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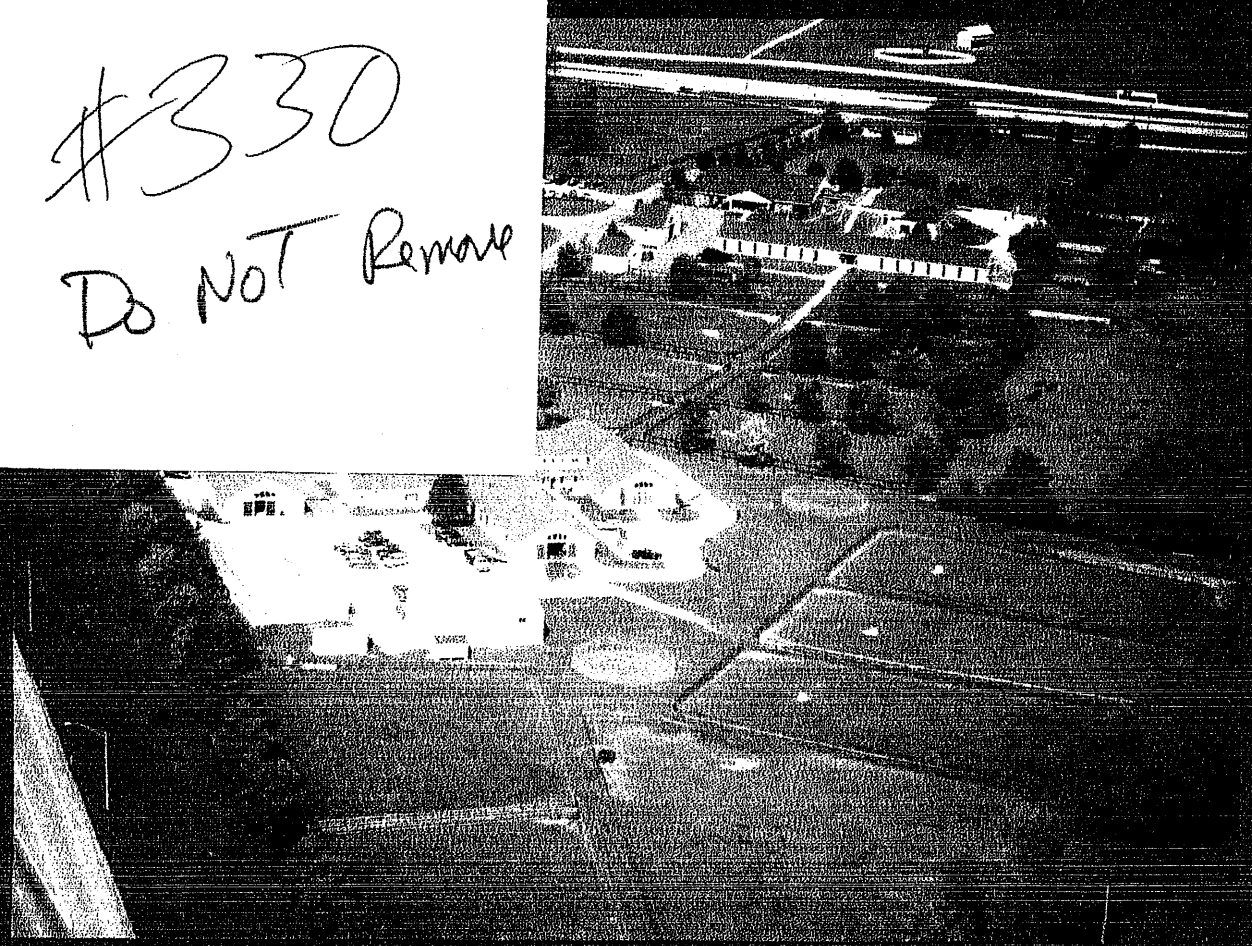

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National Horsemen's Benevolent & Protective Association, Inc

Proposed National Policy on Drug Testing and Therapeutic Medication

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1. EXECUTIVE SUMMARY

The National Horsemen's Benevolent & Protective Association (National HBPA) herein presents its 2002 updated National Policy on Drug Testing and Therapeutic Medication for Association of Racing Commissioners International (ARCI) class 1, 2, 3, and 4 substances. This document defines the relevant terms and sets forth the regulatory need and scientific basis for:

1.1 ZERO TOLERANCE TESTING for performance-altering substances that have no legitimate use in horses in training or racing. This ZERO TOLERANCE policy also applies to prohibited practices, including but not limited to administration of milkshakes, erythropoietins, growth hormones, or unregulated shockwave therapy.

1.2 THRESHOLDS/REGULATORY LIMITS for substances recognized by racing jurisdictions and/or the American Association of Equine Practitioners (AAEP) as therapeutic medications for the horse. The thresholds/regulatory limits herein are based on published scientific research and/or thresholds/regulatory limits adopted by one or more racing jurisdictions.

1.3 THRESHOLDS/REGULATORY LIMITS for the following therapeutic medications: acepromazine, albuterol, bupivacaine, butorphanol, clenbuterol, dantrolene, dexamethasone, flumethasone, flunixin, furosemide, glycopyrrolate, hydrocortisone, isoflupredone, isoxsuprine, ketoprofen, lidocaine, meclofenamic acid, mepivacaine, methocarbamol, methylprednisolone, naproxen, pentazocine, phenylbutazone, prednisolone, prednisone, procaine, promazine, pyrilamine, and terbutaline.

1.4 THRESHOLDS/REGULATORY LIMITS for dietary or environmental substances that are also ARCI substances, namely atropine, benzoylecgonine, caffeine, morphine glucuronides, salicylic acid/salicylates and theobromine.

1.5 SALIX (LASIX) CONTROL: Application of these thresholds/regulatory limits for substances in urine requires that Salix (furosemide, Lasix) administration be controlled such that urinary dilution does not interfere with testing.

1.6 WITHDRAWAL TIME GUIDELINES: The need for practical withdrawal time guidelines keyed to the relevant specific thresholds/regulatory limits set forth herein is explicitly recognized. Research to establish the best possible scientific basis for such withdrawal time guidelines should be a high priority.

1.7 BLOOD TESTING provides a significantly superior scientific basis for the regulation of therapeutic medication. All testing laboratories should have LC-MS or LC-MS-MS instrumentation to optimize regulatory practices through application of blood testing.

1.8 STANDARDS are proposed for administrative procedures, laboratory accreditation, the reporting of chemical identifications and their quantitative determination, independent analysis, and review, with an emphasis on the importance of expert professional review.

1.9 RESEARCH: The development of new therapeutic medications and analytical technologies means that the specifics of this policy will evolve with time.

2. PREAMBLE

2.1 SCOPE OF THE POLICY: The National HBPA herein presents its National Policy on Drug Testing and Therapeutic Medication for ARCI class 1, 2, 3, and 4 substances.

2.2 GOAL OF THE POLICY: The goal of this policy is to harmonize medication policies and their regulation across the United States. In approaching this goal, the National HBPA has chosen to build on established regulatory precedent. Established regulatory precedent includes thresholds or regulatory limits, as set forth in this and the previous draft of this document. This policy now also explicitly sets forth the need for withdrawal time guidelines keyed to the regulatory thresholds, as set forth in Section 12.2 and Appendix I.

2.3 REGULATORY PRECEDENTS FOR THE POLICY: In presenting this document, the National HBPA recognizes and endorses the approaches first set forth in the long-established Canadian policy of limited sensitivity testing for therapeutic medications, the McKinsey Report (1991),[1] the National Thoroughbred Racing Association Racing Integrity and Drug Testing Task Force report (May 2002),[2] and communications from the Racing Medication and Drug Testing Consortium. Beyond this, however, this document draws freely on terms, definitions, and specific thresholds/limits/decision levels/regulatory limits (hereinafter "thresholds/regulatory limits") already in place in North American racing jurisdictions, including Arizona, Arkansas, California, Colorado, Delaware, Florida, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Michigan, Minnesota, Montana, Nebraska, New Hampshire, New Jersey, New Mexico, Ohio, Oklahoma, Oregon, Pennsylvania, Texas, Virginia, Washington, West Virginia, Wyoming, Canada, and other national and international jurisdictions.

2.4 TECHNICAL AND SCIENTIFIC BASIS FOR THE POLICY: As set forth in this document, standardized national medication rules cannot be put in place without access to appropriate analytical standards, validated analytical methods, and appropriate research bases. In this regard, the National and local HBPAs, in cooperation with other groups, have supported research on the synthesis of analytical standards, the development of vali-

dated analytical methods, and the development of appropriate research bases for many of the listed therapeutic medications. This research base is summarized in the attached scientific review (Appendix IX) and the scientific papers that are referenced throughout the text and listed in Appendix VIII.

2.5 ADMINISTRATIVE BASIS FOR THE POLICY: Horses are commonly entered to race at 48 hours prior to post. Where possible, the therapeutic medication policies presented here have been structured, or on revising should be structured, so as to minimize interference with the process of entering horses to race while preserving the health and welfare of the horse.

2.6 DEFINITIONS: Central to any regulatory or scientific process is the precise definition of terms. This document, therefore, defines the relevant regulatory and scientific terms and sets forth the regulatory need and the best available scientific basis for this policy (superscript letters throughout text refer to the definitions presented in Appendix II).

3. ZERO TOLERANCE TESTING POLICY ON PROHIBITED PRACTICES AND PERFORMANCE-ALTERING SUBSTANCES

3.1 ZERO TOLERANCE for prohibited practices, including but not limited to administration of milkshakes, erythropoietins, growth hormones, or unregulated shock-wave therapy.

3.2 ZERO TOLERANCE TESTING[A] for performance-altering substances[B] that have no legitimate use in horses in training or racing; for these substances, any quantity detected is violative.

3.3 ZERO TOLERANCE TESTING means, in practice, utilizing the most sensitive testing procedures available that encompass the full scope and sensitivity of modern analytical methods.

3.4 ZERO TOLERANCE TESTING, therefore, includes the fullest possible range of highly sensitive ELISA tests and instrumental and other screening[C] and confirmation[D] methods.

3.5 ZERO TOLERANCE TESTING for performance-altering substances mandates vigorous research efforts to develop highly sensitive tests for performance-altering substances.

3.6 ZERO TOLERANCE TESTING for performance-altering substances, with the application of appropriate penalties, is unequivocally supported and endorsed by the National HBPA and all HBPA affiliates throughout North America.

3.7 Endorsement of this ZERO TOLERANCE TESTING approach is based on the assumption that all analytical results and proposed administrative actions shall be reviewed by appropriate experts. Within the limits of available knowledge and technology, innocent explanations of the practices or substances in question shall have been rigorously examined prior to consideration of any regulatory action.

4. TESTING FOR THERAPEUTIC MEDICATIONS

4.1 Therapeutic medications[E,F] are necessary to preserve the health and welfare of horses. The National HBPA recognizes that horses in training, like all athletes, may at times require the administration of certain therapeutic medications to preserve their health.

4.2 The National HBPA specifically recognizes the role of the AAEP in identifying substances as therapeutic medications (Appendix III). The National HBPA further recognizes, encourages, and supports the AAEP's role in defining appropriate standardized therapeutic dosage regimens[G] of these therapeutic medications with the primary goal of preserving the health of horses. These standardized therapeutic dosage regimens will also serve to guide analytical chemists, pharmacologists, regulators, and other industry professionals across the nation.

4.3 Zero tolerance testing, as established and set forth above for performance-altering substances, is inappropriate for use in the regulation of therapeutic medication. Zero tolerance testing can lead to the detection of insignificant trace concentrations[H] of therapeutic medications long after their therapeutic effects are over. Additionally, zero tolerance testing continually increases in sensitivity as analytical methods improve. As such, zero tolerance testing is, by definition, inappropriate for application to testing for therapeutic medications.

5. THE PROBLEM: LACK OF NATIONAL STANDARDS

5.1 In the absence of national standards, zero tolerance testing for ineffective traces of therapeutic medications or dietary or environmental substances/contaminants[I] is a significant problem that causes damage to the sport of racing in the following ways.

5.2 First, and foremost, it damages the health and welfare of horses through prohibition of the administration of therapeutic medications, thereby interfering with proper and humane preservation of the health of racing horses.

5.3 Second, it damages the reputation of racing through media stories that are inaccurate or incomplete and that unfairly and unnecessarily harm public confidence in the integrity of racing.

5.4 Third, it damages the reputations of individual trainers by associating them in the minds of owners and the racing public with supposedly improper medication practices.

5.5 Fourth, it causes damage to the reputations of affected owners and, by extension, all owners, thereby discouraging their participation in racing.

5.6 Fifth, individual regulators may utilize tests of differing sensitivities for therapeutic medications, resulting in industry-wide confusion and inequitable penalties, further exacerbating these problems.

6. THE SOLUTION: NATIONAL THRESHOLDS/REGULATORY LIMITS FOR THERAPEUTIC MEDICATIONS AND DIETARY AND ENVIRONMENTAL SUBSTANCES/CONTAMINANTS

6.1 The solution is for racing to adopt uniform national testing standards, in effect, national thresholds/regulatory limits[J] for therapeutic medications, based on published research and thresholds/regulatory limits already in place in Arizona, Arkansas, California, Colorado, Delaware, Florida, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Michigan, Minnesota, Montana, Nebraska, New Hampshire, New Jersey, New Mexico, Ohio, Oklahoma, Oregon, Pennsylvania, Texas, Virginia, Washington, West Virginia, Wyoming, Canada, and other national and international racing jurisdictions.

6.2 As set forth below, the National HBPA has supported research in these areas and has contributed to the synthesis of a substantial number of specific equine medication metabolites and analytical standards[K] required for quantification of analyte concentrations in horse urine or plasma (Appendix IV). The National HBPA, therefore, proposes the following uniform national thresholds/regulatory limits for various ARCI class 1, 2, 3, and 4 substances.[3-7]

6.3 Withdrawal Time Guidelines[L]: Thresholds/regulatory limits are concentrations[M] of substances in biological fluids above which regulatory processes may be initiated. As a practical matter, however, horsemen need "withdrawal time guidelines" keyed[N] to the specific thresholds/regulatory limits set forth hereafter. Current availability of such information is very limited; this area is, therefore, a high priority for research.

7. NATIONAL THRESHOLDS/REGULATORY LIMITS FOR THERAPEUTIC MEDICATIONS

7.1 ARCI CLASS 2 THERAPEUTIC MEDICATIONS

Thresholds/regulatory limits in place in North America for three ARCI class 2 local anesthetics are presented below. All of these thresholds/regulatory limits are in urine and are well documented in published research supported in part by the National and several local Horsemen's Benevolent & Protective Associations (Appendix V). No withdrawal time guidelines for these local anesthetics keyed to these thresholds/regulatory limits are currently available. To prevent the improper use of synergistic combinations of local anesthetics ("cocktails"), these thresholds/regulatory limits will not apply if more than one pharmacologically-related ARCI class 2 local anesthetic is detected. Thresholds/regulatory limits for local anesthetics in blood are within current technical capabilities and would better serve the industry.

7.1.1 BUPIVACAINE (LOCAL ANESTHETIC).

Target Analyte[O]: 3-hydroxybupivacaine.
Threshold/Regulatory Limit: 5 ng/mL, from/in urine.

Ohio and Washington have adopted this threshold/regulatory limit for bupivacaine, an ARCI class 2 therapeutic medication. This threshold/regulatory limit is well supported by published research, and the target analyte, 3-hydroxybupivacaine, is commercially available.[6,8]

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of bupivacaine at the above threshold/regulatory limit are available at this time.

7.1.2 LIDOCAINE (LOCAL ANESTHETIC).

Target Analyte: 3-hydroxylidocaine.
Threshold/Regulatory Limit: 50 ng/mL, from/in urine.

Ohio and Washington have adopted this threshold/regulatory limit for lidocaine, an ARCI class 2 therapeutic medication. This threshold/regulatory limit is well supported by published research.[9,10] The target analyte, 3-hydroxylidocaine, is a major urinary metabolite of lidocaine in the horse and is commercially available.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of lidocaine at the above threshold/regulatory limit are available at this time.

7.1.3 MEPIVACAINE (LOCAL ANESTHETIC).

Target Analyte: 3-hydroxymepivacaine.

Threshold/Regulatory Limit: 10 ng/mL, from/in urine.

California, Washington, and New Mexico have adopted this threshold/regulatory limit for mepivacaine, an ARCI class 2 therapeutic medication. This threshold/regulatory limit is well supported by published research.[11,12] The target analyte, 3-hydroxymepivacaine, is a major urinary metabolite of mepivacaine in the horse and is commercially available.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of mepivacaine at the above threshold/regulatory limit are available at this time.

7.1.4 Five other ARCI class 2 therapeutic medications,

namely diazepam (sedative), fluphenazine (long-acting tranquilizer), hydroxyzine (anti-histaminic), ketamine (tranquilizer/anesthetic), and reserpine (long-acting tranquilizer) are recognized therapeutic medications (Appendix III) for which no published thresholds/regulatory limits or withdrawal time guidelines are currently available.

7.2 ARCI CLASS 3 THERAPEUTIC MEDICATIONS

Thresholds/regulatory limits in place in North America for ten ARCI class 3 therapeutic medications are presented below. With the exception of clenbuterol, all of these thresholds/regulatory limits are in urine. Also, with the exception of clenbuterol, no withdrawal time guidelines keyed to these thresholds/regulatory limits are available.

Recent research on blood testing supported in part by the National and several local Horsemen's Benevolent & Protective Associations has presented data suggesting a withdrawal time guideline of four days in blood serum for clenbuterol.[13] This research is apparently consistent with in-house research from Ohio, New York, and Pennsylvania. With regard to the other listed substances, withdrawal time guidelines keyed to the indicated thresholds/regulatory limits are needed for either the presented urinary thresholds/regulatory limits or their equivalent thresholds/regulatory limits in blood plasma or serum.

To prevent the improper use of synergistic combinations of ARCI class 3 therapeutic medications ("cocktails"), these thresholds/regulatory limits will not apply if more than one pharmacologically related ARCI class 3 therapeutic medication is detected.

7.2.1 ACEPROMAZINE (TRANQUILIZER).
Target Analyte: 2-(1-hydroxyethyl) promazine sulfoxide (HEPS).
Threshold/Regulatory Limit: 25 ng/mL, from/in urine.

California, New Mexico, Ohio, and Washington have adopted this threshold/regulatory limit for acepromazine, an ARCI class 3 therapeutic medication. The target analyte 2-(1-hydroxyethyl) promazine sulfoxide (HEPS) is a major urinary metabolite of acepromazine and is commercially available.[5,6]

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of acepromazine at the above threshold/regulatory limit are available at this time.

7.2.2 ALBUTEROL (BRONCHODILATOR).
Target Analyte: Albuterol.
Threshold/Regulatory Limit: 1 ng/mL, from/in urine.
California and New Mexico have adopted this threshold/regulatory limit for albuterol, an ARCI class 3 therapeutic medication. The threshold/regulatory limit for albuterol in one unidentified American jurisdiction is reportedly 2 ng/mL in urine.[2]

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of albuterol at the above threshold/regulatory limit are available at this time.

7.2.3 BUTORPHANOL (ANALGESIC).
Target Analyte: Butorphanol.
Threshold/Regulatory Limit: 10 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for butorphanol, an ARCI class 3 therapeutic medication.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of butorphanol at the above threshold/regulatory limit are available at this time.

7.2.4 CLENBUTEROL (BRONCHODILATOR).
Target Analyte: Clenbuterol.
Thresholds/Regulatory Limits: 10 pg/mL, from/in plasma/serum; 5 ng/mL, from/in urine.

The 10 pg/mL plasma/serum threshold/regulatory limit for clenbuterol, an ARCI class 3 therapeutic medication, is supported by published research[13] and in-house research (Ohio, New York) and is consistent with Canadian policy. The 5 ng/mL urinary threshold/regulatory limit is supported by research performed at the University of California, Davis, and is in place in California and Washington. The threshold/regulatory limit for clenbuterol in one unidentified American jurisdiction is reportedly 10 ng/mL in urine.[2]

Withdrawal Time Guideline: Data suggesting a 4-day withdrawal time and keyed to the 10 pg/mL plasma/serum threshold for clenbuterol at a dose of 0.8 µg/kg of Ventipulmin orally b.i.d. for 10 days are published in the scientific literature.[13] This research was supported in part by the National and several local Horsemen's Benevolent & Protective Associations.

7.2.5 GLYCOPYRROLATE (BRONCHODILATOR).
Target Analyte: Glycopyrrolate.

Threshold/Regulatory Limit: 5 ng/mL, from/in urine.
Ohio has adopted this threshold/regulatory limit for glycopyrrolate, an ARCI class 3 therapeutic medication. This threshold/regulatory limit is supported by published Canadian research.

Withdrawal Time Guideline: To our knowledge, no

withdrawal time guidelines keyed to a standardized therapeutic dosage of glycopyrrolate at the above threshold/regulatory limit are available at this time.

7.2.6 PENTAZOCINE (ANALGESIC).
Target Analyte: Pentazocine.
Threshold/Regulatory Limit: 50 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for pentazocine, an ARCI class 3 therapeutic medication.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of pentazocine at the above threshold/regulatory limit are available at this time.

7.2.7 PROCAINE (LOCAL ANESTHETIC).
Target Analyte: Procaine.
Threshold/Regulatory Limit: 50 ng/mL, from/in urine.

Ohio has adopted a 50 ng/mL threshold/regulatory limit for procaine, an ARCI class 3 therapeutic medication. This threshold/regulatory limit is well supported by published research.[14] Procaine penicillin is an important therapeutic medication in racing horses. Development of a blood/plasma threshold/regulatory limit for this substance would likely permit its more effective use closer to post than this currently in place urine threshold/regulatory limit. Currently in place blood/plasma thresholds/regulatory limits include 25 ng/mL in plasma in Canada and 20 ng/mL in plasma in Pennsylvania, with strict reporting requirements concerning the pre-race administration of procaine penicillin.[15]

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of procaine at the above urinary threshold/regulatory limit are available at this time.

7.2.8 PROMAZINE (TRANQUILIZER).
Target Analyte: 3-hydroxpromazine.
Threshold/Regulatory Limit: 50 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for promazine, an ARCI class 3 therapeutic medication. The target analyte, 3-hydroxypromazine, is a major urinary metabolite of promazine in the horse and is commercially available.[5,6]

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of promazine at the above threshold/regulatory limit are available at this time.

7.2.9 PYRILAMINE (ANTIHISTAMINIC).
Target Analyte: O-desmethylpyrilamine.
Threshold/Regulatory Limit: 50 ng/mL, from/in urine.
Ohio has adopted a Thin Layer Chromatography threshold/regulatory limit for pyrilamine, an ARCI class 3 therapeutic medication, estimated at 50 ng/mL. The target analyte, O-desmethylpyrilamine, is a major urinary metabolite of pyrilamine in the horse and is commercially available.[5,6,16-18]

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of pyrilamine at the above threshold/regulatory limit are available at this time.

7.2.10 TERBUTALINE (BRONCHODILATOR).
Target Analyte: Terbutaline.
Threshold/Regulatory Limit: 10 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for terbutaline, an ARCI class 3 therapeutic medication.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of terbutaline at the above threshold/regulatory limit are available at this time.

7.2.11 Three other ARCI class 3 therapeutic medications, namely aminophylline (theophylline with ethylenediamine, a bronchodilator), detomidine (analgesic/sedative), and xylazine (analgesic/sedative) are recognized therapeutic medications (Appendix III) for which no published thresholds/regulatory limits or withdrawal time guidelines are currently available.

7.3 ARCI CLASS 4 THERAPEUTIC MEDICATIONS
ARCI class 4 substances have less ability to influence the performance of horses, and many are recognized therapeutic medications. Many are also readily detected and regulated in blood as well as urine.

Because these substances have been detectable for many years, most jurisdictions have long-established regulatory policies for them. Beyond this, it should be made clear that in certain jurisdictions some of these substances are accepted as therapeutic medications whose administration on race day is approved by rule or statute.

At least part of the reason that certain of these substances have been approved by rule, statute, or regulatory limit as race day medications is the considerable technical difficulty in establishing realistic "no race day medication" thresholds/regulatory limits along with the associated withdrawal time guidelines for these agents, as set forth in detail in 7.3.4: Flunixin, 7.3.13: Phenylbutazone, and Appendix I below.

This section of the medication policy recognizes these

long-established regulatory precedents for ARCI class 4 therapeutic medications and simply lists regulatory policies and thresholds/regulatory limits currently in place.

7.3.1 DANTROLENE (MUSCLE RELAXANT).
Target Analyte: Dantrolene.
Threshold/Regulatory Limit: 100 ng/mL, from/in plasma.

Ohio has adopted this threshold/regulatory limit for dantrolene, an ARCI class 4 therapeutic medication, and this threshold/regulatory limit is also under review in another state.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of dantrolene at the above threshold/regulatory limit are available at this time.

7.3.2 DEXAMETHASONE (STEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Dexamethasone.
Threshold/Regulatory Limit: 60 ng/mL, from/in urine.
Ohio has adopted this threshold/regulatory limit for dexamethasone, an ARCI class 4 therapeutic medication, and this threshold/regulatory limit is also under review in another state.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of dexamethasone at the above threshold/regulatory limit are available at this time.

7.3.3 FLUMETHASONE (STEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Flumethasone.
Threshold/Regulatory Limit: 10 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for flumethasone, an ARCI class 4 therapeutic medication, and this threshold/regulatory limit is also under review in another state.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of flumethasone at the above threshold/regulatory limit are available at this time.

7.3.4 FLUNIXIN (NONSTEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Flunixin.
Threshold/Regulatory Limit: 1000/500/100/10 ng/mL, from/in plasma/serum.

New Mexico has adopted a 1000 ng/mL threshold/regulatory limit for flunixin, an ARCI class 4 therapeutic medication. California has adopted a 500 ng/mL threshold/regulatory limit for flunixin. Ohio and Idaho have adopted a 100 ng/mL threshold/regulatory limit for flunixin, and this threshold/regulatory limit is also under review in at least one other state. Pennsylvania has adopted a 10 ng/mL threshold/regulatory limit for flunixin. Pennsylvania guidelines state that "flunixin at 1.1 mg/kg administered IV or PO [orally] 24 hours prior to race day should not result in a violation."[19] This 100-fold range in thresholds/regulatory limits for flunixin suggests that the times prior to post that flunixin can be withdrawn in each of these jurisdictions may also be very different.

Withdrawal Time Guideline: To our knowledge, other than as set forth above for Pennsylvania, no withdrawal time guidelines keyed to a standardized therapeutic dosage of flunixin at the above thresholds/regulatory limits are available at this time.

7.3.5 HYDROCORTISONE (STEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Hydrocortisone.
Threshold/Regulatory Limit: 1000 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for hydrocortisone, an ARCI class 4 therapeutic medication.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of hydrocortisone at the above threshold/regulatory limit are available at this time.

7.3.6 ISOFLUPREDONE (STEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Isoflupredone.
Threshold/Regulatory Limit: 60 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for isoflupredone, an ARCI class 4 therapeutic medication.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of isoflupredone at the above threshold/regulatory limit are available at this time.

7.3.7 ISOXSUPRINE (VASODILATOR).
Target Analyte: Isoxsuprine.
Threshold/Regulatory Limit: 1000 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for isoxsuprine, an ARCI class 4 therapeutic medication, and this threshold/regulatory limit is also under review in at least one other state. This threshold/regulatory limit is supported by Canadian research.[20]

Withdrawal Time Guideline: To our knowledge, no with-

drawal time guidelines keyed to a standardized therapeutic dosage of isoxsuprine at the above threshold/regulatory limit are available at this time.

7.3.8 KETOPROFEN (NONSTEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Ketoprofen.
Thresholds/Regulatory Limits: 100/50 ng/mL, from/in plasma.

Ohio has adopted a 100 ng/mL threshold/regulatory limit for ketoprofen, an ARCI class 4 therapeutic medication, and this threshold/regulatory limit is also under review in another state. California has adopted a 50 ng/mL threshold/regulatory limit for ketoprofen.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of ketoprofen at the above thresholds/regulatory limits are available at this time.

7.3.9 MECLOFENAMIC ACID (NONSTEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Meclofenamic Acid.
Threshold/Regulatory Limit: 1000 ng/mL, from/in plasma.

Ohio and New Mexico have adopted this threshold/regulatory limit for meclofenamic acid, an ARCI class 4 therapeutic medication.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of meclofenamic acid at the above threshold/regulatory limit are available at this time.

7.3.10 METHOCARBAMOL (MUSCLE RELAXANT).
Target Analyte: Methocarbamol.
Threshold/Regulatory Limit: 1000 ng/mL, from/in plasma.

Ohio has adopted this threshold/regulatory limit for methocarbamol, an ARCI class 4 therapeutic medication, and this threshold/regulatory limit is also under review in at least one other state.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of methocarbamol at the above threshold/regulatory limit are available at this time.

7.3.11 METHYLPREDNISOLONE (STEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Methylprednisolone.
Threshold/Regulatory Limit: 1000 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for methylprednisolone, an ARCI class 4 therapeutic medication.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of methylprednisolone at the above threshold/regulatory limit are available at this time.

7.3.12 NAPROXEN (NONSTEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Naproxen.
Threshold/Regulatory Limit: 5000 ng/mL, from/in plasma/serum.

Idaho has adopted this threshold/regulatory limit for naproxen, an ARCI class 4 therapeutic medication, and this threshold/regulatory limit is also under review in at least one other state. This threshold/regulatory limit is supported by Canadian research.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of naproxen at the above threshold/regulatory limit are available at this time.

7.3.13 PHENYLBUTAZONE (NONSTEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Phenylbutazone.
Threshold/Regulatory Limit: 5000/3000/2600/2200/2000 ng/mL, from/in plasma/serum.

Arizona, California, Colorado, Florida, Idaho, Indiana, Kansas, Louisiana, Michigan, Montana, Nebraska, New Mexico, Ohio, Oklahoma, Oregon, Pennsylvania, Texas, Washington, West Virginia, and Wyoming have adopted a threshold/regulatory limit of 5000 ng/mL for phenylbutazone, an ARCI class 4 substance. Arkansas and Minnesota have adopted a threshold/regulatory limit of 3000 ng/mL for phenylbutazone. Delaware, Maryland, New Jersey, and Virginia have adopted a threshold/regulatory limit of 2600 ng/mL for phenylbutazone. Iowa has adopted a threshold/regulatory limit of 2200 ng/mL for phenylbutazone. Illinois has adopted a threshold/regulatory limit of 2000 ng/mL for phenylbutazone. Phenylbutazone is, by rule or law, a race-day medication in Kentucky and New Hampshire. According to the AAEP Guidelines for Drug Detection Times, "a detection time of 48 hours is likely if phenylbutazone has been administered in a multiple dosing regimen and the threshold is 5 µg/mL. Single intravenous doses of 2 grams of phenylbutazone produce plasma concentrations that are below the 5 µg/mL threshold by 24 hours after the dose."[21]

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized ther-

apeutic dosage of phenylbutazone at any of the above thresholds/regulatory limits are available at this time. Most jurisdictions apparently consider their thresholds/regulatory limits to be consistent with a 24-hour rule.

7.3.14 PREDNISOLONE (STEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Prednisolone.
Threshold/Regulatory Limit: 1000 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for prednisolone, an ARCI class 4 therapeutic medication. Prednisolone is, by law, a race-day medication in Florida.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of prednisolone at the above threshold/regulatory limit are available at this time.

7.3.15 PREDNISONE (STEROIDAL ANTI-INFLAMMATORY).
Target Analyte: Prednisone.
Threshold/Regulatory Limit: 100 ng/mL, from/in urine.

Ohio has adopted this threshold/regulatory limit for prednisone, an ARCI class 4 therapeutic medication, and this threshold/regulatory limit is also under review in at least one other state.

Withdrawal Time Guideline: To our knowledge, no withdrawal time guidelines keyed to a standardized therapeutic dosage of prednisone at the above threshold/regulatory limit are available at this time.

7.3.16 Nine other ARCI class 4 therapeutic medications, namely betamethasone (steroidal anti-inflammatory), dembrexine (mucolytic), dipyrone (muscle relaxant), guaifenesin (expectorant/muscle relaxant), ibuprofen (nonsteroidal anti-inflammatory), methylergonovine (vasoconstrictor), phenytoin (muscle relaxant), triamcinolone (steroidal anti-inflammatory), and trichlormethiazide (diuretic) are recognized therapeutic medications (Appendix III) for which no published thresholds/regulatory limits or withdrawal time guidelines are currently available.

8. POLICY ON FUROSEMIDE AND OTHER AGENTS USED TO PREVENT AND/OR TREAT EXERCISE-INDUCED PULMONARY HEMORRHAGE (EIPH)

Medications to reduce the incidence of Exercise-Induced Pulmonary Hemorrhage (EIPH) include furosemide (Salix), aminocaproic acid (Amicar), carbazochrome, Premarin, and tranexamic acid. No EIPH-related medication should be administered closer than 3 hours prior to post.

8.1 FUROSEMIDE Furosemide (as Salix) may be administered on race day for the prevention or alleviation (prophylaxis) of EIPH. Five states permit administration of furosemide up to 3 hours prior to post. The recommended dose of furosemide varies from 250 to 500 mg by single intravenous injection. Optimal regulatory control of the use of furosemide is by quantification of urinary specific gravity and serum furosemide concentrations. A violation of the furosemide rule may be deemed to have occurred if the urinary specific gravity is less than 1.010 and the serum concentration of furosemide is greater than 100 ng/mL. Care should be taken to ensure that regulatory samples are drawn from the opposite side on which Salix was administered (Appendix I, Section 7.2).

8.2 OTHER ADJUNCT MEDICATION FOR EIPH The use of certain approved adjunct bleeder and other adjunct medications in combination with Salix should be permitted, with appropriate information communicated to the betting public. The use of adjunct prophylactic medications such as aminocaproic acid (Amicar), carbazochrome, Premarin, and tranexamic acid should be permitted at the discretion of the treating veterinarian, as is the practice in a number of jurisdictions.

9. POLICY ON DIETARY AND ENVIRONMENTAL SUBSTANCES/CONTAMINANTS

For the purposes of this document, dietary and environmental substances/contaminants are ARCI substances that unavoidably become part of the food supply or environment of the horse. Environmental and/or dietary substances/contaminants that are also ARCI substances include atropine, cocaine/benzoylecgonine, caffeine, morphine/morphine glucuronides, salicylic acid/salicylates, and theobromine. A number of states have established thresholds/regulatory limits for the following environmental contaminants:

9.1 ATROPINE
Target Analyte: Atropine. Threshold/Regulatory Limit: 10 ng/mL from/in urine.

California and New Mexico have adopted this threshold/regulatory limit for atropine, an ARCI class 3 substance.

Withdrawal Time Guideline: No withdrawal time guidelines, since these are neither relevant nor applicable to dietary and environmental substances/contaminants.

9.2 BENZOYLECGONINE
Target Analyte: Benzoylecgonine.
Threshold/Regulatory Limit: 150 ng/mL, in urine.

Ohio and Louisiana have adopted this threshold/regulatory limit for benzoylecgonine, the major urinary metabolite of an ARCI class 1 substance and an environ-

mental contaminant.[22] This threshold/regulatory limit is also under review in more than one jurisdiction.
Withdrawal Time Guideline: No withdrawal time guidelines, since these are neither relevant nor applicable to dietary and environmental substances/contaminants.

9.3 CAFFEINE
Target Analyte: Caffeine. Threshold/Regulatory Limit: 100 ng/mL in urine.

Ohio and Washington have adopted this threshold/regulatory limit for caffeine, an ARCI class 2 substance and a common environmental contaminant. This threshold/regulatory limit is well supported by published research[23] and is apparently in place in three other unidentified American jurisdictions. This threshold/regulatory limit is also under review in more than one jurisdiction.

Withdrawal Time Guideline: No withdrawal time guidelines, since these are neither relevant nor applicable to dietary and environmental substances/contaminants.

9.4 MORPHINE GLUCURONIDES
Target Analyte: Morphine.
Threshold/Regulatory Limit: 100 ng/mL, in urine.

Three thresholds/regulatory limits for morphine glucuronides, the major urinary metabolites of an ARCI class 1 substance, a not uncommon addition to human foodstuffs as poppy seeds and also a potential environmental contaminant, are in place in the United States. The threshold/regulatory limit in one unidentified American jurisdiction is 100 ng/mL,[2] and it is also under review in another. In Louisiana, it is 75 ng/mL; a slightly lower (50 ng/mL) limit is in place in Ohio. This threshold/regulatory limit is also under review in more than one jurisdiction. These thresholds/regulatory limits are well supported by more recent research from the Horseracing Forensic Laboratory (HFL) in England,[24] which shows urinary concentrations of 110 ng/mL after administration to horses of 2-g doses of poppy seeds containing 3 mg of morphine per dose. These thresholds/regulatory limits are dramatically lower than the 2000 ng/mL "cut-off" in place in human workplace medication testing.[19,24,25]

Withdrawal Time Guideline: No withdrawal time guidelines, since these are neither relevant nor applicable to dietary and environmental substances/contaminants.

9.5 SALICYLIC ACID/SALICYLATES
Target Analyte: Salicylic Acid.
Threshold/Regulatory Limit: 750,000 ng/mL, from/in urine.

Ohio, Texas, California, Washington and New Mexico have adopted this threshold/regulatory limit for salicylic acid, an ARCI class 4 substance. This is also the generally accepted international threshold/regulatory limit for salicylates.

Withdrawal Time Guideline: No withdrawal time guidelines, since these are neither relevant nor applicable to dietary and environmental substances/contaminants.

9.6 THEOBROMINE
Target Analyte: Theobromine.
Threshold/Regulatory Limit: 2000 ng/mL, from/in urine.

Ohio and Texas have adopted this well-established international threshold/regulatory limit for theobromine, an ARCI class 4 substance. This is also the generally accepted international threshold/regulatory limit for theobromine.

Withdrawal Time Guideline: No withdrawal time guidelines, since these are neither relevant nor applicable to dietary and environmental substances/contaminants.

9.7 Scopolamine is an example of an ARCI class 3 dietary and/or environmental substance/contaminant for which a threshold/regulatory limit is required.

10. POLICY ON TESTING LABORATORIES, ADMINISTRATIVE PROCEDURES, AND ANALYTICAL FINDINGS

10.1 The National HBPA policy on testing laboratories[P] is consistent with those of ARCI and the North American Pari-Mutuel Regulators Association (NAPRA) in that all testing laboratories shall be accredited to American Association for Laboratory Accreditation (A2LA) standards, or International Standards Organization (ISO)/International Electrotechnical Commission (IEC) 17025 standards, or their equivalent, as set forth in Appendix VI.

10.2 All administrative procedures associated with medication violations should remain confidential until completion of the entire administrative process.

10.3 These administrative procedures shall include a split sample rule following the principles set forth in the ARCI and NAPRA Model Rules.[26,27]

10.4 For all analytical findings for target analytes with thresholds/regulatory limits, the regulatory process shall include determination of the concentration of analytes in the test sample by a validated, peer-reviewed method[Q] or, failing that, the best available method.

10.5 If the primary laboratory reports the presence of a target analyte at a concentration greater than the threshold/regulatory limit, then the trainer or the trainer's designated representative shall have the opportunity to designate any laboratory accredited to A2LA or ISO/IEC 17025 standards as set forth in 10.1 above as

his or her "split sample" or "reference" laboratory to obtain a quantitative[R] determination of the analyte. He/she shall be free to request any additional testing of the sample, including genetic testing, as may be required to assist in his or her defense and/or the authorities in their review of the circumstances giving rise to the chemical identification in question.

10.6 All quantitative results/reports shall include a statistical estimate of the MEASUREMENT UNCERTAINTY.[S] No target analyte shall be reported unless the lower limit of the 95% CONFIDENCE LIMIT[T] for the measured concentration of the target analyte is greater than the threshold/regulatory limit.

11. POLICY ON EXPERT PROFESSIONAL REVIEW

11.1 The National HBPA hereby endorses and supports the 1995 recommendation of the ARCI that "all chemical findings in official test samples be subjected to a documented review process by a veterinary pharmacologist prior to any regulatory action."

11.2 The National HBPA endorses the use of an independent Equine Medical Director (EMD), as set forth by the California Horse Racing Board. The EMD should oversee implementation of the guidelines established above and promote research aimed at identifying thresholds/regulatory limits for therapeutic medications, dietary and environmental substances/contaminants. The EMD should also contribute to the development of withdrawal time guidelines for therapeutic medications and educate the racing community at large on matters affecting preservation of the health and welfare of horses.

12. FURTHER RESEARCH

12.1 BLOOD TESTING The National HBPA recognizes that blood, as a regulatory sample, yields data that are, in forensic terms, much more confidently interpretable than urinary data. The National HBPA also notes that recent advances in analytical chemistry, specifically LC-MS and LC-MS-MS technology, increasingly make possible the quantitative confirmation of therapeutic medications in blood plasma and serum samples.

The National HBPA, therefore, recommends that all testing laboratories have in place LC-MS or LC-MS-MS testing technology to optimize regulatory practices for horse racing and to better preserve the health and welfare of horses.

Application of LC-MS and LC-MS-MS testing technology will allow racing chemists to confirm and quantify an increasing number of ARCI class 2, 3, and 4 therapeutic medications in blood, thereby avoiding many of the problems associated with urine testing.

Urine testing does not allow confident interpretation of the pharmacological significance of quantitative data from urine because of the very large inherent variability in urinary concentrations of therapeutic medications and/or their metabolites (Appendix I, Section 4).

Quantitative blood data can be much more confidently interpreted than urinary data. The advantage for horses, horsemen, and the industry at large is that urinary findings may be found to be without significance based on negative or subthreshold quantitative data from the blood sample, a very significant regulatory advance.[13]

A further problem with urine testing has been that the analytes detected in urine are often unique metabolites of the medication in question. Analytical standards of these metabolites can be difficult to obtain, of uncertain chemical stability, and challenging to quantify, all of which lead to significant technical problems and difficulties with quantitative urine testing.

On the other hand, the analyte detected in a blood test is almost always the parent medication. Advantages of this technique are that suitable standards are virtually always available, these standards are generally stable, and it is almost always easier to accurately recover and quantify parent medications in blood than the more complex and poorly characterized metabolites of unknown stability identified in or recovered from urine. This is a problem that has been specifically addressed by research supported by the National and local HBPAs (Appendix V).

Additionally, to our knowledge, Salix administration does not interfere with the detection or quantification of any medication in blood plasma or serum, again leading to more equitable regulation of therapeutic medication.

A further problem with urine testing is that some substances are slow to accumulate in urine and thus may be nondetectable shortly after their administration. This deficit in urine testing could be exploited through the administration of performance-altering substances close to post. Blood testing suffers from no such limitations and can be a very reliable method of detecting the administration of performance-altering substances close to post.

In summary, because it avoids the many technical problems associated with urine testing, blood or serum-based testing provides a significantly superior scientific basis for the regulation of therapeutic medication. As such, blood-based testing has the potential to significantly benefit horses, horsemen, and the industry at large.

On this basis, the National HBPA recommends and strongly supports the accelerated implementation of LC-

MS or LC-MS-MS blood testing technology for therapeutic medications, with the goal of avoiding the many regulatory uncertainties inherent in urine testing.

12.2 WITHDRAWAL TIME GUIDELINES As set forth in this National Policy on Drug Testing and Therapeutic Medication, thresholds/regulatory limits are a critical regulatory tool; thresholds/regulatory limits, however, are not practically usable by most industry professionals. What industry professionals need are withdrawal time guidelines keyed to the specific thresholds/regulatory limits in place in the jurisdiction.

A withdrawal time guideline is a suggested period before an event during which administration of a medication should cease in order to minimize the probability of exceeding the threshold/regulatory limit for the substance.

All withdrawal time guidelines are "best estimates." Adherence to a withdrawal time guideline merely serves to reduce the risk of inadvertently exceeding the threshold/regulatory limit; it never guarantees that exceeding the regulatory limit will not occur.

A more detailed definition of withdrawal time guidelines and their limitations is set forth under Appendix II: Definitions. A listing of "Factors Affecting Withdrawal Times" is set forth in Appendix I.

To our knowledge, the only scientifically well-established withdrawal time guidelines keyed to a standardized therapeutic dosage and a specific regulatory limit currently in place are those for clenbuterol in serum and flunixin in serum Pennsylvania (7.3.4).[13]

In summary, the development of withdrawal time guidelines keyed to each specific in place threshold/regulatory limit and the appropriate standardized dosage regimen for each therapeutic medication is a high research priority.

12.3 The National HBPA recognizes that the specifics of forensic testing and therapeutic medication and the sensitivity and scope of analytical methods change with time. Nothing in this policy shall be interpreted to preclude its modification in the light of increasing knowledge about the detection, actions, effects, and uses of performance-altering substances and the capability of identifying therapeutic medications or dietary or environmental substances/contaminants in horses in training or racing.

APPENDIX I: FACTORS AFFECTING WITHDRAWAL TIMES

It is important to allow an adequate withdrawal time between administration of a therapeutic medication and competition. Withdrawal times, however, are affected by a large number of poorly characterized or understood factors. Any guideline, therefore, is unlikely to be inclusive of all the possible variations that can affect a withdrawal time in any individual horse.

The following, in approximate order of their importance, is a list of factors that influence withdrawal times.

1. Dose. Medications administered at gram doses (2 to 10 g/horse) are much more likely to be detectable for longer periods than medications administered at low milligram doses (5 mg or less/horse).
Precaution: Be aware of the actual quantity, in grams, milligrams, or micrograms per administration, of the medications you administer.

2. Sensitivity of the testing process. Increasing the sensitivity of a test by 100-fold or more is likely to greatly extend (perhaps triple) the withdrawal time.
Precaution: If an ELISA test for an agent has been developed/introduced, a general rule is to at least double the withdrawal time that was used prior to development/introduction of the ELISA test.

3. Local testing procedures. Testing methods are not standardized, so what constitutes a violation in one jurisdiction may not necessarily constitute a violation in another. For example, Canada has limited sensitivity testing for therapeutic medications and certain Canadian "detection times"[U] are shorter than the "detection times" for the same medications in the United States.
Precaution: Because the Canadian authorities have limited the sensitivity of their tests for many medications, all Canadian detection times should be treated with caution outside of Canada.
Note: The setting of a threshold/regulatory limit immediately standardizes testing for that medication in all jurisdictions adhering to that threshold/regulatory limit. Setting a threshold/regulatory limit immediately requires the laboratory to put into place specific analytical procedures that allow it to quantify medication concentrations at the level of the threshold/regulatory limit.

4. Urine pH and volume. The pH of the urine (whether the urine is acidic or alkaline) that the horse produces post race can be a major factor (potentially 100-fold or greater) in determining urinary medication or medication metabolite concentrations and, therefore, the withdrawal time. While this factor is outside the control of the horseman, it may play an important role in determining the withdrawal time and/or the significance of a urinary finding. Urine may also be concentrated or diluted, depending on the state of hydration of the horse or the presence of diuretics, which can also affect detection and withdrawal times.

Note: This potentially very large (100-fold or greater) variability in the urinary concentrations of therapeutic medications makes blood testing a much more equitable forensic procedure than urine testing.

5. Route of administration. Oral administration can greatly prolong withdrawal times. It may take up to 5 days for pills or tablets to pass through the intestinal tract of a horse; a pill or tablet that breaks down slowly in the intestinal tract can potentially release medication into a horse's system for 5 days.

Precaution: Avoid oral administrations close to post. Therapeutic medications that are administered close to post should, where appropriate, be administered intravenously.

6. Frequency of medication use. Repeated or long-term administrations of some medications, especially repeated oral administrations, can greatly extend withdrawal times. Good examples of such medications include isoxsuprine and the acepromazine family of tranquilizers.

Precaution: Where possible, avoid repeated or prolonged schedules of administration.

Note: The potential effect of repeated administrations on detection times/withdrawal times is the reason that withdrawal time guidelines must be keyed to the regulatory threshold, the formulation used, the daily dose, and the number of days for which the medication is administered (see AAEP comments on phenylbutazone detection times, 7.3.13). All of these are veterinary matters and, as such, should be specified by appropriately trained and experienced veterinarians.

7. Contamination.

7.1 Contamination of the horse's environment. Any stall that a horse inhabits during a course of therapy becomes contaminated with the medication in question. This has been shown to occur even if the medication is administered parenterally (other than orally). Contamination is obviously much more likely to occur if the medication is administered orally or in the feed at relatively large doses. Isoxsuprine, for example, is notorious in this regard, but this effect holds at some level for all therapeutic medications.[28-30]

Precaution: Care should be taken with orally administered medication to ensure that the stall does not become contaminated or that other horses in the stable do not become exposed to the medication. Move a treated horse to a fresh stall during the withdrawal period prior to competition to eliminate the possibility of stall or environmental contamination extending the withdrawal time.

7.2 Contamination of the sample prior to collection. Research with furosemide has unequivocally demonstrated the necessity of drawing the test blood sample on the contralateral side from the site of administration. This is because inadvertent extravascular administration of even miniscule volumes of therapeutic medications has the potential to release medication from these extravascular sites into the jugular vein, giving rise to spuriously high readings from the injection site vein.[31]

Precaution: With the increasing emphasis on blood testing, every effort should be made to ensure that blood samples drawn for regulatory purposes are drawn from the opposite side of the horse on which the administrations were made.

7.3 Postcollection contamination. Postcollection contamination can occur during the collection of urine samples. It usually occurs with prescription medications or substances otherwise present in the detention barn. When it occurs, the principal protection for the horseman is the absence of metabolized forms of the medication in the urine sample; the absence of such metabolites may be prima facie evidence that such postcollection contamination occurred, as it indicates that the substance did not pass through the horse's system prior to collection.

Note: In the event of postcollection contamination, the blood sample may be expected to be negative, a further advantage of blood testing.

8. Time of last meal. If medications are administered orally, recent food intake is likely to reduce the peak blood concentration attained and delay the time at which peak blood concentration is reached, as food may interfere with absorption of the medication into the bloodstream.

9. Release times of the medication preparation. Sustained-release preparations[V] for either oral or intramuscular use may be specifically formulated to delay release of the medication into the horse's system, thereby extending withdrawal times.

Precaution: Where possible, avoid sustained-release preparations.

10. Medication formulation. For any dosage form other than simple intravenous (IV) administration, variations in the formulation of a medication may result in substantially different withdrawal times. These variations can be quite significant among different oral formulations.

Precaution: Never assume that seemingly similar products from different manufacturers will have the same withdrawal times.

11. Other factors. Individual variation between animals (eg, amount of body fat), the breed and gender of the horse, coadministration of other medications, the health of the horse, and the amount of stress that the horse is subjected to are some additional factors that may affect withdrawal times.

For more detailed information, consult your veterinarian

and the appropriate regulatory body for your particular sport and jurisdiction. See also the AAEP's *Guidelines for Drug Detection Times*, Vols 1-3 (American Association of Equine Practitioners, 1999, 2000, 2001), as well as *Equine Drugs and Vaccines: A Guide for Owners and Trainers* by Eleanor M. Kellon, VMD (Breakthrough Publications, 1995) and Drugs and the Performance Horse by Thomas Tobin (Springfield, Ill: Charles C. Thomas; 1981) or relevant publications that may be available in the scientific literature.

APPENDIX II: DEFINITIONS

A. ZERO TOLERANCE TESTING: For the purposes of this document, zero tolerance testing shall mean utilization of the most sensitive and rigorous testing procedures possible for performance-altering substances, encompassing the full scope and sensitivity of modern analytical technology. As such, the analytical limit defined by zero tolerance testing is simply the "Limit of Detection" (LOD) of the most sensitive testing technique available. Zero tolerance testing, therefore, continually increases in sensitivity as analytical methods improve.

B. PERFORMANCE-ALTERING SUBSTANCE: For the purposes of this document, a performance-altering substance shall be any ARCI class 1, 2, 3, or 4 substance not identified as a therapeutic medication by an American racing authority or the AAEP or any substance with no accepted therapeutic use in horses in training or racing.

C. SCREENING TEST: For the purposes of this document, a screening test is a preliminary test that is used to rapidly evaluate whether a sample may or may not contain a prohibited substance. By definition, a screening test is merely suggestive and does not constitute definitive evidence of the presence of the prohibited substance. Thin Layer Chromatography (TLC) and Enzyme-Linked ImmunoSorbent Assay (ELISA) tests are classic examples of screening tests. By definition, a screening test yields a "presumptive" identification, which may or may not be correct.

D. CONFIRMATORY TEST: For the purposes of this document, a confirmatory test is a definitive chemical test performed under rigorously controlled conditions that unequivocally establishes the presence of the identified substance in the sample in question. Confirmatory tests are optimally independent of and operate on different chemical principles from the screening test. Mass spectrometry is the current basis for most of the confirmatory tests used in equine forensic science. By definition, a confirmatory test is extremely good evidence for the presence of the reported substance.

E. THERAPEUTIC: For the purposes of this document, therapeutic means "serving to cure or heal or to preserve health." It is derived from the Greek word therapeuein, meaning to nurse (Webster's Dictionary, 1995).

F. THERAPEUTIC MEDICATION: For the purposes of this document, a therapeutic medication shall be any ARCI class 2, 3, or 4 substance recognized as a therapeutic medication by an American racing jurisdiction or the AAEP and/or any substance "administered by or under the supervision of a veterinarian that supports the health, welfare, and fitness of horses during training and racing or facilitates their safe and humane handling during routine procedures" (draft AAEP definition of therapeutic medication, communicated November 11, 2002).

G. STANDARDIZED THERAPEUTIC DOSAGE REGIMEN: For the purposes of this document, a standardized therapeutic dosage regimen refers to a defined formulation of a therapeutic medication, administered at a defined daily dose for a defined number of days. These criteria are defined so as to reflect optimal therapeutic use of the medication in veterinary practice. These defined therapeutic dosage regimens will serve to guide analytical chemists, pharmacologists, regulators, and other industry professionals across the nation.

H. TRACE CONCENTRATION: For the purposes of this document, a trace concentration is defined as a pharmacologically insignificant concentration of the substance in question in the biological fluid.[5] The term "trace" is well established in the field and is the term used in the pivotal ARCI resolutions in this area, adopted in Oklahoma in April 1995.[26]

I. DIETARY OR ENVIRONMENTAL SUBSTANCES/ CONTAMINANTS: For the purposes of this document, a dietary or environmental substance/contaminant shall be any ARCI class 1, 2, 3, or 4 substance that is or may become part of the food supply and/or environment of horses.

J. THRESHOLD/REGULATORY LIMIT: For the purposes of this document, a threshold/regulatory limit (or "decision level"/"cut-off"/"reporting level") is any defined concentration of an analyte in a biological fluid that relates to a regulatory event. Concentrations greater than the threshold/regulatory limit may initiate regulatory action; concentrations below the threshold/regulatory limit are of no regulatory interest. The terms "threshold/regulatory limit," "cut-off," "limitation on the sensitivity of testing," "reporting level," and "decision level" are, for all practical purposes, equivalent in scientific and regulatory terms.[5] "Threshold" is the historically established term in this area (Appendix IX). A current list of world thresholds/regulatory limits is presented in Appendix VII.

K. ANALYTICAL STANDARDS: For the purposes of this document, an analytical standard is a certified chemically pure sample of a medication or medication metabolite used by an analyst as a reference in order to reliably and reproducibly identify and quantify medications and medication metabolites in a forensic sample (Appendix IV).

L. WITHDRAWAL TIME GUIDELINES: For the purposes of this document, a withdrawal time is a suggested period before an event to cease administration of a medication so as to minimize the risk of post-race detection of a residue of the medication. When establishing a withdrawal time, veterinarians must take numerous factors into account, including but not restricted to the longest known "detection times" for the medication, the dose used, the form in which the medication was/is administered, the route of administration, the duration of treatment, the sensitivity of testing/known detection time, the chemical and pharmacokinetic characteristics of the medication, the appropriate level of risk, and any unique characteristics of the horse or the event in which the horse is participating.

Withdrawal time estimates are almost always significantly longer than the longest reported detection time for the medication and can vary from jurisdiction to jurisdiction depending on the testing methodology and/or the specific thresholds/regulatory limits employed by the laboratory or the authority.

Withdrawal times should be based on consideration of these and other factors and are best recommended by practicing veterinarians who have a unique knowledge of the physiological characteristics of the horse in question and also their accumulated professional experience with regard to the jurisdiction, medication, and horse in question.

Based on the above considerations, it is clear that any withdrawal time recommendation carries with it a finite possibility of error. The probability of a residue being detected increases in direct proportion to the number of times that a given withdrawal time guideline is applied.

M. CONCENTRATION ("LEVEL"): In forensic science, a concentration is the weight, generally expressed as micrograms, nanograms, or picograms, of the substance in question dissolved in a unit volume, usually 1 mL of plasma/serum or urine.

A microgram is one millionth of a gram. A concentration of 1 microgram (mcg, µg) per milliliter, represents a concentration of one part per million (ppm). For example, a common regulatory threshold for phenylbutazone is 5 mcg per mL (5 µg/mL) in plasma/serum (7.3.13).

A nanogram is one billionth of a gram. A concentration of 1 nanogram (ng) per milliliter represents a concentration of 1 part per billion (ppb). For example, a common regulatory threshold for furosemide is 100 nanograms per mL (100 ng/mL) in plasma/serum (8.2).

(To relate one part per billion to everyday life, one part per billion represents one second in your life if you are 32 years of age.)

A picogram is one trillionth of a gram. A concentration of 1 picogram (pg) per milliliter represents a concentration of 1 part per trillion. For example, the proposed plasma/serum threshold for clenbuterol is 10 picograms per mL (10 pg/mL) of plasma/serum (7.2.4).

Obviously, following the point of reference established above, one part per trillion represents one second in your life if you are 32,000 years of age.

While "concentration" is the correct scientific term, some technical journals (clinical journals) and most lay publications speak of blood or urinary "levels," which are equivalent to blood or urinary "concentrations."

N. KEYED: For the purposes of this document, with reference to a withdrawal time guideline, the term "keyed" means that the guideline is based on research that specifies: 1, the formulation used; 2, the dose and route of administration; 3, the duration of administration; 4, the measured rate of decline of the concentration of the target analyte in the forensic sample being analyzed; 5, the relevant threshold/regulatory limit; and 6, the best estimate of the uncertainty associated with any withdrawal time guideline presented. (See 7.2.4, clenbuterol, for an example of a keyed withdrawal time guideline.)

O. TARGET ANALYTE: For the purposes of this document, the target analyte refers to the specific analyte detected and, where appropriate, quantified in the forensic sample. The target analyte may be the parent material or medication administered to the horse or a metabolite or portion of a metabolite of the material identified in or recovered from the forensic sample. Unless otherwise specified, the target analyte is the analyte on which regulatory action is based and, for the purposes of thresholds/regulatory limits, the target analyte is the only analyte quantified.

P. TESTING LABORATORY: For the purposes of this document, a testing laboratory is a laboratory employed by or under contract to a racing authority that meets the criteria set forth by NSFTC, A2LA, or ISO/IEC 17025, as presented in Appendix VI.

Q. VALIDATED METHOD: For the purposes of this document, a validated method is a qualitative or quantitative analytical method that has been rigorously characterized and tested, in more than one laboratory, so that it reliably performs as described in the Standard Operating Procedure[W] (SOP).

R. QUANTITATIVE TEST: For the purposes of this document, a quantitative test is a test that both unequivocally identifies and defines the concentration of the prohibited substance in the test sample.

S. MEASUREMENT UNCERTAINTY: For the purposes of this document, the result of any measurement of the

concentration of a substance is only an estimate of the true value. Therefore, the result is complete only when accompanied by a quantitative statement of its uncertainty (eg, a confidence interval) as established by appropriate statistical methods.

T. 95% CONFIDENCE LIMIT: For the purposes of this document, the 95% confidence interval is a range of concentration values within which 95% of all measurements will fall. In order for a "positive" to be called, the lower limit of the 95% confidence interval for a determined concentration must be greater than the threshold/regulatory limit.

U. DETECTION TIME: For the purposes of this document, a detection time is an officially or scientifically reported period of time after administration during which a medication, or a metabolite thereof, has been detected in the blood, urine, or other body fluid of a horse.

Detection times are almost always based on results obtained in experimental situations with small numbers of horses that are not actually racing. These limitations must be kept in mind when extrapolating from reported detection times to actual withdrawal time guidelines.

Good sources of detection time information include the *AAEP Guidelines for Drug Detection Times*, and the Canadian, Australian, and European guides to detection times summarized in *An Overview of the Effective World Rules on Therapeutic Medications*, available from the Gluck Equine Research Center.[32]

V. SUSTAINED-RELEASE PREPARATIONS: Many therapeutic medications are formulated as sustained-release or controlled-release preparations. These formulations are typically administered intramuscularly, and the therapeutic medication is then slowly released from the formulation.

Slow release of the medication serves the very useful purpose of prolonging its therapeutic effect. It also, however, prolongs the detection time of the medication and other substances used in the formulation.

Procaine penicillin is a typical sustained-release formulation, administered intramuscularly, in which the prolonged release of procaine, a substance used in the formulation, becomes a regulatory problem for horseracing.

W. STANDARD OPERATING PROCEDURE: For the purposes of this document, a Standard Operating Procedure (SOP) is a complete description of an analytical method or procedure that enables its confident replication in the hands of an appropriately trained and equipped individual.

APPENDIX III: AMERICAN ASSOCIATION OF EQUINE PRACTITIONERS' THERAPEUTIC MEDICATIONS LIST, 1995

Note: An American Association of Equine Practitioners "Therapeutic Medication Committee" under the chairmanship of Dr. Rick Arthur has been at work updating this therapeutic medication list for some time. As well as updating the actual medication list, the AAEP also needs to extend this list of therapeutic medications to include defined dosage schedules, as set forth under item 7 in Appendix II: Definitions. As set forth throughout this document and explicitly set forth under item 7 in Appendix II, these are absolute prerequisites for standardized testing. In the absence of defined medication schedules and specified thresholds/regulatory limits, withdrawal time guidelines for horsemen, veterinarians, and the racing industry at large cannot be developed (see AAEP comments on phenylbutazone detection times, 7.3.13).

Name	ARCI Class	Name	ARCI Class
Diazepam	2	Dipyrone	4
Fluphenazine	2	Flumethasone	4
Hydroxyzine	2	Flunixin	4
Ketamine	2	Guaifenesin	4
Lidocaine	2	Hydrocortisone (Cortisol)	4
Mepivacaine	2	Ibuprofen	4
Reserpine	2	Isoflupredone (Fluoroprednisolone)	4
Acepromazine	3	Isoxsuprine	4
Albuterol	3	Ketoprofen	4
Aminophylline	3	Meclofenamic Acid4	
Atropine	3	Methocarbamol	4
Butorphanol	3	Methylergonovine	4
Clenbuterol	3	Methylprednisolone	4
Detomidine	3	Nandrolone	4
Glycopyrrolate	3	Naproxen	4
Pentazocine	3	Pentoxifylline	4
Procaine	3	Phenytoin	4
Promazine	3	Prednisolone	4
Pyrilamine	3	Stanozolol	4
Terbutaline	3	Testosterone	4
Xylazine	3	Thiosalicylate	4
Acetylsalicylic Acid	4	Triamcinolone	4
Aminocaproic Acid	4	Trichlormethiazide	4
Betamethasone	4	Cimetidine	5
Boldenone	4	Cromolyn	5
Dantrolene	4	Dimethylsulfoxide	5
Dembrexol (Dembrexine)	4	Dimethylsulphone	5
Dexamethasone	4	Ranitidine	5

This table was generated by circulating a list of several hundred medications to AAEP members and asking them to indicate which agents they routinely used in their practice. The data were collected and reviewed by the AAEP and presented for publication as Appendix G in the Proceedings of the "Testing for Therapeutic Medications, and Environmental and Dietary Substances in Racing Horses," pp. 191-192, 1995, Lexington, KY.[3,5]

APPENDIX IV: EQUINE MEDICATION AND MEDICATION METABOLITE STANDARDS SYNTHESIZED

As set forth throughout this document, most urinary identifications of therapeutic medications are based on the detection of specific urinary metabolites of the medication, herein specified as the target analyte. Until recently, few if any of these target analytes were available to equine forensic scientists. Starting in 1995, and supported by the National and local Horsemen's Benevolent & Protective Associations, the Kentucky Equine Drug Council, and the University of Kentucky, a chemical synthesis program has been instituted to make these target analytes/standards/metabolites available to the racing industry.

The left hand column of the table below lists the parent therapeutic medication, while the right hand column lists the metabolite/target analyte as the specific chemical name of the target analyte/standard.

	Parent therapeutic	Chemical name of medication target analyte/standard
1	Acepromazine	2-(1-hydroxyethyl) promazine sulfoxide
2	Acepromazine	(1-hydroxyethyl) promazine (uncrystallized)
3	Acepromazine	Acepromazine sulfoxide
4	Amitraz	d6-N-2,4-Dimethylphenyl-N'-methylformamidine
5	Bupivacaine	3-hydroxybupivacaine
6	Chlorpromazine	7-hydroxychlorpromazine
7	Clenbuterol	1-(4-Amino-3,5-Dichlorophenyl) ethane-1,2-diol
8	Clenbuterol	2-(2-)4-Amino-3,5-2-Dichlorophenyl) Hydroxyethylamino]-2-Methyl-Propan-1-Ol
9	Clenbuterol	Clenbuterol-D9
10	Colterol and Bitolterol	3-O-Methylcolterol
11	Fluphenazine	7-hydroxyfluphenazine
12	Furosemide	Furosemide-D5
13	Guanabenz	Hydroxyguanabenz
14	Lidocaine	3-hydroxylidocaine
15	Lidocaine	4-hydroxylidocaine
16	Mazindol	2-(2-Aminoethyl)-3-(4-chlorophenyl)-3-hydroxy-2,3-dihydro-isoindol-1-one
17	Mepivacaine	3-hydroxymepivacaine
18	Mepivacaine	4-hydroxymepivacaine
19	Phenylbutazone	Phenylbutazone-D9
20	Procaine	Procaine-D10
21	Promazine	3-hydroxypromazine
22	Promethazine	Promethazine sulfoxide
23	Propanolol	4-hydroxypropanolol
24	Propiomazine	2-(1-hydroxypropyl) promethazine sulfoxide
25	Propionylpromazine	2-(1-hydroxypropyl) promazine sulfoxide
26	Pyrilamine	O-desmethylpyrilamine
27	Ropivacaine	3-hydroxyropivacaine
28	Ropivacaine	4-hydroxyropivacaine
29	Selegiline	Desmethylselegiline
30	Tramadol	Desmethyltramadol
31	Tripelennamine	3-OH-Tripelennamine

APPENDIX V: NATIONAL AND LOCAL HORSEMEN'S BENEVOLENT AND PROTECTIVE ASSOCIATIONS THAT HAVE SUPPORTED EQUINE MEDICATION RESEARCH

National HBPA
National Horse Center
Building B Suite 2
4063 Iron Works Parkway
Lexington, KY 40511-8905

Canada HBPA
609 West Hastings Street, Suite 888
Vancouver, BC
V6B 4W4

Florida HBPA
Calder Race Course
PO Box 1800
Opa-Locka, FL 33055

Nebraska HBPA
6406 South 150th Street
Omaha, NE 68137

Kentucky HBPA
PO Box 9317
Louisville, KY 40209

Ontario HBPA
135 Queen's Plate Drive, Suite 370
Rexdale, Ontario
M9W 6V1

Charles Town HBPA
PO Box 581
Charles Town, WV 25414

Ohio HBPA
3684 Park Street
Grove City, OH 43123

Arkansas HBPA
PO Box 1670
Hot Springs, AR 71902

Michigan HBPA
4800 South Harvey
Muskegon, MI 49444-9762

Pennsylvania HBPA
PO Box 88
Grantville, PA 17028

Alabama HBPA
1523 Hidden Hills
Hartsdale, AL 35640

Total support approaching $500,000 since 1994.

APPENDIX VI: LABORATORY STANDARDS*

In order to receive accreditation under National Forensic Science Technology Center (NFSTC), American Association for Laboratory Accreditation (A2LA), or International Standards Organization (ISO)/International Electrotechnical Commission (IEC) 17025, laboratories must meet a series of minimum requirements. These standards include the following:

The laboratory must have a suitably qualified technical leader having either a 4-year baccalaureate with college credit courses in chemistry, pharmacology and toxicology, or related subjects, course work in statistics, and 5 years of experience as an analytical chemist in a laboratory analyzing substances in body fluids, including experience in giving evidence, or a graduate degree with college credit courses in chemistry, pharmacology and toxicology, or related subjects, course work in statistics, and 2 years of experience as an analytical chemist in a laboratory analyzing substances in body fluids, including experience in giving evidence.

The laboratory must demonstrate that it has effective systems in place to manage information collection, analysis, and dissemination.

The laboratory shall maintain a list of all analysts, the tests they are authorized to perform, and the reports they are authorized to sign.

All authorized analysts must have successfully completed a competency test before being allowed to perform unsupervised analyses and sign reports.

The laboratory must prepare a list of critical reagents, which are those materials utilized in analyses which can determine the accuracy of testing and the nonfunctioning of which would result in significant loss of sample. All critical reagents must be shown to be of suitable quality before being released for routine use.
The laboratory must be able to establish and maintain the forensic integrity of samples.

Samples must be received, identified, have their receipt recorded, and be stored under conditions which protect them from loss, contamination, and deleterious change. All analytical data, including quality control data, manual data transfers, calculations, chain of custody records, and conclusions must be verified by another authorized analyst.

All equipment and laboratory apparatus, the performance of which could affect the quality of test results, must be calibrated and maintained at appropriate intervals. The calibration status of all equipment must be clearly noted on or by that equipment.

The laboratory must have measures to ensure that the incidence of false-negative results is kept to a minimum.

**Courtesy of the National Forensic Science Technology Center, 2002.*

	Medication	Concentration	Fluid	Jurisdiction	Ref #
1	Acepromazine	25 ng/mL	urine	Ohio	1
	Acepromazine	25 ng/mL	urine	California	2
	Acepromazine	25 ng/mL	urine	Washington	3
	Acepromazine	25 ng/mL	urine	New Mexico	4
2	Albuterol	1 ng/mL	urine	California	2
	Albuterol	1 ng/mL	urine	New Mexico	1
3	Arsenic	200 ng/mL	urine	Texas	5
	Arsenic	300 ng/mL	urine	International	6
4	Atropine	10 ng/mL	urine	California	2
	Atropine	10 ng/mL	urine	New Mexico	4
5	Benzocaine	50 ng/mL	urine	California	2
	Benzocaine	50 ng/mL	urine	Washington	3
	Benzocaine	50 ng/mL	urine	New Mexico	4
6	BZE* (Benzoylecgonine)	50 ng/mL	urine	Unattributed	7
	BZE (Benzoylecgonine)	150 ng/mL	urine	Ohio	1
	BZE (Benzoylecgonine)	150 ng/mL	urine	Louisiana	8
7	Betamethasone	60 ng/mL	urine	Ohio	1
8	Bupivacaine	5 ng/mL	urine	Ohio	1
	Bupivacaine	5 ng/mL	urine	Washington	3
9	Butorphanol	10 ng/mL	urine	Ohio	1
10	Caffeine	250 ng/mL	serum	Canada	9
	Caffeine	1,000 ng/mL	urine	Canada	9
	Caffeine	10 ng/mL	plasma	Hong Kong	1
	Caffeine	10 ng/mL	urine	Jockey Club of Brasileiro	11
	Caffeine	30 ng/mL	urine	Hong Kong	1
	Caffeine	100 ng/mL	urine	Ohio (see 7.2.4)	1
	Caffeine	100 ng/mL	urine	Louisiana	8
	Caffeine	100 ng/mL	urine	Washington	9
11	Carbon Dioxide	37 mmol/mL	plasma	International	6
12	Clenbuterol	1 ng/mL	urine	Ohio	1
	Clenbuterol	5 ng/mL	urine	Washington	3
	Clenbuterol	5 ng/mL	urine	California	1
13	Dantrolene	100 ng/mL	plasma	Ohio	1
14	Dexamethasone	60 ng/mL	urine	Ohio	1
15	Dimethylsulfoxide	10,000 ng/mL	urine	Ohio	1
	Dimethylsulfoxide	5,000 ng/mL	urine	International	6
	Dimethylsulfoxide	1,000 ng/mL	plasma	International	6
16	Dipyrone	1,000 ng/mL	plasma	Jockey Club of Brasileiro	11
17	Flumethasone	10 ng/mL	urine	Ohio	1
18	Flunixin	1,000 ng/mL	plasma	New Mexico	4
	Flunixin	500 ng/mL	plasma	California	2, 2a
	Flunixin	100 ng/mL	plasma	Idaho	13
	Flunixin	100 ng/mL	plasma	Ohio	1
	Flunixin	10 ng/mL	plasma	Pennsylvania	12
	Flunixin	40 ng/mL	urine	Sweden	3
19	Furosemide	50 ng/mL	plasma	Oklahoma	10
	Furosemide	100 ng/mL	plasma	Others	7
	Furosemide	100 ng/mL	plasma	Jockey Club of Brasileiro	11
	Furosemide	60 ng/mL	plasma	Illinois	14
	Furosemide	100 ng/mL	plasma	Texas	5
20	Glycopyrrolate	5 ng/mL	urine	Ohio	1
21	Hydrocortisone	1,000 ng/mL	urine	Ohio	1
	Hydrocortisone	1,000 ng/mL	urine	International	6
22	Imipramine	20 ng/mL	plasma	Jockey Club of Brasileiro	11
23	Indomethacin	50 ng/mL	plasma	Jockey Club of Brasileiro	11
24	Isoflupredone	60 ng/mL	urine	Ohio	1
25	Isoxsuprine	1,000 ng/mL	urine	Ohio	1
26	Ketoprofen	100 ng/mL	plasma	Ohio	1
	Ketoprofen	50 ng/mL	plasma	California	2
27	Lidocaine	25 ng/mL	plasma	Jockey Club of Brasileiro	11
	Lidocaine	50 ng/mL	urine	Ohio	1
	Lidocaine	50 ng/mL	urine	Washington	3
	Lidocaine	25 ng/mL	urine	Louisiana	8
28	Meclofenamic Acid	1,000 ng/mL	plasma	Ohio	1
	Meclofenamic Acid	1,000 ng/mL	plasma	New Mexico	4
	Meclofenamic Acid	2,500 ng/mL	plasma	USA Equestrian	15
	Meclofenamic Acid	1,000 ng/mL	blood	Idaho	13
29	Mephenesin	200 ng/mL	plasma	Jockey Club of Brasileiro	11

Continued on next page

APPENDIX VII: *Continued*

	Medication	Concentration	Fluid	Jurisdiction	Ref #
30	Mepivacaine	5 ng/mL	urine	Ohio	1
	Mepivacaine	10 ng/mL	urine	California	2
	Mepivacaine	10 ng/mL	urine	Washington	3
	Mepivacaine	10 ng/mL	urine	New Mexico	4
31	Methocarbamol	1,000 ng/mL	plasma	Ohio	1
32	Methoxytramine	4,000 ng/mL	urine	International	6
33	Methylprednisolone	1,000 ng/mL	urine	Ohio	1
34	Morphine	50 ng/mL	urine	Ohio	1
	Morphine	75 ng/mL	urine	Louisiana	8
	Morphine	110 ng/mL	urine	HFL	16
35	Naproxen	5,000 ng/mL	blood	Idaho	13
36	Oxyphenbutazone	5,000 ng/mL	plasma	North America (ARCI)	17
	Oxyphenbutazone	5,000 ng/mL	plasma	Ohio	1
	Oxyphenbutazone	5,000 ng/mL	plasma	Louisiana	8
	Oxyphenbutazone	5,000 ng/mL	blood	Idaho	13
	Oxyphenbutazone	165,000 ng/mL	urine	Louisiana	8
37	Pentazocine	50 ng/mL	urine	Ohio	1
38	Phenylbutazone	5,000 ng/mL	plasma	North America (ARCI)	17
	Phenylbutazone	700 ng/mL	plasma	Jockey Club of Brasileiro	11
	Phenylbutazone	5,000 ng/mL	plasma	Louisiana	8
	Phenylbutazone	5,000 ng/mL	plasma	Texas	5
	Phenylbutazone	5,000 ng/mL	plasma	California	2
	Phenylbutazone	5,000 ng/mL	plasma	Pennsylvania	12
	Phenylbutazone	5,000 ng/mL	plasma	New Mexico	4
	Phenylbutazone	5,000 ng/mL	blood	Idaho	13
	Phenylbutazone	165,000 ng/mL	urine	Louisiana	8
	Phenylbutazone	165,000 ng/mL	urine	Idaho	13
39	Prednisolone	1,000 ng/mL	urine	Ohio	1
40	Prednisone	100 ng/mL	urine	Ohio	1
41	Procaine	750 ng/mL	urine	Hong Kong	18
	Procaine	25 ng/mL	plasma	Canada	10
	Procaine	100 ng/mL	plasma	Jockey Club of Brasileiro	11
	Procaine	50 ng/mL	urine	Ohio	1
	Procaine	10 ng/mL	urine	California	2
	Procaine	25 ng/mL	urine	Washington	3
	Procaine	10 ng/mL	urine	New Mexico	4
42	Promazine	20 ng/mL	plasma	Jockey Club of Brasileiro	11
	Promazine	50 ng/mL	urine	Washington	3
	Promazine	25 ng/mL	urine	New Mexico	4
	Promazine	25 ng/mL	urine	Ohio	1
	Promazine	25 ng/mL	urine	California	2
43	Pyrilamine	5 ng/mL	plasma	Jockey Club of Brasileiro	11
	Pyrilamine	50 ng/mL	plasma	Ohio	1
44	Salicylates	750,000 ng/mL	urine	California	2
	Salicylates	750,000 ng/mL	urine	Washington	3
	Salicylates	750,000 ng/mL	urine	Ohio	1
	Salicylates	750,000 ng/mL	urine	New Mexico	4
45	Salicylic Acid	750,000 ng/mL	urine	Ohio	1
	Salicylic Acid	750,000 ng/mL	urine	International	6
	Salicylic Acid	750,000 ng/mL	urine	Texas	5
	Salicylic Acid	6,500 ng/mL	plasma	International	6
46	Terbutaline	10 ng/mL	urine	Ohio	1
47	Testosterone (epitestosterone)	20 ng/mL (geldings)	urine	International	6
	Testosterone	55 ng/mL (fillies & mares)	urine	International	6
48	Tetramisole	80 ng/mL	plasma	Jockey Club of Brasileiro	11
49	Theobromine	2,000 ng/mL	urine	Ohio	1
	Theobromine	2,000 ng/mL	urine	International	6
	Theobromine	2,000 ng/mL	urine	Texas	5

**BZE is the major urinary metabolite of cocaine.*

For comparative purposes, the "thresholds" for human urine concentrations, as established by the Department of Health and Human Services' Substance Abuse and Mental Health Services Administration (SAMHSA), are listed below.

NB: The opiate testing cutoff concentrations were increased, effective December 1, 1998, from 300 ng/ml to 2,000 ng/ml.

Continued on next page

APPENDIX VII: *Continued*

Marijuana metabolite[1]	15 ng/ml	urine	SAMHSA	19
Cocaine metabolite[2]	150 ng/ml	urine	SAMHSA	19
Morphine	2,000 ng/ml	urine	SAMHSA	20
Codeine	2,000 ng/ml	urine	SAMHSA	20
6-Acetylmorphine[3]	10 ng/ml	urine	SAMHSA	20
Phencyclidine	25 ng/ml	urine	SAMHSA	19
Amphetamine	500 ng/ml	urine	SAMHSA	19
Methamphetamine[4]	500 ng/ml	urine	SAMHSA	19

1: Delta-9-tetrahydrocannabinol-9-carboxylic acid.

2: Benzoylecgonine.

3: Test for 6-AM when the morphine concentration exceeds 2,000 ng/ml.

4: Specimen must also contain amphetamine at a concentration > 200 ng/ml.

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APPENDIX IX: ACKNOWLEDGEMENTS

This National Policy was inspired by Mr Ted Bassett of the Keeneland Association, who suggested to Don Sturgill, General Counsel to the National HBPA, that the HBPA develop a national medication policy. This suggestion of Mr Bassett's resonated with that made by Kent Stirling of the Florida HBPA at the summer HBPA meeting in Boston in 2001. Don immediately alerted President John Roark and Executive Director Remi Bellocq of the National HBPA, and within days, Kent and Dr Thomas Tobin, with the assistance of Remi Bellocq and the National HBPA Medication Committee, began drafting this policy. This document, therefore, is a tribute to the leadership and foresight of Ted Bassett, Kent Stirling, Don Sturgill, John Roark, and Remi Bellocq, and all the members of the National HBPA Medication Committee.

The Medication Committee was well positioned to draft this document. Starting in 1994, under President Mel Bowman, the HBPA began supporting and encouraging research on therapeutic medication regulation. In August of that year, they supported an international workshop on Testing for Therapeutic Medications, Environmental and Dietary Substances in Racing Horses at the Maxwell H. Gluck Equine Research Center at the University of Kentucky. This workshop represented an intellectual turning point, in that it marked the formal academic acceptance of the concept of limited sensitivity testing for therapeutic medications in the United States.

The HBPA has also tackled the scientific problems facing medication control programs. In 1995, the Florida HBPA, under President Kent Stirling, initiated a chemical synthesis program for equine drug metabolite standards at the University of Kentucky (Appendix IV). Additionally, local HBPAs and the National HBPA under Presidents Bill Walmsley and Rick Hiles supported research on developing a scientific basis for regulatory thresholds for therapeutic medications (Appendix V).

This work on regulatory thresholds for therapeutic medications was accepted and published in the scientific literature, and it also attracted the attention of researchers. In 1998, the Journal of Veterinary Pharmacology and Therapeutics requested an overview of HBPA-supported research in this area. This review, which summarizes much of the work supported by the HBPA up to 1999, is attached to and made a part of this report.
This research on regulatory thresholds for therapeutic medications was also supported by the Kentucky Racing Commission, the Kentucky Equine Drug Council, and the dedicated efforts of members of the Equine Pharmacology, Experimental Therapeutics and Toxicology group at the University of Kentucky. Additionally, it is a pleasure to recognize the ongoing support of the faculty of the Gluck Equine Research Center and its director, Dr Peter Timoney. Finally, much of this document reflects the editorial contributions of Mrs Linda Keisel of Agricultural Communications Services in the College of Agriculture at the University of Kentucky and the ongoing support and contributions of Ms Amy Troppmann of the Gluck Equine Research Center.

APPENDIX X: SCIENTIFIC REVIEW

For a full scientific review of the thresholds material presented herein, please consult "Testing for therapeutic medications: analytical/pharmalogical relationships and 'limitations' on the sensitivity of testing for certain agents."J Vet Pharmacol Ther 1999;22:220-33 [KY AG Exp sta #98-14-134]

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