techniques for testing employed by the respective laboratories were slightly different but both facilities used state-of-the-art drug detection procedures and adhered to best laboratory practices. The test procedures employed by Cornell University's Equine Drug Testing Program included Enzyme-Linked Immunosorbant Assay (ELISA), High Performance Liquid Chromatography (HPLC), and Thin Layer Chromatography (TLC) for screening and target testing, with Gas Chromatography/Mass Spectrometry (GC/MS), HPLC and Liquid Chromatography/Mass Spectrometry (LC/MS) used for drug confirmations.

The University of California-Davis' Analytical Chemistry Laboratory subjected Supertest samples to an instrumentally based drug-testing program. Screening techniques employed LC/MS and GC/MS rather than TLC procedures. In addition, all samples were subjected to a broad array of ELISA tests. Drug confirmations were done by LC/MS or GC/MS.

The Supertest focused on Class 1, 2 and 3 drugs in the Association of Racing Commissioners International (RCI) Guidelines for Foreign Substances, due to their relative potential to influence the performance of the horse. There was some testing for RCI Class 4 medications—specifically, steroidal anti-inflammatories and non-steroidal anti-inflammatories other than phenylbutazone, flunixin (Banamine®), naproxen (Naprosyn®), and meclofenamic acid (Arquel®).

The findings presented herein are from the first 1,272 samples of a total of 1,800 to be analyzed. Only RCI Class 1, 2 and 3 drugs will be discussed because not enough samples have been analyzed for the presence of the selected steroidal and non-steroidal Class 4 medications as of the writing of this report. The Task Force expects to release results for all samples in December 2001.

As a prelude to the release of the first phase of the Supertest results, two detailed surveys (Appendices D and E) were sent to the 28 racing jurisdictions that submitted samples for Supertest analysis and to the four jurisdictions that did not submit samples. The surveys were returned by 30 of the 32 jurisdictions, a 94% response rate. The two jurisdictions not returning the survey were also two of the jurisdictions that did not participate in the Supertest. These results constitute the first-ever benchmark survey of equine drug testing practices and procedures in the United States.

The benchmark study serves two purposes. First, it constitutes an archive of information that can be communicated to state racing commissions so that they can make more informed decisions regarding their own jurisdiction's procedures. Second, it provides a national context for the Supertest results.

In this report, jurisdictions are designated by random letters to ensure confidentiality and avoid compromising any state's current testing program or exposing any jurisdiction to undue criticism.

NTRA RACING INTEGRITY AND DRUG TESTING TASK FORCE REPORT

EXECUTIVE SUMMARY

The NTRA Racing Integrity and Drug Testing Task Force Report, the result of two years of research into drug testing of racehorses competing in the United States, is both the first-ever comprehensive survey of the country's current testing programs and practices (representing 30 of 32 racing jurisdictions, or 94 %) as well as a summary of "Supertest" findings from post-race test samples submitted by 28 of those 32 jurisdictions (88%). A list of states submitting samples appears in the report as Appendix B.

A total of 1,800 samples were submitted for the Supertest, with this report covering the results of 1,272 samples (71%) for the presence of Class 1, 2 and 3 drugs in the Association of Racing Commissioners International (RCI) Guidelines for Foreign Substances. Results from the remaining 528 samples, including the results for selected Class 4 medications, are to be released before the end of 2001.

Key Findings from the Jurisdiction Survey

Screening of Laboratory Samples: Enzyme-Linked Immunosorbant Assays (ELISA) and Thin Layer Chromatography (TLC) remain the dominant screening methodologies. ELISA is drug-specific, while TLC can detect multiple drugs, but generally not at low concentrations (below 100 nanograms/ml). All responding jurisdictions use ELISA testing, with 93% also using TLC. The average number of ELISA tests used per sample is 20.3, or 14.2% of the 143 ELISA kits available, while the median is 15. Jurisdictions report widespread reliance on "group" ELISA kits, which test for multiple drugs, and rotation of ELISA tests on a random basis.

Drug Classifications: RCI has classified drugs into five categories based on pharmacology, ability to influence the outcome of a race, therapeutic value in the racehorse or other evidence that they may be used improperly. The Task Force survey, covering 508,737 samples tested between 1997-1999, found 385 reported violations for 45 different medications categorized as Class 1, 2 or 3—those that have the highest to moderate potential, respectively, to affect performance in the racehorse. Only 10 of the 45 medications were detected on more than 10 occasions. Four of the 10, (clenbuterol, promazine, glycopyrrolate and lidocaine), are routinely used for therapeutic purposes.

Threshold Levels for Select Drugs and Therapeutic Medications: Regulatory thresholds refer to the point at which administrative action is taken against a trainer for the presence of a prohibited drug or an unacceptably high level of a permitted, therapeutic medication. What constitutes an actionable medication finding in one state may be ignored in another. Jurisdictions surveyed on threshold levels for nine drugs overwhelmingly reported "zero tolerance" levels for the following: acepromazine/promazine (22/28), albuterol (24/28), atropine (25/28), caffeine (22/28), clenbuterol (19/26), cocaine (24/28), morphine (25/27) and scopolamine (26/27).

Animal Selection in the Testing Process: Eighty-two percent of all jurisdictions test only the race winner, with 18% testing the one-two finishers. In stakes races, 63% of jurisdictions report selecting additional finishers, usually the second- and third-place horses. Other horses that may be selected include beaten favorites, runners showing dramatic form reversals and instances where racing commissions have investigative leads.

Test Research and Methods Development: Pari-mutuel wagering is the single largest funding source for improvements in drug testing methodologies, contributing \$1.35 million or 25% of all monies allocated to equine medical research through the pari-mutuel mechanism. The bulk of this money is spent in four states with university laboratories equipped to conduct equine drug detection.

Expenditures on Drug Testing: Based on modeled survey results, it is estimated that individual jurisdictions spend between \$70 and \$325 per race on sample testing. Although this difference appears significant, there is an imperfect correlation between testing expenditures and effective testing. Sixty-eight percent of jurisdictions surveyed report that lab services and collection expenses are borne by racing commissions.

Laboratory-Commission Drug Testing Agreements: Twenty-one jurisdictions (63%) have contractual agreements with laboratories; four-fifths of them use the Request For Proposal (RFP) process to determine laboratory selection, and more than half use the RFP as a means of ensuring prescribed levels of performance. Twenty percent have statutory agreements, with the remainder having either combination systems or some other arrangement.

The Supertest Project

Test Background

The Supertest samples had been declared free of prohibited substances by the participating racing jurisdictions prior to being submitted for testing. Sample collection began in April 2000, with testing performed by Cornell University's Equine Drug Testing Program (under the direction of Dr. George Maylin) and the University of California-Davis' Equine Analytical Chemistry Laboratory (under the direction of Dr. Scott Stanley). The techniques for testing employed by the respective laboratories were slightly different but both facilities used state-of-the-art drug detection procedures and adhered to best laboratory practices.

Test Summary

Twenty-two confirmations were found in 1,272 samples: two Class 1s, two Class 2s and 18 Class 3s. Clenbuterol accounts for 50% of the Class 3 confirmations and 41% of all confirmations. Alpha-2 adrenergic drugs, which have anti-hypertensive effects as well as analgesic and sedative properties, account for 32% of all confirmations.

Summary of Conclusions

Despite wide differences in testing programs, 98.3% of Supertest samples contained no RCI Class 1, 2 or 3 drugs.

In the remaining 1.7% of samples, 18 of 22 confirmations (82%) were for Class 3 drugs, which may have a generally accepted medical use in the racehorse and whose pharmacology suggests less potential to affect performance than Class 2 or Class 1 medications. Of the 18 Class 3 confirmations, nine were for clenbuterol, an FDA-approved medication used to treat horses suffering from chronic obstructive pulmonary disease (COPD).

That the Supertest detected drugs and/or therapeutic medications in samples declared free of prohibited substances by racing jurisdictions is not surprising when viewed in the proper context. The Supertest utilized more comprehensive screening and confirmation regimens than those used by most racing jurisdictions. In addition, some racing jurisdictions apply threshold concentrations for certain therapeutic medications, notably clenbuterol, below which the presence of the medication is declared a non-finding. The Supertest employed only one threshold level (clenbuterol at 1ng/ml) while all other confirmations were reported regardless of concentration.

New, more potent, multi-action drugs continue to be marketed for therapeutic use in human patients. These drugs can affect the performance of racehorses at extremely low doses and result in urine and blood concentrations in the low nanogram per milliliter range. As illustrated by the Supertest findings, more rigorous testing must be performed, utilizing state-of-the-art techniques, to detect these types of drugs.

Task Force Recommendations

The material below is excerpted from the Recommendations section of the full report, which begins on page 34.

1. Jurisdictions should use more rigorous screening processes.

Key Actions:

- Transition away from TLC while relying more on ELISA and instrumental testing methods;
- Rotate and develop more ELISA tests; and
- Pursue strategies, including cooperative alliances for the purchase of drug testing kits, to reduce overall testing costs.

2. Jurisdictions should re-assess medication rules and enforcement policies in light of new and more sophisticated testing technologies.

Key Actions:

- Reassess medication rules and enforcement policies—largely formulated on the basis of outmoded TLC methodologies—in light of ELISA and instrumental testing methods, which can detect substances in very low concentrations;
- Evaluate a medication's pharmacology (i.e., its ability to affect a horse's performance) in light of new and more sophisticated testing methods to determine whether, and to what extent, administrative action is appropriate; and
- Research the role that permitted medications may play in interfering with the detection of prohibited substances.

3. The racing industry should support the development of withdrawal guidelines for commonly administered therapeutic medications.

Key Actions:

- Develop an alliance of industry stakeholders to determine if, when and how withdrawal times (or, alternatively, decision levels) can be made the standard for specific therapeutic medications;
- Continue and expand research on the pharmacology of therapeutic medications; and
- Develop a program for communicating proper systems for medication withdrawal and for reporting violations in a manner consistent with protecting the image and integrity of horseracing.

4. A national, external quality assurance program for drug-testing laboratories should be established.

Key Actions:

- Monitor the performance of laboratories through oversight by a consortium of industry stakeholders, including racing commissions, laboratory analysts and national racing organizations;
- Establish a list of substances to be tested for, and develop programs to document and verify the accuracy and reliability of testing methods; and
- Disseminate findings to industry stakeholders and to participating laboratories to ensure full compliance with accepted testing procedures.

5. Create a national organization to implement improvements in drug testing and provide leadership in jurisprudence and public communication practices relating to drug testing issues.

Key Actions:

- Form a national organization, representing regulators, owners, trainers, racetracks, veterinarians and drug testing researchers to implement recommendations outlined in the Task Force Report;
- Coordinate judicial and drug testing research efforts between states and racing jurisdictions; and
- Reduce litigation relating to medication violations and increase horseracing's credibility in the area of drug testing by promoting judicially sound, "best practices" relating to public disclosure of suspected medication violations.

I. SCREENING OF LABORATORY SAMPLES

As indicated by survey responses, Thin Layer Chromatography (TLC) and Enzyme Linked Immunosorbant Assays (ELISA) are the dominant screening methodologies employed in post-race testing. All responding jurisdictions used ELISA testing to some degree. Two responding jurisdictions indicated that they no longer perform any TLC screening and instead utilize instrumental screening. Several jurisdictions responded that instrumental screening techniques were used, usually in addition to ELISA and TLC. The survey asked about jurisdictions' use of Gas Chromatography (GC), High Performance Liquid Chromatography (HPLC), Gas Chromatography/Mass Spectrometry (GC/MS) and Liquid Chromatography/Mass Spectrometry (LC/MS). These results are summarized below:



PERCENT OF JURISDICTIONS USING THESE SCREENING METHODS

ELISA Screening

Use of ELISA screening on post-race samples has grown significantly during the last decade. A primary reason for this growth is the high sensitivity of the method as compared to the TLC method. Another characteristic of ELISA testing is the ability to automate the testing process, which significantly reduces the human labor component.

Two companies dominate the production and distribution of ELISA test kits to racing jurisdictions: Neogen Corporation and Testing Components Corporation (TCC).

Using the order forms from these two companies, we have identified 143 discreet ELISA test kits that are commercially available to racing jurisdictions. The ELISA test kit list, however, contains some general ELISA kits (e.g., opiate group, bronchodilator group, et al.) and fails to include those drugs within certain families that cross-react with the ELISA for another drug in the family. Based on information provided by Neogen and TCC, it is conservatively estimated that the full complement of 143 ELISA kits collectively can detect more than 300 drugs and drug metabolites.

When analyzing the data submitted by the commissions, the number of ELISA tests performed on each sample by responding jurisdictions ranged from one at the low end to a high of 70. The average

number (using the high-end number when a range was given as an answer) of tests per sample was 20.3, which represents 14% of the total number of test kits available. The median number of kits used is 15. The figure below summarizes the number of ELISA tests per jurisdiction with the overall average and median indicated at the far right.



NUMBER OF ELISA TESTS USED FOR SCREENING

The seemingly low average number of ELISA kits used per sample is mitigated by the fact that the "group" ELISA tests are among the most popular. We attempted to determine which kits are used for the purposes of routine screening. Not surprisingly, this was a question that a number of jurisdictions felt was proprietary and therefore did not answer. A number of jurisdictions did answer, though, and some very definite patterns emerged. The most frequently mentioned ELISA kits used for routine screening are, alphabetically: Amphetamine, Bronchodilator group, Buprenorphine, Butorphanol/Nalbuphine, Clenbuterol, Cocaine, Detomidine, Dexamethasone, Etorphine, Fentanyl group, Lidocaine, Opiate group, Oxymorphone, Pentazocine, Promazine group, and Pyrilamine. The four "group" kits (Bronchodilator, Fentanyl, Opiate and Promazine) mentioned above detect more than 30 different drugs or drug metabolites, while there is significant cross reactivity on the Amphetamine, Dexamethasone, Oxymorphone and Pyrilamine tests.

Another strategy used by commission laboratories to attempt to increase the coverage provided by ELISA testing is to rotate different types of ELISA kits. In fact, 91% of the jurisdictions answered that new ELISA tests are rotated into the mix. The 9% that do not rotate are among those that run the highest number of tests per sample. The time frame during which new tests are rotated in ranged significantly from weekly to infrequently.

Two procedural areas in which there were significant differences between respondents involved the pooling of test samples and the setting of limits of detection of the test kits. More than half (55%) of

the jurisdictions allow for samples to be pooled on kits with sensitivities high enough to avoid compromising results. The number of samples pooled ranged from two to five. Limits of detection refer to the lowest concentration of drug or metabolite that can be detected by the ELISA test. The majority of the jurisdictions (60%) allow this detectable concentration to be set by the manufacturer of the test kit. However, 40% exert at least some control over this concentration. Reasons for setting unique limits included the capability of the laboratory to confirm the presence of the drug at that particular concentration and the ability of the laboratory to conduct internal performance evaluations.

Thin Layer Chromatography

Thin layer chromatography has been the dominant screening methodology for more than 30 years. This position though, is starting to give way to instrumental screening and the aforementioned ELISA kits. Two jurisdictions have moved away entirely from TLC methodology. Two others indicated that TLC was used only as a targeted test method to test for drugs for which there was no coverage with ELISA kits or instrumental screening.

Simplified, TLC involves mixing the urine sample with a solvent to extract various drugs. This extracted sample is then "spotted" on a plate containing a porous medium, usually silica gel. This plate is then placed in a solvent that travels up the plate, carrying the drugs and other extracted substances with it. Drugs are identified based on differing degrees of migration up the plate and by color once the plate has been exposed to visualization reagents.

The main advantages of TLC over ELISA screening are cost and the ability to test a high number of samples for a large number of drugs. The cost advantage is diminished by the fact that TLC is not a process that can be automated easily, and therefore labor costs are much higher than for ELISA testing. TLC is also a relatively rapid screening technique and is a broad-spectrum technique, meaning that multiple drugs can be screened versus ELISA, which is drug or drug-group specific. TLC may not detect drugs found in very low concentrations (generally below 100 nanograms/ml). As a result, TLC has a higher rate of false negatives than does ELISA testing.

On average, those laboratories still screening 100% of samples on TLC run three to six extracts per sample. The most commonly identified extracts were

- base urine
- acid urine
- ion pair
- enzyme hydrolysis with base extract
- base hydrolysis with acid extract

There was a significant difference in the number of plates per sample, with the low being one and the high being 15. The average of all the responses was 8.5 plates per sample. Extracts of approximately 10 to 20 individual samples can be run on one TLC plate, and multiple drugs may be detected.

II. RCI CLASS 1, 2 AND 3 DRUGS

The RCI classification scheme was developed in 1991 and continues to be updated. The classification system is widely used by commissions in determining penalties for medication violations. Drugs are classified into five categories based on their pharmacology, their ability to influence the outcome of a race, whether they have legitimate therapeutic uses in the racing horse or other evidence that they may be used improperly. A committee of regulators, veterinarians and analytical chemists developed and update the classification system.

- Class 1 drugs are those with the highest potential to affect performance and with no generally accepted medical use in the racing horse.
- Class 2 drugs have a high potential to affect performance but less so than for Class 1 drugs. They also either have no generally accepted therapeutic use, or if they do, they have high potential for abuse.
- Class 3 medications may or may not have a generally accepted medical use in the racing horse, but their pharmacology suggests less potential to affect performance than Class 2 drugs.
- Class 4 and 5 medications are generally accepted as therapeutic medications with less potential to affect performance than Class 3 medications.
- In the most recent version of the classification, 748 drugs and metabolites have been classified into the five groups: 40 in Class 1, 302 in Class 2, 143 in Class 3, 244 in Class 4, and 19 in Class 5.

As a context for the Supertest results, the survey asked each commission to list all medication violations for the period 1997-1999 for Class 1, 2 and 3 drugs. To prevent skewing the results, commissions were asked to identify those calls that were blind or quality assurance samples so that they could be removed from the overall rates. Standardbred positives also were culled out.

Of the 508,737 samples tested from Thoroughbreds and Quarter Horses, there were 385 violations for 45 different medications categorized as Class 1, 2 and 3 drugs. (One violation not included in the breakdown by class was a sildenafil (Viagra®) positive. Because it is a relatively new drug, sildenafil has not yet been classified but is likely to fall into either Class 2 or 3.)

- 57 Class 1 calls
- 105 Class 2 calls
- 228 Class 3 calls

Only 10 of the 45 medications were detected on more than 10 occasions. They are (alphabetically) albuterol, caffeine, clenbuterol, cocaine, ephedrine, glycopyrrolate, lidocaine, metaraminol, promazine and pyrilamine. Clenbuterol alone accounts for 47% of the Class 3 violations and a statistically significant 28% of all Class 1, 2 and 3 violations reported during this time period. No other agent comes close to these numbers.

The list of the most commonly used kits for screening discussed in the ELISA testing section has a direct correlation with the list of most common Class 1, 2 and 3 positive calls. Of the 10 double-digit medications, only caffeine, glycopyrrolate and metaraminol would not be detectable from the list of 17 ELISAs. Metaraminol is a special case, as all 23 calls were made in a single jurisdiction and involved only Quarter Horse racing. The impact of new methodologies is shown by these calls, as they occurred shortly after the introduction of a new instrumental screening technique for the medication.

Bronchodilators, as a group, accounted for 130 of the 385 violations. Medication findings are classified below, based on the pharmacological action of the drug. This breakdown is somewhat subjective, as some of the drugs may have multiple effects.

| CLASSIFICATION | NUMBER | PERCENTAGE |
|-------------------|--------|------------|
| BRONCHODILATORS | 130 | 30% |
| STIMULANTS | 105 | 29% |
| LOCAL ANESTHETICS | 47 | 13% |
| SEDATIVES | 33 | 9% |
| ANALGESICS | 19 | 5% |
| OTHER (MISC.) | 51 | 14% |

Certain drugs and classifications of drugs are seen with greater regularity in all jurisdictions. These patterns will be helpful in channeling the development of new testing methodologies toward medications, and even families of medications, that have the highest potential for abuse. These patterns can also prove valuable in any discussion regarding threshold levels or the point at which administrative action is taken. For example, two of the drugs (caffeine and cocaine) with more than 10 violations have a high potential for environmental exposure, and three of the medications (promazine, glycopyrrolate and lidocaine) are used routinely for therapeutic purposes. The complete list of detected drugs can be found in Appendix F.

III. REGULATORY THRESHOLDS

Regulatory thresholds refer to the point at which administrative action is taken when a medication is detected. Regulatory thresholds are sometimes referred to as decision levels. The limit of detection discussed in the ELISA testing section is one form of a regulatory threshold. Regulatory thresholds are not necessarily derived from the limit of detection of a particular screening methodology, however. They can be set arbitrarily or by the best scientific evidence available on the point at which a particular medication has no therapeutic effect.

Because the Supertest samples were submitted in complete anonymity, it was important to determine what regulatory thresholds, if any, are used for various medications in each jurisdiction. The survey asked specifically for the regulatory thresholds on nine different medications, which are listed in the tables below. Acepromazine and promazine have been grouped together in the tables since the regulatory thresholds were the same for each medication. The list was derived from the RCI Class 1, 2 and 3 drugs with the most violations and also included medications that are thought to have the potential for environmental exposure.

Concentrations vary between states and on a medication-to-medication basis. As a consequence, what constitutes an actionable medication finding in one state may be ignored in another.

Abbreviation: ng/ml = nanograms/milliliter

Acepromazine/Promazine

| THRESHOLD | 25 ng/ml | 10 ng/ml | 2 ng/ml | 0 ng/ml | OTHER* |
|------------------|----------|----------|---------|---------|---------------|
| NUMBER REPORTING | 3 | 1 | 1 | 22 | 1 |

Albuterol

| THRESHOLD | 2 ng/ml | 1 ng/ml | 0 ng/ml | OTHER* |
|------------------|---------|---------|---------|---------------|
| NUMBER REPORTING | 1 | 2 | 24 | 1 |

Atropine

| THRESHOLD | 10 ng/ml | 0 ng/ml | OTHER* |
|------------------|----------|---------|---------------|
| NUMBER REPORTING | 2 | 25 | 1 |

Caffeine

| THRESHOLD | 100 ng/ml | 0 ng/ml | OTHER* |
|------------------|-----------|---------|---------------|
| NUMBER REPORTING | 4 | 22 | 2 |

Clenbuterol

| THRESHOLD | 10 ng/ml | 1 ng/ml | .5 ng/ml | .01 ng/ml** | 0 ng/ml | OTHER* |
|------------------|----------|---------|----------|-------------|---------|---------------|
| NUMBER REPORTING | 1 | 3 | 1 | 1 | 19 | 1 |

Cocaine and Metabolites

| THRESHOLD | 150 ng/ml | 100 ng/ml | 50 ng/ml | 0 ng/ml |
|------------------|-----------|-----------|----------|---------|
| NUMBER REPORTING | 2 | 1 | 1 | 24 |

Morphine

| THRESHOLD | 100 ng/ml | 50 ng/ml | 0 ng/ml |
|------------------|-----------|----------|---------|
| NUMBER REPORTING | 1 | 1 | 25 |

Scopolamine

| THRESHOLD | 0 ng/ml | OTHER* |
|------------------|---------|---------------|
| NUMBER REPORTING | 26 | 1 |

OTHER*

For jurisdictions credited with an "other" response, the survey answer indicated that the regulatory threshold was equal to the limit of detection of the testing methodology. A specific concentration was not provided.

****** This particular concentration is for clenbuterol in serum, while all others are concentrations in urine samples.

IV. ANTI-INFLAMMATORY MEDICATIONS

Steroidal Anti-Inflammatory Medications

The *corticosteroid*, or anti-inflammatory steroid group, is used in all types of medical practice, both human and veterinary. Corticosteroids most commonly are prescribed in the treatment of allergic conditions due to their ability to resolve inflammation quickly. They also are helpful in the treatment of asthmatic patients since inflammatory cells play a significant role in the disease mechanism. These conditions are seen in fairly high frequencies in stabled racehorses and generally are termed inflammatory airway disease. A more serious condition that is seen in some horses is chronic obstructive pulmonary disease (COPD). The layperson's term for this condition is "heaves." This condition also may be treated with steroidal anti-inflammatory medications. Corticosteroids also are used to relieve the general aches and pains associated with athletic performance, whether they are administered orally, parenterally (intravenously or intramuscularly) or intrarticularly (in the joint). Some of these medications also are used for an apparent calming effect that occurs when administered intravenously.

The table below summarizes the responses by the commissions when asked whether the presence of each of the steroidal anti-inflammatory medications outlined below constitutes a violation in their jurisdiction. Although many more anti-inflammatory steroids exist, these four were selected because they are very commonly used in routine veterinary practice.

| | Betamethasone | Dexamethasone | Prednisone | Prednisolone |
|------------------------------|---------------|---------------|------------|--------------|
| Yes, presence is a violation | 27 | 27 | 26 | 26 |
| No, presence not a violation | 2 | 2 | 3 | 3 |

NOTE: *Anabolic steroids* are those used for increasing muscle mass. They are a class of drug distinct from the corticosteroids. Although there are numerous variations, they are typically similar in makeup and in action to the male hormone testosterone. Two of the most popular brand names used in equine veterinary practice are Equipoise® and Winstrol®. Anecdotally, their usage in the racing Thoroughbred is usually to promote the building and repair of muscle mass and to increase aggressiveness in otherwise "timid" fillies or mares. As a group, they are rarely tested for by racing jurisdictions.

Non-Steroidal Anti-Inflammatory Drugs

The use of non-steroidal, anti-inflammatory drugs (NSAIDs) is more difficult to assess. Jurisdictions not only allow a differing menu of NSAIDs to appear in post-race samples but also allow different concentrations of the same medication to appear as well. Phenylbutazone, or "bute," which works in the horse like aspirin (another NSAID) does in humans, is a case in point.

Race-day administration of phenylbutazone is unrestricted in a number of jurisdictions, while in others it can appear only at permitted concentrations. These permitted concentrations can range from 2 micrograms/ml to 5 micrograms/ml in plasma. To adjust Supertest results for these significant differences would be virtually impossible, and, because the results would have little meaning, the non-steroidal anti-inflammatory medications phenylbutazone, flunixin (Banamine®), naproxen (Naprosyn®), and meclofenamic acid (Arquel®) were eliminated from the testing regimen.

A search of the various rulebooks indicated that these were the four most common NSAIDs allowed to appear in post-race samples. The survey then asked the commissions whether the presence of a non-steroidal anti-inflammatory medication, other than those listed above, would constitute a violation.

| | NUMBER OF JURISDICTIONS |
|------------------------------|----------------------------|
| Yes, presence is a violation | 26* |
| No, presence not a violation | 1** |

* In one responding "yes" jurisdiction, the non-steroidal anti-inflammatory medication ketoprofen is allowed to appear if present below a threshold concentration.

** In one responding "no" jurisdiction, the non-steroidal anti-inflammatory medication ketorolac, which is an RCI Class 3 drug, is not allowed to appear in post-race samples.

V. ANIMAL SELECTION

One of the key recommendations of "Building a World Class Drug Detection System for the Racing Industry," authored by McKinsey and Company, was to change the manner in which animals were selected for post-race testing. Specifically, the report recommended reducing the number of winners selected to 50% of the races and developing a practical system for determining when to test longshots and beaten favorites. Ideally, using this system would reduce the average number of animals selected to 1.5 per race, resulting in a significant reduction in testing costs while still serving as a deterrent.

The survey submitted to the jurisdictions attempted to determine whether, 10 years later, any of the commissions had adopted these strategies. The commissions were asked which of the top three finishers in a race were selected routinely for post-race testing. The survey also asked whether jurisdictions routinely select additional animals from stakes races, whether the wagering choices affect animal selection, and what circumstances would lead to the selection of a random horse.



Routine Animal Selection

The number of races run in 1999, using figures supplied by Equibase Company and the American Quarter Horse Association (AQHA), was 60,116, for the 30 jurisdictions responding to the survey. Therefore, the total number of winners tested in those 30 jurisdictions was 60,116 (not accounting for dead heats). The total number of races run in those five jurisdictions routinely selecting the place horse was 10,065. Assuming both blood and urine samples were taken from these animals, the total number of samples generated by routine animal selection equates to 140,362. Survey responses indicated that approximately 207,000 blood and urine samples were submitted for analysis in 1999. In other words, 68% of samples tested are from either first or second place finishers.

Stakes Race Animal Selection



ARE ADDITIONAL HORSES SELECTED IN STAKES RACES?

The majority of the jurisdictions do send additional horses to the test barn after stakes races. Virtually all jurisdictions that do more extensive testing in stakes routinely select the second- and third-place finishers. An additional 50% of those jurisdictions also collect samples from the fourth-place horse. (One jurisdiction, however, used the purse distribution to determine the additional runners selected, taking samples from horses that earned more than \$5,000 in the race.)

There were 2,317 races classified as stakes during the year 1999. Multiplying this figure by the 63% of the jurisdictions selecting additional horses in stakes races means that in some 1,460 races additional horses are selected. If an assumption is made that two additional horses are selected beyond the number selected in any other race, this would translate to 2,920 additional urine and blood samples from routine selections in stakes races. Adding these 2,920 samples to the total number of samples generated from the top finishers in all races brings the total number of routine samples to 143,282, or 69% of all samples tested.

Wagering Menu and Animal Selection



DOES THE WAGERING MENU AFFECT ANIMAL SELECTION?

The types of wagers offered in a particular race generally have little bearing on which animals are sent to the test barn; however, the stewards, in a number of jurisdictions, have discretion to direct horses for testing if unusual wagering trends are observed. Of the jurisdictions that responded the wagering menu does affect selection, the trifecta seems to have the most influence of all wagers, with some jurisdictions requiring the second- and third-place finishers to be tested. Overall, the impact of the wagering menu on routine animal selection statistics is negligible.

Random Animal Selection

Random selections account for the remaining 31% of the samples submitted for analysis. The commissions were asked what circumstances would dictate the selection of a random sample. The most frequent response for selecting a non-winner was the presence of a beaten favorite. Seventy-seven percent of the jurisdictions mentioned that this would likely result in the horse being directed to the test barn. Other circumstances frequently mentioned include

- horses showing dramatic form improvements / longshots finishing in the money (42%),
- horses that the commission has an investigative lead on (42%) and
- claimed horses, whether they are winners or not (31%)

The stewards are given wide discretion by most jurisdictions in selecting the random samples as well. Situations infrequently mentioned included horses that were pulled up or injured and horses that had previously tested positive.

VI. RESEARCH AND METHOD DEVELOPMENT

In a previous study conducted by the National Thoroughbred Racing Association and the University of Arizona Race Track Industry Program, the amount of money directed toward equine medical research directly from pari-mutuel handle topped \$5 million in the year 1999. A conservative estimate is that approximately 25% or \$1.35 million of the 1999 funding was used for studies that could lead to the development of new methods for drug detection. Four states-each having a university with laboratory facilities equipped for post-race sample analysis-are responsible for the vast majority of this research. Since all pari-mutuel funding mechanisms call for grants to be awarded intrastate, however, the capabilities of the research facilities within the state may limit growth in this area. Despite this fact, parimutuel wagering is, by far, the largest funder of research into drugs and drug detection.

Research into drug metabolism and detection also occurs at some of the state-run laboratory facilities. It is difficult to quantify the exact dollar contribution because research and development are typically components of a blanket contract cost. The figure in the chart below represents only those laboratories that were able to define the amount devoted to research.

The most mentioned source of funding for method development by the commissions was the Association of Racing Commissioners International (RCI) or Testing Integrity Program (TIP) quality assurance program. Jurisdictions that participate in this program pay dues annually, ranging between \$10,000 and \$20,000. The laboratory of the member jurisdiction is then allowed to participate in proficiency testing, method development and validation and drug administration programs. These administration programs lead to the ultimate development of standard operating procedures. Most commissions pay these dues from budgeted funds.



SOURCE OF MONEY FOR RESEARCH

VII. NUMBER OF SAMPLES TESTED AND DOLLARS SPENT

It is difficult to make valid comparisons between racing jurisdictions based on the number of samples submitted for analysis and the dollars expended by the various states. One reason is that states have vastly different breakdowns of Thoroughbred, Quarter Horse, Standardbred and Greyhound racing. Accounting for sample cost differences among various breeds is virtually impossible in a number of racing jurisdictions. Another obvious problem is the tremendous differences in the number of racing days and in the economic impact the sport has in any one jurisdiction.

The following model, based on survey responses and the assumptions outlined below, approximates spending on drug testing.

Assumptions

- 1. All expenses for equine testing, regardless of breed, are equal.
- 2. All expenses associated with Greyhound testing are 20% less than for equine samples.
- 3. Standardbred samples are not counted, and in jurisdictions with standardbred and Thoroughbred racing, figures are prorated based on the percentage of Thoroughbred samples.
- 4. Quarter Horse racing is included because many jurisdictions run mixed meets and/or mixed races for Quarter Horses and Thoroughbreds.
- 5. In jurisdictions with Greyhound racing, figures are prorated based on the percentage of Thoroughbred samples, but 20% of the total dollar expenditure is added back to account for the reduced expense of Greyhound testing as compared to equine testing.

The result is the adjusted chart that appears below:



DOLLARS EXPENDED ON THOROUGHBRED AND QUARTER HORSE POST-RACE SAMPLE TESTING

These figures are inadequate for comparative purposes, because they fail to account for the amount of racing occurring in a particular jurisdiction. In order to make this modification to the numbers, data was obtained from the Equibase Company and the American Quarter Horse Association regarding the number of races for 1999 in each racing jurisdiction. The charts below represent the number of races per jurisdiction.



NUMBER OF RACES BY JURISDICTION

We then simply divided the testing expense figure for each jurisdiction (Chart 1) by the number of races (Chart 2) to produce an average per race (Chart 3). Rather than organize these jurisdictions from highest to lowest, Chart 3 places the jurisdictions in the same order they appear in Chart 1 (dollars expended by jurisdictions). Jurisdictions AA and T do not appear on the first and third charts because Greyhound and/or Standardbred samples could not be segregated from the total number reported by the commission on the survey.



DOLLARS SPENT ON SAMPLE TESTING PER RACE

As shown in Chart 3, some jurisdictions with a limited amount of racing (e.g., jurisdiction BB) spend a relatively significant amount of money on post-race testing. The converse (e.g., jurisdiction Y) is also true. In any event, however, the correlation between spending and test effectiveness is not perfect. A jurisdiction may spend large amounts on testing, but those test methods may not be as effective as others costing less.

The survey also attempted to distinguish between costs associated with sample collection and laboratory services. Monetary comparisons between jurisdictions are extremely difficult due to the fact that a number of jurisdictions had blanket contracts or agreements that included both expenses. Comparisons can be made, however, as to which party was financially responsible for the expenses. In the vast majority of the jurisdictions, the racing commission was the entity responsible for payment, both for laboratory services and the expenses associated with collection.



WHO PAYS FOR LAB SERVICES?

WHO PAYS FOR COLLECTION EXPENSES?



VIII. AGREEMENTS BETWEEN LABS AND COMMISSIONS

Most jurisdictions have contractual agreements with their testing laboratories; however, 20% of the states-all having laboratory facilities intrastate-have statutory agreements in place. One inherent advantage of contracts that the survey revealed was the ability to insist on specific requirements that the laboratories had to live up to. Of the jurisdictions that had statutory agreements, only one had specific performance parameters for the laboratory built in.

Conversely, only two jurisdictions had contractual agreements with their laboratories that contained no specific performance parameters. The types of contract requirements listed by the majority of the jurisdictions included

- analytical methodologies the lab was required to perform;
- the number of tests to be done;
- the chain of custody procedures;
- quality assurance and accreditation requirements and
- the term and renewal process of the agreement.



COMMISSION-LABORATORY AGREEMENTS

RFP DOCUMENTATION

There is a strong correlation between the use of contractual agreements and the implementation of the Request for Proposal (RFP) process. Of the 21 jurisdictions employing contractual agreements, 81% used the RFP document to aid in determining which laboratory would be awarded a contract. None of the six jurisdictions with statutory agreements indicated that RFP's were utilized. Further, only one of the 13 jurisdictions (8%) with state-run or university-affiliated laboratories within the state used the RFP.

The usefulness of the RFP document is demonstrated by the survey responses. Fifty-seven percent of the respondents who indicated that RFPs were used said the document contained penalty clauses for failure of the laboratory to adhere to prescribed requirements. The penalties ranged from cancellation of the contract to fines for the late reporting of test results. Related to that issue, fully 92% of those jurisdictions using RFP's had some degree of monitoring capability written into the document, including visits to the lab and internal and external auditing procedures.

IX. SUPERTEST FINDINGS

A. <u>Buspirone hydrochloride</u>

1 confirmation in 1,272 samples

Trade name: BuSpar® RCI Classification: 2

Mechanism of Action:

Buspirone is an azapirodecanedione derivative. It is prescribed in human patients for the relief of mild to moderate anxiety and nervous tension.

Veterinary Indications:

The use of buspirone in veterinary medicine is extra label, as the U.S. Food and Drug Administration does not approve it for use in animals. There are anecdotal reports that buspirone does have a beneficial effect in the treatment of stereotypical behavior patterns in the horse such as stall weaving and cribbing. A literature search, however, could find no published references on the use of this drug in the horse, although there were several studies on the use of this drug in the dog and cat. Ancecdotally, it is used for its mood-altering effect prior to a horse's performance.

Explanation of Finding:

An ELISA test kit to screen samples for buspirone is available from TCC. Neogen does not currently have an ELISA kit capable of detecting this drug. There are four potential explanations as to why the Supertest was able to find this medication in the sample:

- The laboratory from the originating jurisdiction uses Neogen test kits exclusively;
- The buspirone kit was not in the rotation pattern at the time the sample was submitted;
- The concentration of this drug or its metabolites in the sample was too low to be detectable by TLC or other screening test;

1 confirmation in 1,272 samples

• The laboratory may have detected but did not recognize this relatively new drug.

B. <u>Caffeine</u> Trade name: multiple RCI Classification: 2

cation: 2

Mechanism of Action:

Caffeine is a naturally occurring xanthine derivative that exerts a mild and direct stimulating effect on the central nervous and cardiovascular systems. It also relaxes bronchial smooth muscle and has a mild diuretic effect. Theophylline, another xanthine derivative, is used widely for the treatment of pulmonary disease. Theophylline and theobromine are both metabolites of caffeine and often are reported together when found in post-race samples.

Veterinary Indications:

Although caffeine's metabolite theophylline has a number of indications in the treatment of respiratory disease in the horse, the parent compound is of limited value in the course of normal veterinary practice. Because of the presence of xanthines in coffee, soft drinks, and chocolate, caffeine has a high potential for environmental exposure, which is often the most likely explanation for positive findings.

Explanation of Finding:

Because of caffeine's high potential for environmental exposure, several states have adopted thresholds below which the finding does not constitute a violation. Using the survey responses, the most commonly mentioned threshold concentration is 100 ng/ml. This sample may have originated from such a jurisdiction. Since caffeine is widely tested for in post-race samples, a second possibility is that the laboratory missed detecting the presence of the drug.

C. <u>Clenbuterol hydrochloride</u> 9 confirmations in 1,272 samples

Trade name: Ventipulmin®, Spiropent® RCI Classification: 3

Mechanism of Action:

Clenbuterol is a beta-2 selective adrenoceptor agonist. Beta-2 adrenoceptors are found in a number of tissues in the body, including smooth muscles (involuntary) and the heart. By binding to the beta-2 adrenoceptors, clenbuterol allows the smooth muscle in the upper respiratory tract to relax, thus providing relief from restricted airways. This is the main therapeutic use of the drug. Clenbuterol also has a mild anabolic effect on muscle tissue, while at the same time exerting a catabolic effect on fat tissue when administered at doses higher than those used to produce a bronchodilating effect. It also stimulates the central nervous and cardiovascular systems.

Veterinary Indications:

Clenbuterol is not approved by the U.S. Food and Drug Administration for use in humans, but Ventipulmin® is approved for use in the horse. It typically is used for the treatment of inflammatory airway disease and chronic, obstructive pulmonary disease (COPD), often termed "heaves." There are numerous studies indicating that it is an effective symptomatic treatment for COPD.

Explanation of Finding:

For the purposes of the Supertest, a 1 ng/ml threshold concentration was employed. The 1 ng/ml threshold concentration was the most commonly mentioned on the survey responses. Had a lower threshold concentration been used in the Supertest, there would have been a much higher confirmation rate. There are several explanations for the Supertest findings:

- Because of its potential therapeutic benefits, jurisdictions aren't testing for it;
- Jurisdictions are using a threshold concentration that is higher than the threshold concentration used to report results from the Supertest;
- Jurisdictions are relying on TLC for the detection of this medication;
- There may be differences in the specificity between the Clenbuterol ELISA test and the Bronchodilator group ELISA test.

D. Clonidine hydrochloride

3 confirmations in 1,272 samples

Trade name: Catapres® RCI Classification: 3

Mechanism of Action:

Clonidine is an alpha-2 selective adrenergic agonist. Clonidine also acts on the central nervous system to produce a reduction in heart rate and dilation of the peripheral blood vessels. It is because of this central nervous system effect that clonidine has been widely prescribed for humans with high blood pressure. Very recently, clonidine also has been used in patients suffering from the effects of drug withdrawal and in patients with nervous tics and attention deficit disorder (ADD). Clonidine has mild analgesic and sedative properties.

Veterinary Indications:

Clonidine seems to have limited veterinary applications, unlike other alpha-2 agonists, xylazine and detomidine, which are used frequently as pre-anesthetic drugs and as sedatives in the horse. Most studies on clonidine have focused on its cardiopulmonary effects, with one study indicating a possible bronchodilating effect in the horse. With its recent success in treating humans with ADD, future studies may focus on equine repetitive behaviors such as cribbing, head shaking and stall weaving. The use in the horse is extra-label as the U.S. Food and Drug Administration does not approve it for use in animals.

Explanation of Finding:

Clonidine cross-reacts on an ELISA test with another alpha-2 adrenergic agent, romifidine. This particular ELISA kit is available only through TCC. This sample may have originated from a jurisdiction employing only Neogen kits. Until very recently, a method for detecting the presence of the drug was unavailable. This may explain why clonidine was not listed by any jurisdiction in response to the survey, which asked for positives called in the years 1997-1999. This demonstrates the impact of new testing methodologies, as clonidine was found not only in the Supertest but also in multiple samples in a single jurisdiction earlier this year. The other potential explanation is that clonidine may not have been used until recently.

E. <u>Cocaine</u>

1 confirmation in 1,272 samples

Trade name: none RCI Classification: 1

Mechanism of Action:

Cocaine is a sympathomimetic amine that has a direct, stimulating effect on the central nervous system. The effects of the drug are somewhat similar to those of amphetamine. In the same pharmacologic class as procaine and tetracaine, cocaine was studied years ago as a local anesthetic. Administered parenterally, the drug produces profound euphoria in humans and also has significant effects on the cardiopulmonary system. The metabolites of cocaine, benzoylecgonine and ecgonine methyl ester, usually are found in urine due to the fact that the parent drug is rapidly metabolized. The presence of cocaine in urine is an unusual finding.

Veterinary Indications:

There is no legitimate therapeutic use for cocaine in the horse. Although it could be potentially used as a local anesthetic, there are more effective local anesthetic drugs that are not controlled substances. Because it is a highly abused drug among humans, horses may be exposed to this drug environmentally.

Explanation of Finding:

Because of cocaine's potential for environmental exposure, several racing commissions have adopted thresholds below which the finding does not constitute a violation. This sample may have originated from such a jurisdiction. Using the survey responses, four jurisdictions have threshold concentrations for cocaine ranging from 50 ng/ml to 150 ng/ml. Since cocaine is widely tested for in post-race samples, a second possibility is that the laboratory missed detecting the presence of the drug.

F. <u>Dextromoramide bitartrate</u>

1 confirmation in 1,272 samples

Trade name: Palfium®, Narcolo® RCI Classification: 1

Mechanism of Action:

Dextromoramide, a synthetic analogue of methadone, is a narcotic analgesic. The analgesic potency of the drug is two to four times that of morphine. It has a rapid onset of effect with a relatively short duration of action. Dextromoramide is used to relieve severe pain associated with surgery or long-term illnesses such as cancer. It has no U.S. Food and Drug Administration approval for any use, human or animal, in this country.

Veterinary Indications:

There is no legitimate therapeutic use in the horse. A literature search found only one reference to the drug for veterinary use, a study on post-operative pain relief in the cat.

Explanation of Finding:

An ELISA test kit is available to screen samples for dextromoramide through TCC. Neogen does not currently have an ELISA kit capable of detecting this drug. There are four potential explanations as to why the Supertest was able to find this drug in the sample:

- The laboratory from the originating jurisdiction uses Neogen test kits exclusively;
- The dextromoramide kit was not in the rotation pattern at the time the sample was submitted;
- The concentration of the drug in the sample was too low to be detectable by TLC;
- The laboratory detected the drug or its metabolites but failed to identify it.

G. Guanabenz acetate

4 confirmations in 1,272 samples

Trade name: Wytensin® RCI Classification: 3

Mechanism of Action:

Like clonidine, guanabenz is an alpha-2 selective adrenergic agonist. Guanabenz also acts on the central nervous system to produce a reduction in heart rate and dilation of the peripheral blood vessels. As a result of these effects, guanabenz has been prescribed for humans with high blood pressure. Guanabenz, like the other alpha-2 agonists, also has analgesic and sedative properties.

Veterinary Indications:

A literature search on guanabenz could find no references to its use in veterinary medicine. The use in the horse is extra-label, as the U.S. Food and Drug Administration does not approve it for use in animals.

Explanation of Finding:

A guanabenz-specific ELISA test kit is now available through Neogen. Guanabenz cross reacts with the TCC ELISA kit for detomidine, another alpha-2 agent. However, until very recently, a method for confirming the presence of guanabenz in urine was unavailable. This new technique for the identification of the parent drug in urine requires instrumental techniques, which are not used by a number of jurisdictions but were used in the Supertest. This leads to a number of explanations for these findings:

- The laboratory from the originating jurisdiction does not use the instrumental technique necessary for confirmation;
- The laboratory from the originating jurisdiction was unaware of this confirmation technique;
- The concentration of drug in the sample was too low to be detectable by TLC;

- The guanabenz or detomidine kit was not in the rotation pattern at the time the sample was submitted;
- The sample emanated from a racing jurisdiction permitting the use of guanabenz as a bleeder medication.

H. <u>Tripelennamine hydrochloride</u> 2

2 confirmations in 1,272 samples

Trade name: Re-Covr®, PBZ® RCI Classification: 3

Mechanism of Action:

Tripelennamine is an ethylenediamine anti-histamine. Anti-histamines block H1 or H2 receptors, preventing the effects of histamine on the respective tissues involved. This particular class of anti-histamines blocks H1 receptors, which are important in the symptomology of allergic conditions. At low doses, tripelennamine has a mild sedating effect, while at high doses it can act as a central nervous system stimulant.

Veterinary Indications:

Tripelennamine and another anti-histamine in the same class, pyrilamine (Histavet®), are both approved by the FDA for use in horses. They are used primarily to treat the symptoms associated with allergies. Since inflammatory airway disease is thought to have an allergic component, these anti-histamines would be routinely used in the therapy of this condition. They also would likely be used for the treatment of skin conditions associated with allergies, such as hives.

Explanation of Finding:

An ELISA test kit is available to screen samples for pyrilamine through Neogen. Tripelennamine cross-reacts with this kit. TCC does not currently have an ELISA kit capable of detecting this drug. There are five potential explanations as to why the Supertest was able to find this medication in the sample:

- The laboratory from the originating jurisdiction uses TCC test kits exclusively;
- The pyrilamine kit was not in the rotation pattern at the time the sample was submitted;
- The concentration of drug metabolite in the sample was too low to be detectable by TLC;
- Because of its potential therapeutic benefits, jurisdictions aren't testing for it;
- The laboratory detected the metabolite of the drug but didn't report it because an authentic standard is not available.

Summary of RCI Class 1, 2 and 3 Findings

- 22 confirmations in 1,272 samples
- Two Class 1 confirmations in 1,272 samples
- Two Class 2 confirmations in 1,272 samples
- Eighteen Class 3 confirmations in 1,272 samples
- Clenbuterol accounts for 50% of the Class 3 calls and 41% of the overall calls
- Bronchodilating medications account for 41% of the calls
- Alpha-2 adrenergic medications account for 32% of the calls

X. RECOMMENDATIONS

RECOMMENDATION 1

Post-race samples should undergo a more rigorous screening process than is currently performed in most jurisdictions.

Background:

Based upon the survey responses, most jurisdictions use a combination of TLC and ELISA to screen samples. TLC has an advantage in that it is very cost effective and can analyze samples for a wide variety of drugs. ELISA's advantages are that it is a highly sensitive method and very specific. Because TLC generally lacks the sensitivity of ELISA, it may not detect some drugs in low concentrations (below 100 ng/ml). The Supertest used no TLC, instead focusing on ELISA and instrumental methodologies. Because of this difference in screening technique, the Supertest was able to identify gaps in the detection of certain medications.

Implementation:

- Develop a database of drugs and metabolites that can be detected by current screening methodologies.
- Using the database, determine which drugs can be detected by multiple screening techniques and which can be detected only by using a single available technique.
- Transition away from TLC (other than for drugs and metabolites that only this technique can find or that do not affect the performance of horses if found in sub-TLC amounts) toward more sensitive techniques such as ELISA and instrumental techniques.
- Develop strategies to reduce costs associated with post-race testing.
- Urge states to contract with separate laboratories and submit a small number of samples for more rigorous testing.
- Pursue the development of cooperative alliances for the purchasing of test kits and equipment.
- Rotate ELISA test kits frequently to increase the number of drugs covered in the screening scheme.
- Utilize ELISA kits from more than one producing company.
- Support the development and validation of new tests including ELISA tests.

- Increases likelihood of detecting high-potency, low-concentration drugs.
- Possibly increases efficiency due to utilization of screening methodologies that can be automated.
- Creates a drug and metabolite database accessible to both laboratories and commissions.
- Makes ELISA kits more widely available.
- Potentially reduces cost once a cooperative purchasing system is established.
- Lessens likelihood of differing methodologies when split samples are tested.

Jurisdictions should re-assess medication rules and enforcement policies in light of new and more sophisticated testing methodologies.

Background:

Under current testing protocols, a sample is not reported as positive for a prohibited substance unless a drug is identified and the drug's identity is confirmed. Except for those few permitted medications or substances for which decision levels have been established, e.g., phenylbutazone, the presence of a drug in a sample at any level is deemed to be a positive test. This may have been a reasonable policy when the only screening method was TLC. However, with the development of more sensitive screening techniques such as ELISA and instrumental methods, there is now the ability to detect drugs in very low concentrations. This has presented the industry with a dilemma. This has been a significant improvement in testing, since many drugs may affect performance at very low doses and result in urine and blood concentrations in the low nanogram per milliliter range. On the other hand, such testing also can result in a medication violation even when a drug has been administered solely for therapeutic purposes in the course of routine veterinary treatment or where environmental exposure is alleged to have occurred. Moreover, this dilemma is further complicated by the fact that certain permitted medications may affect the laboratory's ability to detect the presence of drugs in the samples being tested. The industry needs to address this issue so that it effectively punishes those who damage the integrity of the sport vet recognizes the therapeutic aspects of animal management and scientifically documented environmental causes. A review of regulations regarding the administration of permitted medications also should be conducted to ensure that these permitted medications are not causing interference with laboratory capabilities.

Implementation:

- Obtain from laboratories the inherent limits of detection of the screening methodologies employed to detect each substance.
- Using information developed from Recommendation 1, determine where differences between inherent limits of detection and recommended thresholds occur.
- Review existing literature on the pharmacology of drugs and, if necessary, conduct research on those drugs with little or no previously published information.
- Conduct research on the effect permitted medications have on the ability to screen samples accurately.
- Conduct research to shed additional light on potential environmental sources altering test results.
- Alter the wording in rulebooks accordingly.
- Communicate this regulatory threshold concept to trainers and veterinarians.

- Focuses resources more on intentional administrations of drugs to affect the race-day performance of the horse.
- Lessens the negative publicity for the industry from errors in medication administration.
- Lessens the need for analysts to provide expert testimony regarding analytical findings.
- Increases public confidence in the ability to detect performance-altering drugs.
- Facilitates the shipping of horses between jurisdictions for race competition.
- Creates a framework for dealing with new medications on the market or others with significant therapeutic value.

Begin the development of withdrawal guidelines for commonly used therapeutic medications.

Background:

Based on the findings of the survey, which benchmarked the medication violations of 30 racing jurisdictions over a three-year period, a total of nine drugs account for almost 75% of all the violations reported for RCI Class 1, 2 or 3 drugs. Of those nine medications, six can be considered therapeutic. In addition to the survey results, 11 of the Supertest confirmations were for medications that are FDA approved for use in the horse, e.g., clenbuterol and tripelennamine. Despite this fact, the negative publicity the sport receives when a violation is reported is independent of the usage of the medication or the concentration at which it was found. In order to minimize this negative publicity and to provide veterinarians and trainers with guidelines, the recommendation is to begin the development of therapeutic medication guidelines similar to the system used in Canada. These nine medications that comprise the most frequently called positives are suggested as a starting point, with other medications added as they are researched.

Implementation:

- Develop an alliance of stakeholders, including commissions, to discuss the current research and reach a consensus on whether thresholds or withdrawal times for specific therapeutic medications should be set.
- For those drugs for which the alliance desires to have thresholds set or withdrawal times established, develop procedures for determining what those thresholds/withdrawal times should be.
- Survey practicing veterinarians to identify those medications that have a true therapeutic value in the racing animal.
- Perform a literature search to accumulate research already conducted on the pharmacokinetic and pharmacodynamic properties of this list of medications.
- Commence research on the properties of medications with little or no previously published information.
- Publish educational materials for practicing veterinarians and trainers to inform them of withdrawal periods for each medication and thereby minimize violations.
- Develop a standard written agreement between the commission and laboratory to report violations only when concentrations exceed an established threshold.
- Provide a method for administrative handling of routine overages of designated therapeutic medications without publicly charging trainers and owners with rule violations.

- Reduces violations for mistakes in medication administration due to inadequate or insufficient information.
- Reduces time and expense of litigation.
- Lessens the need for analysts to provide expert testimony regarding analytical findings.
- Provides horsemen and veterinarians with administrative guidelines for the use of medications most critical to the welfare of the racing animal.
- Lessens negative publicity for the industry from errors in medication administration.
- Creates a structure for ongoing dialogue on new medications that reach the marketplace and for establishing research priorities on a national level.
- Facilitates the shipping of horses between jurisdictions for race competition.

Develop and implement a national external quality assurance program for laboratories conducting post-race sample testing.

Background:

There have been two independent reports in the last 10 years on the state of post-race drug testing. Both have recommended the development or enhancement of quality assurance programs. In response to the first report, RCI developed a quality assurance program, which is still in existence and administered by RCI and utilizing the services of the Testing Integrity Program (TIP) and the Interstate Drug Testing and Research Program (IDTRP). Unfortunately, laboratory participation in a single QAP program is not 100%. There are a number of reasons for this, including an ideological rift between analysts belonging to TIP and IDTRP. The most recent assessment of post-race testing, "Equine Drug Testing: An Assessment of Current Practices and Recommendations for Improvement," was authored by a scientific advisory committee put together by the National Thoroughbred Racing Association's Task Force on Racing Integrity and Drug Testing (see Appendix A). The committee, which was composed of analytical chemists outside the racing industry, noted, "With the wide variance in testing procedures, it is crucial that a quality assurance program be in place to monitor the performance of the analysts and to document the accuracy and reliability of the test measurements." Due to the lack of a cohesive national program, commissions are sometimes left to their own limited resources to determine laboratory performance.

Implementation:

- Develop an oversight body composed of racing commissions, laboratory analysts and national organizations.
- Reach consensus on substances to be tested for in a quality assurance program.
- For those substances to be tested for by the quality assurance program, determine by administration what the range in concentration is likely to be in post-race samples.
- Prepare urine and blood samples taken from horses that have been administered drugs of interest at doses used to affect the performance of horses in races.
- Send these samples to testing laboratories as routine samples taken from horses at racetracks after preparing forensically sound confirmatory samples.
- Report results to the oversight body, including accuracy and reproducibility specifications.
- Analyze results via oversight body, and provide feedback to commissions and laboratories.
- Provide analytical aid to laboratories with testing problems for any of the substances.

- Fosters a spirit of communication and cooperation between analysts and commissions.
- Develops and disseminates best practices and standard operating procedures.
- Provides a framework for assistance and improvement of laboratory procedures when problems are identified.
- Could lead to the development of a national accreditation program for laboratories.

A national organization, including regulators, should be formed to implement improvements in drug testing and provide leadership in jurisprudence and public communication practices related to drug-testing issues.

Background:

The racing industry is fragmented in the area of drug testing, regulatory enforcement and medication research. For example, based upon our survey, it can be estimated that the post-race collection and testing of samples is a \$25 million industry in the United States. Given the litigious nature of some medication findings, it is possible an equal amount may be spent adjudicating these cases nationwide. However, it appears that less than \$1.5 million is spent annually studying the effects of medications on the horse and on the development of new screening and confirmation methods. Of this amount, most is spent on an intrastate basis, and there is little evidence that ongoing research in other jurisdictions is taken into account, invariably leading to duplication and wasted resources. These inconsistencies can have the unintended effect of undermining the credibility of testing and enforcement, because the general public often cannot differentiate between a serious violation and a therapeutic medication used too close to race-day.

Implementation:

- Form a national organization, including representatives of regulators, owners and trainers, racetracks, veterinarians and scientists, to implement recommendations in this report.
- Develop mechanisms to avoid duplication of research efforts.
- Commission the additional research necessary to address voids in current testing and to identify funding resources.

Potential Research Projects:

- Comparative performance-enhancing effects of bronchodilators on racehorse populations in the racetrack environment.
- Absorption, distribution, metabolism and elimination studies on medications delivered via nebulization.
- Absorption, distribution, metabolism and elimination studies on medications delivered via intrarticular injection.
- Development of experimental models to differentiate accidental environmental exposure from purposeful administration.
- Differentiation of opiates using analytical markers.
- Absorption, distribution, metabolism, and elimination studies on human mood-altering medications in the horse.
- Systemic effects of clenbuterol and other beta agonists on the racing horse.
- Development of new ELISA test kits.
- Development of more extensive libraries for instrumental screening techniques.
- Effects of multiple permitted medications on the ability to screen samples accurately.

- Improves efficiency of communication on drug testing matters within the industry.
- Coordinates research priorities so duplication can be avoided.
- Provides leadership in jurisprudence reform and the development of uniform penalties.
- Provides a framework for scientific discussion on new medications brought to the marketplace.

ACKNOWLEDGMENTS

We are truly grateful to the people listed on these pages. Without their time and effort, this document would not have been possible. Our hope is that the information presented here is worthy of that time and effort. We look forward to much future collaboration.

Mr. A. Melvin McDonald Chairman Arizona Department of Racing

Mr. Wade Turner Executive Director Arizona Department of Racing

Dr. Leslie Salmons State Veterinarian Arizona Department of Racing

Mr. Cecil Alexander Chairman Arkansas State Racing Commission

Mr. Robert Cohee Manager Arkansas State Racing Commission

Dr. Dean Hunter State Veterinarian Arkansas State Racing Commission

Mr. Robert Tourtelot Chairman California Horse Racing Board

Mr. Roy Wood, Jr. Executive Director California Horse Racing Board

Dr. Ron Jensen Equine Medical Director California Horse Racing Board

Dr. Scott Stanley Director Davis Equine Analytical Chemistry Lab

Mr. Gale Davey Chairman Colorado Racing Commission Mr. David Reitz Director Colorado Racing Commission

Dr. Earl Carlson State Veterinarian Colorado Racing Commission

Mr. Bernard Daney Chairman Delaware Racing Commission

Mr. John Wayne Administrator Delaware Racing Commission

Mr. Joseph Strug Laboratory Director Dalare Associates

Dr. Paul Kirsch Chairman Florida Division of Pari-Mutuel Wagering

Dr. Ian Tebbett Director University of Florida Racing Laboratory

Ms. Margaret Wilding Associate Director University of Florida Racing Laboratory

Mr. David Tiffany Scientific Research Manager University of Florida Racing Laboratory

Mr. Marvin Aslett Chairman Idaho State Racing Commission

Mr. Dick Cade Commissioner Idaho State Racing Commission Mr. Ralph Gonzalez Chairman Illinois Racing Board

Mr. Jack Kubik Executive Director Illinois Racing Board

Ms. Shelley Kalita Director Illinois Racing Board Laboratory

Mr. Mark Benoit Assistant Laboratory Director Illinois Racing Board Laboratory

Mr. Nicholas Stein Chairman Indiana Horse Racing Commission

Mr. Joe Gorajec Executive Secretary Indiana Horse Racing Commission

Mr. W. R. Hansen Chairman Iowa Racing and Gaming Commission

Mr. Jack P. Ketterer Administrator Iowa Racing and Gaming Commission

Dr. Walter Hyde Iowa State University Veterinary Diagnostic Laboratory

Mr. Gene M. Olander Chairman Kansas Racing Commission

Mr. Tracy Diel Executive Director Kansas Racing Commission

Dr. Bryce Peckham State Veterinarian Kansas Racing Commission

Mr. Frank Shoop Chairman Kentucky Racing Commission Mr. Bernard J. Hettel Executive Director Kentucky Racing Commission

Dr. Mitzi Fisher State Veterinarian Kentucky Racing Commission

Dr. Thomas Tobin Professor of Toxicology Gluck Equine Research Center

Mr. Albert M. Stall Chairman Louisiana State Racing Commission

Mr. Charles A. Gardiner III Executive Director Louisiana State Racing Commission

Dr. Steven Barker LSU Equine Medication Surveillance Laboratory

Mr. John Franzone Chairman Maryland Racing Commission

Mr. Kenneth A. Schertle Executive Director Maryland Racing Commission

Mr. Michael Hopkins Deputy Executive Director Maryland Racing Commission

Mr. Thomas Lomangino Director Maryland Racing Commission Laboratory

Mr. Robert Hutchinson Chairman Massachusetts Racing Commission

Ms. Elizabeth M. Barry Executive Secretary Massachusetts Racing Commission Mr. Bruce Aspeslagh Director Massachusetts State Racing Commission Laboratory

Ms. Annette Bacola Commissioner Michigan-Office of Racing Commissioner

Mr. Jim Bowes Deputy Commissioner Michigan-Office of Racing Commissioner

Mr. Thomas Whalen Director Geagley Laboratory

Dr. Steve Reh Director of Operations Geagley Laboratory

Ms. Cindy Piper Chairwoman Minnesota Racing Commission

Mr. Richard Krueger Director Minnesota Racing Commission

Mr. Joe Erickson Chairman State of Montana Board of Horse Racing

Mr. Sam Murfitt Executive Secretary State of Montana Board of Horse Racing

Mr. Dennis Lee Chairman Nebraska State Racing Commission

Mr. Dennis Oelschlager Executive Secretary Nebraska State Racing Commission

Mr. Timothy J. Connors Chairman New Hampshire Pari-Mutuel Commission Mr. Paul Kelley Director New Hampshire Pari-Mutuel Commission

Ms. JoAnne Dufort Head Racing Chemist New Hampshire Pari-Mutuel Commission Laboratory

Ms. Noel Love Gross Chairwoman New Jersey Racing Commission

Mr. Frank Zanzuccki Executive Director New Jersey Racing Commission

Mr. Tony Socci Assistant Director New Jersey Racing Commission

Mr. Greg Copsetta Chief Inspector New Jersey Racing Commission

Mr. Phil Lorimer Director Meadowlands Laboratory

Mr. Billy R. Blackburn Chairman New Mexico Racing Commission

Mr. Julian Luna Executive Director New Mexico Racing Commission

Mr. Wayne Conwell Medication Manager New Mexico Racing Commission

Mr. Michael J. Hoblock, Jr. Chairman NYS Racing and Wagering Board

Mr. Edward Martin Executive Director NYS Racing and Wagering Board Mr. Joseph Lynch Manager of Racing Operations NYS Racing and Wagering Board

Dr. George A. Maylin Director Equine Drug Testing Program

Mr. C. Luther Heckman Chairman Ohio State Racing Commission

Mr. Clifford A. Nelson II Executive Director Ohio State Racing Commission

Mr. Steve Zaper Investigator Ohio State Racing Commission

Dr. Rick Sams Director Analytical Toxicology Laboratory Ohio State University

Mr. Gordon Hare Executive Director Oklahoma Horse Racing Commission

Mr. Benny Lovett Director of Law Enforcement Oklahoma Horse Racing Commission

Dr. Rudy Garrison State Veterinarian Oklahoma Horse Racing Commission

Mr. Stephen S. Walters Chairman Oregon Racing Commission

Mr. Steve Barham Executive Director Oregon Racing Commission

Mr. Ben H. Nolt, Jr. Executive Secretary Pennsylvania Horse Racing Commission Mr. Cuyler H. Walker Chairman Pennsylvania Horse Racing Commission

Mr. Joe Mushalko Director Pennsylvania Horse Racing Commission

Dr. Cornelius Uboh Director Pennsylvania Equine Toxicology and Research Laboratory

Ms. Terri Lacy Chairwoman Texas Racing Commission

Mr. Mike Burleson Deputy Director-Racing Operations Texas Racing Commission

Ms. Paula Flowerday Executive Secretary Texas Racing Commission

Dr. Stewart Marsh Chief Veterinarian Texas Racing Commission

Dr. Allen Ray Texas Veterinary Medical Diagnostic Laboratory

Ms. Robin Traywick Williams Chairwoman Virginia Racing Commission

Mr. Stanley K. Bowker Executive Secretary Virginia Racing Commission

Ms. Barbara Shinpoch Chairwoman Washington Horse Racing Commission

Mr. Bruce Batson Executive Secretary Washington Horse Racing Commission Mr. James T. McClure Chairman West Virginia Racing Commission

Ms. Linda Lacy Executive Secretary West Virginia Racing Commission

Mr. Kent Orchard Chairman Wyoming State Pari-Mutuel Commission Mr. Frank Lamb Executive Director Wyoming State Pari-Mutuel Commission

Ms. Petra Hartmann Manager Industrial Laboratories

Mr. Chris Nattrass Racing Chemistry Manager Truesdail Laboratories

Ms. Jeanne B. Mahoney President Center of Tox Services

APPENDIX A

The Scientific Advisory Committee was composed of the following individuals:

- Dr. Melvin V. Koch-Chairman (Director, Center for Process Analytical Chemistry, University of Washington, Seattle, Washington)
- Wayne W. Blaser (WBI Associates, Midland, Michigan)
- Kent L. Hodges (Michigan Molecular Institute, Midland, Michigan)
- Dr. Roger A. Parker (Nobilent, Inc., Cincinnati, Ohio)
- Dr. James C. Tou (Chief Analytical Scientist, retired, Dow Chemical, Midland, Michigan)

APPENDIX B

STATES AND RACETRACKS PARTICIPATING IN THE SUPERTEST

<u>ARIZONA</u>

Turf Paradise

ARKANSAS Oaklawn Park

CALIFORNIA

Bay Meadows Del Mar Golden Gate Fields Hollywood Park Oak Tree at Santa Anita Santa Anita

DELAWARE

Delaware Park

FLORIDA

Calder Gulfstream Park Hialeah Tampa

ILLINOIS

Arlington Park Hawthorne Sportsman's Park

INDIANA Hoosier Park

IOWA Prairie Meadows

<u>KANSAS</u>

Eureka Downs The Woodlands

KENTUCKY

Churchill Downs Ellis Park Keeneland Turfway Park 40 samples

40 samples

19 samples30 samples14 samples61 samples25 samples51 samples

40 samples

- 44 samples 112 samples 28 samples 16 samples
- 60 samples 20 samples 20 samples

40 samples

40 samples

10 samples 10 samples

70 samples 20 samples 90 samples 20 samples

LOUISIANA

Fair Grounds25 samplesLouisiana Downs15 samplesDelta Downs10 samplesEvangeline Downs10 samples

MARYLAND

Laurel Pimlico

MASSACHUSETTS Suffolk Downs

MICHIGAN Great Lakes Downs

<u>MONTANA</u>

Great Falls Great Montana Fair

<u>NEBRASKA</u>

Fonner Park Lincoln Columbus Omaha

NEW HAMPSHIRE

Rockingham Park

NEW JERSEY

Meadowlands Monmouth Park

NEW YORK

Aqueduct Belmont Park Finger Lakes Saratoga

<u>OHIO</u>

Thistledown Beulah Park River Downs 10 samples

50 samples 50 samples

20 samples

20 samples

10 samples 10 samples

10 samples 5 samples 3 samples 2 samples

20 samples

50 samples 50 samples

65 samples75 samples20 samples40 samples

24 samples18 samples18 samples

OKLAHOMABlue Ribbon Downs15 samplesFair Meadows5 samplesRemington18 samplesWill Rogers2 samples

OREGON

Portland Meadows

PENNSYLVANIA

Penn National Philadelphia

TEXAS

Lone Star Park Retama Park Sam Houston

VIRGINIA

Colonial Downs

WASHINGTON

Emerald Downs

WEST VIRGINIA

Charles Town Mountaineer Park

WYOMING

Wyoming Downs

20 samples

20 samples

30 samples

30 samples

40 samples

10 samples

10 samples

20 samples

20 samples

10 samples

10 samples

TOTAL

1,800 samples

APPENDIX C

Standard Operating Procedures for the Handling and Shipping of Samples for NTRA Extensive Testing

- 1. Selected samples should be thawed and transferred to NTRA test cups and refrozen. The shipment and delivery of the polyfoam container to the recipient laboratory should be made during the workweek. Although the Task Force isn't concerned with chain of evidence requirements, we want to ensure that test samples arrive in the best possible condition for extensive testing. We want to avoid having samples shipped any later than a Wednesday, to prevent test samples from arriving when lab personnel might not be available.
- 2. The contents of the test sample should be shaken or stirred to ensure a uniform distribution. It should then be decanted (poured) into a NTRA specimen cup and sealed with a lid. This should be a one-cup to one-cup transfer only. The sample contents should be transferred to an NTRA cup in a cold liquid state and then re-frozen prior to transport to the recipient laboratory.
- 3. The NTRA test cup should only be filled to the shoulder of the cup. The neck of the cup should not be filled. This will prevent leakage when the sample is frozen prior to shipment.
- 4. All samples shall be transported in provided polyfoam packers with an icepack to ensure that test samples arrive in a frozen state the day after shipping.
- 5. Frozen samples should be placed in an upright position. This can be accomplished by lining up test samples along the wall of the polyfoam packer and placing the icepack in the center of the samples.
- 6. Only the pre-printed FedEx invoices should be used. This will provide the NTRA Drug Testing Task Force as the sender with a 444 Madison Ave., Suite 503, New York, NY 10022 address as the billable party. The name and the address of the recipient laboratory will also be pre-printed.
- 7. All packages should be sent via FedEx Standard Overnight Delivery. *Please note: that box should be checked as in the attached sample airbill in Item #4a.
- 8. Item #5 on the airbill should be checked as Other Package.
- 9. If you have any questions regarding these procedures please call Jim Gallagher at 212-907-9288 or write to my e-mail address at jgallagher@ntra.com.

APPENDIX D

First Questionnaire Sent to Commissions

- 1. How much is spent (laboratory/collection expenses) for drug testing in your jurisdiction annually?
 - a. Laboratory Services
 - b. Collection Expenses _____
- 2. What entity (commission or racing association) pays for laboratory services and collection expenses?
 - a. Laboratory Services _____
 - b. Collection Expenses _____
- 3. What are the total costs to the racing jurisdiction or racing association for laboratory services? (Please include all expenses-personnel (# of employees), facility, equipment, total capital costs of instruments and supplies)
 - a. Personnel ()_____
 - b. Facility
 - c. Equipment
 - d. Instruments _____
 - e. Supplies
 - f. Overhead
 - g. QA/QC
 - h. Other

4. What are the total costs to the racing jurisdiction or racing association for sample collection?

(Please include costs for personnel, shipment and supplies)

- a. Personnel
- b. Shipping
- c. Supplies
- d. Other

| 5. | How is the amount | paid to the | testing laborator | y calculated? | Lump S | Sum | Per | Test |
|----|-------------------|-------------|-------------------|---------------|--------|-----|-----|------|
|----|-------------------|-------------|-------------------|---------------|--------|-----|-----|------|

6. Can a specific laboratory fee be attributed to analyzing blood on a per sample basis?

Yes No

7. If yes, please provide that cost ______

8. Can a specific laboratory fee be attributed to analyzing urine on a per sample basis?

____Yes ____No

9. If yes, please provide that cost _____

 Are corresponding blood and urine samples treated as one sample in the determination of laboratory fees? _____Yes _____No

11. If yes, please provide that cost _____

| 12. | What kind of agree | ment does your j | urisdiction have with the laboratory that performs testing? |
|-----|--------------------|------------------|-------------------------------------------------------------|
| | Contract | Statutory | Other (Please explain) |

Are there specific requirements for testing samples detailed in your drug testing agreement? Yes No

- 13. If yes, please enumerate (i.e.- types and number of tests, equipment required, quality assurance/ proficiency/external blind sample requirements, standards for declaring positives, etc.)
- 14. Do you employ a Request for Proposal (RFP) document in contracting with your testing laboratory?
 Yes _____ No

15. If yes, does it contain the elements referred to in Question 14 above? _____ Yes _____ No

16. Are penalties assessed against the laboratory for failure to meet the standards outlined in the RFP?
Yes _____ No

17. If yes, what are they?

 Is there any monitoring capability or responsibility within the jurisdiction to ensure that all the terms of the agreement are being fulfilled? _____ Yes ____ No If yes, please explain.

19. What is the process for renewing an RFP?

20. Does your jurisdiction collect blood samples for testing? ____Yes ____No

21. Are all blood samples analyzed? _____ Yes _____ No

22. What drugs are tested for in blood?

23. Number of samples analyzed in 1999? Please specify the number of bloods and urines tested.

- a. Number of blood samples:
- b. Number of urine samples:

If incorporated in an annual report, please furnish a copy.

24. Names of the drugs and drug metabolites reported by the laboratory during the past 3 years. (If possible, please cite ARCI classification)

If there is insufficient space, please attach a listing.

- 25. What screening techniques led to the detection of each individual ARCI Class 1, 2 and 3 substances reported by the laboratory during the past 3 years?
- 26. What is the total number of ELISA tests routinely run per test sample? Please identify those ELISA tests that comprise the routine test procedure for each test sample.
- 27. Are other ELISA tests rotated into the screening process? If so, please identify them:
- 28. How often are these tests rotated into the screening process?
- 29. Are time limits imposed upon the laboratory to screen samples? _____Yes _____No
- 30. If yes, in what time period must samples be screened?
- 31. Are time limits imposed upon the laboratory to confirm samples? Yes No
- 32. If yes, in what time period must samples be confirmed?
- Does your jurisdiction pool samples in performing ELISA screening?
 Yes No
- 34. If yes, how many samples are pooled?
- 35. Are the limits of detection for the ELISA tests set by the manufacturer?
 - ____Yes ____No
- 36. If not, how are these parameters set and by whom?
- 37. What other screening techniques are routinely employed in urine?

 Number of extracts per sample
 % of samples screened

 Number of plates per sample
 % of samples screened

 Specify which extracts are performed and on what basis.

GC _____ Yes ____ No Number of extracts per sample _____ % of samples screened _____ Specify which extracts are performed and on what basis. HPLC Yes No Number of extracts per sample % of samples screened Specify which extracts are performed and the number or runs made in each case.

GC/MS Yes No Number of extracts per sample % of samples tested Specify which extracts are performed and the number of runs made in each case.

LC/MS Yes No Number of extracts per sample % of samples tested Specify which extracts are performed and the number of runs made in each case.

- 38. Total amount of money spent by the commission or by any other entity in your jurisdiction on research for method development and validation annually?
- 40. Total amount of money spent by the commission or by any other entity in your jurisdiction on research for other purposes?

41 What is the source of this funding?

Type of research performed?

How does the commission determine which research projects to fund?

What entity performs the research?

Is research productivity and quality evaluated? _____ Yes _____ No

- 42. If so, by whom and in what manner?
- 43. What instrumentation is available in the laboratory? Please specify # of instruments and age of equipment?

I

44. Is there any automated equipment in the laboratory? Please specify.

45. Is your laboratory accredited? _____ Yes _____No

46. If so, what accrediting criteria are used?

APPENDIX E

Second Questionnaire Sent to Commissions

| A. 1. | What horses are <u>routinely</u> selected for testing? Please check the box that applies. |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | A. Winners only □ B. Win and Place Finishers only □ C. Win, Place and Show Finishers only □ D. Other (Please explain): □ |
| 2. | What other horses might be selected on a <u>random</u> basis? (examples-beaten favorites or claimed horses) |
| 3. | Are additional horses selected in stakes races? Yes No And No |
| 4. | Does the wagering menu offered affect the horses that are selected? Yes□ No□ 4A. If yes, please give details |
| 5. | How many horses, on average, are tested on a per race basis? |
| 6. | How many horses, on average, are tested on a per card basis? |
| 7. | Please list the laboratories that are allowed by your jurisdiction to analyze referee or split samples: |

8. What is the decision level where administrative action might be taken for the following drug positives in your jurisdiction? Please remember to include the appropriate units. If trace amounts constitute a positive please place a **zero** in the box.

| DRUG | DECISION LEVEL |
|---------------------|-----------------------|
| ACEPROMAZINE | |
| ALBUTEROL | |
| ATROPINE | |
| CAFFEINE | |
| CLENBUTEROL | |
| COCAINE | |
| (BE & EME Analytes) | |
| MORPHINE | |
| PROMAZINE | |
| SCOPALAMINE | |

9. Is the presence of non-steroidal anti-inflammatory medications other than phenylbutazone, flunixin (Banamine), naproxen, or meclofenamic acid (Arquel) considered a positive test in your jurisdiction?

Yes…□ No…□

10. From the following list of steroidal anti-inflammatories please check those that if detected would constitute a positive test:

_

| A. Betamethasone | |
|------------------|---|
| B. Dexamethasone | |
| C. Prednisone | |
| D. Prednisolone | |
| | - |

B.

-

Using the previous survey responses, these were all of the Class 1, 2 and 3 positives reported by racing jurisdictions in the years requested (1997-1999). Please make sure that each Class 1, 2 and 3 positive called in your state appears on this list and indicate the number of such positives called by your jurisdiction during this time frame. In addition, we would like to know the primary screening ("S") and confirmation ("C") methods used to detect the presence each medication. Please denote with the letter "S" or "C" under the appropriate methodology for each medication. If the drug was screened and confirmed via serum please denote with a "B". If your jurisdiction has not called a positive for a listed medication, please leave that row blank.

Example: Medication "A" was called detected using ELISA screening and confirmed with GC/MS using a blood sample on five different occasions. The appropriate response is:

| MEDICATION | # | TLC | ELISA | GC | HPLC | GC/MS | LC/MS |
|----------------|--------|-----|-------|----|------|-------|-------|
| | called | | | | | | |
| Medication "A" | 5 | | SB | | | СВ | |

| | # | METHODOLOGIES | | | | | | |
|--------------------|--------|---------------|-------|----|------|-------|-------|--|
| MEDICATION | called | TLC | ELISA | GC | HPLC | GC/MS | LC/MS | |
| Acepromazine | | | | | | | | |
| Albuterol | | | | | | | | |
| Atropine | | | | | | | | |
| Bromfenac | | | | | | | | |
| Bumetanide | | | | | | | | |
| Buprenorphine | | | | | | | | |
| Buspirone | | | | | | | | |
| Bupivacaine | | | | | | | | |
| Butorphanol | | | | | | | | |
| Caffeine | | | | | | | | |
| Clenbuterol | | | | | | | | |
| Cocaine (BE & EME) | | | | | | | | |
| Detomidine | | | | | | | | |
| Dextromoramide | | | | | | | | |
| Ephedrine | | | | | | | | |
| Etorphine | | | | | | | | |
| Glycopyrrolate | | | | | | | | |
| Guanabenz | | | | | | | | |
| Heptaminol | | | | | | | | |

| MEDICATION | # | TLC | ELISA | GC | HPLC | GC/MS | LC/MS |
|---------------------|--------|-----|-------|----|------|-------|-------|
| | called | | | | | | |
| Imipramine | | | | | | | |
| Ipratropium | | | | | | | |
| Ketorolac | | | | | | | |
| Mepivacaine | | | | | | | |
| Methylphenidate | | | | | | | |
| Lidocaine | | | | | | | |
| Meprobamate | | | | | | | |
| Metaraminol | | | | | | | |
| Morphine | | | | | | | |
| Nalbuphine | | | | | | | |
| Nefopam | | | | | | | |
| Naloxone | | | | | | | |
| Oxycodone | | | | | | | |
| Pentazocine | | | | | | | |
| Phentermine | | | | | | | |
| Phenylpropanolamine | | | | | | | |
| Picrotoxin | | | | | | | |
| Procaine | | | | | | | |
| Promazine | | | | | | | |
| Pyrilamine | | | | | | | |
| Romifidine | | | | | | | |
| Scopalamine | | | | | | | |
| Sertraline | | | | | | | |
| Sildenafil | | | | | | | |
| Strychnine | | | | | | | |
| Terbutaline | | | | | | | |
| Theophylline | | | | | | | |
| Tramadol | | | | | | | |
| Tripelennamine | | | | | | | |

If any of these positive calls were made on proficiency or blind quality assurance samples **ONLY** and **NOT** on an actual post-race sample, please list them below:

APPENDIX F

Summary of Class 1, 2 and 3 Calls 1997-1999

| Drug/Metabolite | RCI | # of | % of all | 1/ | # of | subjective |
|------------------------------------|-------|------------|----------|-----------|---------------|------------------|
| 0 | class | violations | calls | # samples | jurisdictions | classification |
| | | | | | reporting | |
| Albuterol | 3 | 15 | 3.9% | 33,916 | 10 | Bronchodilator |
| Alfentanil | 1 | 3 | 0.8% | 169,579 | 1 | Analgesic |
| Amphetamine | 1 | 2 | 0.5% | 254,369 | 2 | Stimulant |
| Apomorphine | 1 | 2 | 0.5% | 254,369 | 1 | Analgesic |
| Atropine | 3 | 1 | 0.3% | 508,737 | 1 | Spasmodic |
| Atropine/Scopalamine* | 3 | 1 | 0.3% | 508,737 | 1 | Spasmodic |
| Butorphanol | 3 | 2 | 0.5% | 254,369 | 2 | Analgesic |
| Caffeine | 2 | 20 | 5.2% | 25,437 | 8 | Stimulant |
| Caffeine/Theobromine* | 2 | 2 | 0.5% | 254,369 | 2 | Stimulant |
| Caffeine/Theophylline* | 2 | 12 | 3.1% | 42,395 | 3 | Stimulant |
| Caffeine/Theophylline/Theobromine* | 2 | 3 | 0.8% | 169,579 | 2 | Stimulant |
| Clenbuterol | 3 | 107 | 27.8% | 4,755 | 17 | Bronchodilator |
| Cocaine | 1 | 18 | 4.7% | 28,263 | 5 | Stimulant |
| Detomidine | 3 | 2 | 0.5% | 254,369 | 1 | Sedative |
| Dezocine | 2 | 3 | 0.8% | 169,579 | 1 | Analgesic |
| Ephedrine | 2 | 6 | 1.6% | 84,790 | 3 | Stimulant |
| Ephedrine/Pseudoephedrine/PPA* | 2 | 8 | 2.1% | 63,592 | 4 | Stimulant |
| Etorphine | 1 | 1 | 0.3% | 508,737 | 1 | Sedative |
| Glycopyrrolate | 3 | 14 | 3.6% | 36,338 | 3 | Spasmodic |
| Guanabenz | 2 | 3 | 0.8% | 169,579 | 1 | Sedative |
| Imipramine | 2 | 1 | 0.3% | 508,737 | 1 | Anti-depressant |
| Ipratropium | 3 | 3 | 0.8% | 169,579 | 1 | Bronchodilator |
| Ketorolac | 3 | 4 | 1.0% | 127,184 | 2 | Analgesic |
| Lidocaine | 2 | 35 | 9.1% | 14,535 | 9 | Local anesthetic |
| Mephentermine | 1 | 3 | 0.8% | 169,579 | 3 | Stimulant |
| Mepivacaine | 2 | 4 | 1.0% | 127,184 | 3 | Local anesthetic |
| Metaproterenol | 3 | 1 | 0.3% | 508,737 | 1 | Stimulant |
| Metaraminol | 1 | 23 | 6.0% | 22,119 | 1 | Stimulant |
| Methylphenidate | 1 | 1 | 0.3% | 508,737 | 1 | Stimulant |
| Morphine | 1 | 2 | 0.5% | 254,369 | 2 | Analgesic |
| Nalbuphine | 2 | 3 | 0.8% | 169,579 | 2 | Analgesic |
| Picrotoxin | 1 | 1 | 0.3% | 508,737 | 1 | Stimulant |
| Phenylpropanolamine (PPA) | 3 | 5 | 1.3% | 101,747 | 2 | Stimulant |
| Procaine | 3 | 8 | 2.1% | 63,592 | 7 | Local anesthetic |
| Promazine | 3 | 24 | 6.2% | 21,197 | 10 | Sedative |
| Propranolol | 3 | 2 | 0.5% | 254,369 | 2 | Stimulant |
| Pyrilamine | 3 | 25 | 6.5% | 20,349 | 3 | Antihistamine |
| Romifidine | 2 | 2 | 0.5% | 254,369 | 2 | Sedative |
| Scopolamine | 3 | 4 | 1.0% | 127,184 | 1 | Spasmodic |
| Sertraline | 2 | 1 | 0.3% | 508,737 | 1 | Anti-depressant |

| Sildenafil | N/A | 1 | 0.3% | 508,737 | 1 | Unknown |
|--------------|-----|---|------|---------|---|----------------|
| Strychnine | 1 | 1 | 0.3% | 508,737 | 1 | Stimulant |
| Terbutaline | 3 | 1 | 0.3% | 508,737 | 1 | Bronchodilator |
| Theophylline | 3 | 4 | 1.0% | 127,184 | 2 | Bronchodilator |
| Torsemide | 3 | 3 | 0.8% | 169,579 | 1 | Diuretic |
| Tramadol | 2 | 2 | 0.5% | 254,369 | 2 | Analgesic |
| Xylazine | 3 | 1 | 0.3% | 508,737 | 1 | Sedative |

* All positives designated with an asterisk indicate that the parent drug and metabolite(s) were called in the same sample. For the purposes of this report, the parent drug and metabolite(s) were considered to be a single positive test.