The National HBPA, Inc.
NATIONAL HEADQUARTERS
www.hbpa.org

3380 Paris Pike • Lexington, KY 40511
(859) 259-0451 – Telephone (859) 259-0452 – Facsimile
Email: racing@hbpa.org

President & Chairman
Dr. Doug Daniels – VA

Chief Executive Officer
Eric J. Hamelback

Regional Vice Presidents
J. Lloyd Yother – AZ
Joe Davis – IN
Rick Hiles – KY
Sandee Martin – PA

Secretary/Treasurer
Lynne Schuller – NE

General Counsel
Peter Ecabert

Federal Trade Commission:

On behalf of the National Horsemen's Benevolent and Protective Association ("National HBPA") along with guidance from our veterinary advisory group North American Association of Racetrack Veterinarians ("NAARV"), this letter is submitted in response to the FTC request for public comment on the proposed **HISA Anti-Doping and Medication Control Rule and Prohibited Substances Technical Document, posted October 28, 2022**. With that said, it is our belief that the law is unconstitutional, violates the nondelegation doctrine, the Due Process clause, and other provisions of the U.S. Constitution. Thus, the National HBPA is of the opinion the law is fundamentally unworkable and the mitigation efforts to make it work, violate the provisions of HISA. For these reasons and the information set forth below, the National HBPA is of the opinion that the technical document currently posted is in need of a significant corrective overhaul.

The National HBPA is also of the opinion Congress (as is evident by the provisions within HISA) intended the Authority submit both the racetrack safety regulations and the anti-doping and medication regulations at the same time to be evaluated together. Allowing for this piecemeal submission makes it impossible for interested parties to know how these rules will be impacted by the additional proposed rules to come. As a result, several issues that touch on both regulations, (i.e., the fee structure), remain unresolved.

Subject to the objections above, the National HBPA provides the following public comments regarding the proposed HISA Prohibited Substances Technical Document and Anti-Doping and Medication Control Rule . The document and its contents have been reviewed in detail by the scientific and veterinary advisors to the NAARV and National HBPA. We have a number of concerns with the manner in which this document completely reorganizes the existing ARCI Uniform Classifications. The ARCI Uniform Classification Guidelines has been developed and refined over many years with the input of many scientists and chemists, and its classifications are first and foremost focused on the potential for a substance to affect racing performance, or endanger the welfare of the horse. We believe these factors do not appear to have been primary considerations in the development of the HISA Prohibited Substances Document.

We are forced to assume at this point every blank spot in the Prohibited Substances Technical Document is accompanied by regulation at limit of detection (LOD), without regard for its ability to be transferred from the environment or a very long terminal half-life. With that assertion we are convinced more innocent horsemen/women will be penalized than the guilty. A full 12% of substances on the list are at risk of environmental transfer either from their common, legal use as an oral medication, or their stability in the environment. Further, veterinarians will be handicapped as to what can be used for the health and welfare of the horse, because of extremely long terminal half-lives for therapeutics such as aminocaproic acid or trazodone.

Further concern comes from the majority of the substances in the Prohibited Substances Technical Document, even S7 substances, are **listed without a detection time**. We have already experienced that "limit of detection" comes with a high price, rendering many, if not most therapeutic substances out of reach of the veterinary practitioner, who is tasked with the primary responsibility of maintaining the health and welfare of the horse. An example of the disconnect between this HISA document and the European system upon which it appears to be based on - the European Horserace Scientific Liaison Committee (EHSLC) Detection Times List (Feb 2021) – is that the EHSLC has both clodronate and tildronate [tiludronate] listed with 30-day detection times. Yet we now know the detection time as published in November 2021 demonstrates using a higher sensitivity testing

methodology, tiludronic acid can actually be detected for over three years beyond its last administration. This one example along with others reiterate the issues and concerns for this document.

As stated, the HISA Prohibited Substances Technical Document has been reviewed in detail by the scientific and veterinary advisors to the NAARV and National HBPA, and we address our number of concerns within the material and references set forth below. We also wish to reiterate how this document completely ignores the ask that has been aimed at peer reviewed, veterinary science-based research to achieve uniformity that has been heard for many years, but instead completely reorganizes the existing ARCI Uniform Classifications. It is not an understatement to say again as we have in previous comments, the concerns for horsemen and women have been expressed to achieve uniformity, not a complete overhaul of the rules found ARCI Uniform Classification Guidelines themselves.

Our concerns are outlined in the following sections:

1. HISA S0 Prohibited Substances List
    a. Limiting of therapeutic medications not to otherwise LEGAL medications, but only to FDA Approved medications, rather than Approved and Listed;
    b. Including FDA Approved medications in common therapeutic use on the S0, banned at all times list;
    c. Including metabolites of S7 substances in the S0 category;
    d. Banning of Standard of Practice medications required for breeding fillies;
    e. Banning of anesthesia induction and reversal agents;
    f. Banning of long-term tranquilizers used in the peri-operative period for the health and welfare of horses requiring stall rest;
    g. Imposition of a 14-month period of ineligibility for any medication, endangering such horses, with no scientific basis for such a requirement.
2. Endogenous and Dietary Substances List (Specified Substances)
    a. Failure to identify all endogenous and dietary substances as Specified Substances;
    b. Failure to include screening limits for endogenous and dietary substances.
3. Environmental Substances List (Specified Substances)
    a. Failure to recognize that environmental substances are Specified Substances;
    b. Failure to include screening limits for environmental substances.
4. Therapeutic (Controlled) Medication (S7) List
    a. Detection Times are a huge step backwards from reliable withdrawal times;
    b. Multiple errors in the Technical Document require clarification and correction;
    c. A transition or grace period during the early period of implementation of the severe; restrictions on therapeutic medications for horses is essential to preserve the health and welfare of the athlete, and the very existence of the sport.

Respectfully Submitted,

National HBPA and NAARV

HORSEMEN'S BENEVOLENT & PROTECTIVE ASSOCIATION CHARTERED 1940
H·B·P·A

NAARV
NORTH AMERICAN ASSOCIATION OF RACETRACK VETERINARIANS

Dear Lisa Lazarus and HISA members:

On behalf of the National Horsemen's Benevolent and Protective Association ("National HBPA") along with guidance from our veterinary advisory group North American Association of Racetrack Veterinarians ("NAARV"), this letter is submitted in response to your request for public comment on the proposed HISA **Prohibited Substances Technical Document, received July 21, 2022**. With that said, it is our belief that the law is unconstitutional, violates the nondelegation doctrine, the Due Process clause, and other provisions of the U.S. Constitution. Thus, the National HBPA is of the opinion the law is fundamentally unworkable and the mitigation efforts to make it work, violate the provisions of HISA. For these reasons and the information set forth below, the National HBPA is of the opinion that the technical document currently posted is in need of a significant corrective overhaul.

The National HBPA is also of the opinion Congress (as is evident by the provisions within HISA) intended the Authority submit both the racetrack safety regulations and the anti-doping and medication regulations at the same time to be evaluated together. Allowing for this piecemeal submission makes it impossible for interested parties to know how these rules will be impacted by the additional proposed rules to come. As a result, several issues that touch on both regulations, (i.e., the fee structure), remain unresolved.

Subject to the objections above, the National HBPA provides the following public comments regarding the proposed HISA Prohibited Substances Technical Document. The document and its contents have been reviewed in detail by the scientific and veterinary advisors to the NAARV and National HBPA. We have a number of concerns with the manner in which this document completely reorganizes the existing ARCI Uniform Classifications. The ARCI Uniform Classification Guidelines has been developed and refined over many years with the input of many scientists and chemists, and its classifications are first and foremost focused on the potential for a substance to affect racing performance, or endanger the welfare of the horse. We believe these factors do not appear to have been primary considerations in the development of the HISA Prohibited Substances Document.

We are forced to assume at this point every blank spot in the Prohibited Substances Technical Document is accompanied by regulation at limit of detection (LOD), without regard for its ability to be transferred from the environment or a very long terminal half-life. With that assertion we are convinced more innocent horsemen/women will be penalized than the guilty. A full 12% of substances on the list are at risk of environmental transfer either from their common, legal use as an oral medication, or their stability in the environment. Further, veterinarians will be handicapped as to what can be used for the health and welfare of the horse, because of extremely long terminal half-lives for therapeutics such as aminocaproic acid or trazodone.

Further concern comes from the majority of the substances in the Prohibited Substances Technical Document, even S7 substances, are **listed without a detection time**. We have already experienced that "limit of detection" comes with a high price, rendering many, if not most therapeutic substances out of reach of the veterinary practitioner, who is tasked with the primary responsibility of maintaining the health and welfare of the horse. An example of the disconnect between this HISA document and the European system upon which it appears to be based on - the European Horserace Scientific Liaison Committee (EHSLC) Detection Times List (Feb 2021) – is that the EHSLC has both clodronate and tildronate listed with 30-day detection times. Yet we now know the detection time as published in November 2021 demonstrates using a higher sensitivity testing methodology, tildronic acid

can actually be detected for over three years beyond its last administration. This one example along with others reiterate the issues and concerns for this document.

As stated, the HISA Prohibited Substances Technical Document has been reviewed in detail by the scientific and veterinary advisors to the NAARV and National HBPA, and we address our number of concerns within the material and references set forth below. We also wish to reiterate how this document completely ignores the ask aimed at peer reviewed, veterinary science-based research to achieve uniformity that has been heard for many years, but instead completely reorganizes the existing ARCI Uniform Classifications. It is not an understatement to say again as we have in previous comments, the concerns for horsemen and women have been expressed to achieve uniformity, not a complete overhaul of the rules found ARCI Uniform Classification Guidelines themselves.

Our concerns are outlined in the following sections:

1. HISA S0 Prohibited Substances List
    a. Limiting of therapeutic medications not to otherwise LEGAL medications, but only to FDA Approved medications, rather than Approved and Listed;
    b. Including FDA Approved medications in common therapeutic use on the S0, banned at all times list;
    c. Including metabolites of S7 substances in the S0 category;
    d. Banning of Standard of Practice medications required for breeding fillies;
    e. Banning of anesthesia induction and reversal agents;
    f. Banning of long-term tranquilizers used in the peri-operative period for the health and welfare of horses requiring stall rest;
    g. Imposition of a 14-month period of ineligibility for any medication, endangering such horses, with no scientific basis for such a requirement.
2. Endogenous and Dietary Substances List (Specified Substances)
    a. Failure to identify all endogenous and dietary substances as Specified Substances;
    b. Failure to include screening limits for endogenous and dietary substances.
3. Environmental Substances List (Specified Substances)
    a. Failure to recognize that environmental substances are Specified Substances;
    b. Failure to include screening limits for environmental substances.
4. Therapeutic (Controlled) Medication (S7) List
    a. Detection Limits are a huge step backwards from reliable withdrawal times;
    b. Multiple errors in the Technical Document require clarification and correction;
    c. A transition or grace period during the early period of implementation of the severe; restrictions on therapeutic medications for horses is essential to preserve the health and welfare of the athlete, and the very existence of the sport.

Respectfully Submitted,

National HBPA and NAARV

Comprehensive Evaluation for S0 Substances

The first comprehensive evaluation set forth is for the defined **S0 Substances**. As stated, we are assuming every blank spot in the Prohibited Substances Technical Document is accompanied by regulation at limit of detection, without regard for its ability to impact racing integrity or equine health at the levels identified. The entire S0 category of substances reflects a gross misunderstanding by the Authority of what is **legal** to administer to an animal. The FDA's approval status only determines how a product may be marketed, not whether it is legal and **does not** indicate whether a drug is legal to use, dispense or administer. FDA approval actually indicates the marketing status of the drug, and whether or not the labeling can include a drug claim. Drugs are legal to be purchased, dispensed and administered as long as they are manufactured in facilities registered with the FDA and listed with the FDA, or compounded and labeled according to the Pharmacy Board regulations of the state in which they are sold. This was determined by the Drug Listing Act of 1972 (https://www.fda.gov/drugs/electronic-drug-registration-and-listing-system-edrls/annex-b-drug-listing-act-1972-information-bulletin). All FDA approved and FDA listed products are produced in FDA inspected manufacturing facilities (cGMP manufacturing), and their labels reviewed by the FDA, ensuring the strength, quality, purity and potency.

S0 substances are defined in HISA Series 4111 as:

"Any pharmacological substance that is not addressed by Rules 4112 through 4117 and with no current approval by any governmental regulatory health authority for veterinary or human therapeutic use or any substance not universally recognized by veterinary regulatory authorities as a valid veterinary therapeutic Treatment is prohibited at all times." A finding of such a substance is accompanied by period of ineligibility to race for 14 months.

The Act requires that Section 1206(b)(1) *"…Covered horses should compete only when they are free from the influence of medications, other foreign substances, and methods that affect their performance."* This is the FIRST consideration required of HISA, and appears to be completely ignored, in favor of a requirement NOT enumerated in the Act, that of medications being FDA Approved. A clear example of this is the placement of Isoxsuprine (https://ndclist.com/search-animal.php?sNDCAnimal=isoxsuprine), and Carbazochrome Salicylate, legal, listed, ARCI classified substances at 4, the second lowest risk category for integrity or equine welfare, now grossly misplaced into the S0 category. Clearly, the Authority deviates from its mandate in order to push an agenda against non-FDA approved substances.

There are 106 FDA Approved substances and 10 Listed substances in the HISA S0 category. Of these, there are 19 FDA Approved (Table 1a) and 9 Listed substances (Table 1b) that are in therapeutic use in equine practice. A brief review of the veterinary literature and published formularies (Hagyard's, Sanders) reflects the use of these substances. Based on the severe proposed penalty of up to a 14-month period of ineligibility for any horse demonstrated to have been administered an S0 substance, we strongly believe no substances with a valid therapeutic use should ever be in the S0 category.

Additionally, we are alarmed with the fact that several primary metabolites of S7 substances are included in the S0 list. If the S7 substance does not warrant an S0 penalty, then there is no place for its primary metabolites on the S0 list. These substances are indicated with an asterisk (*) in Table 1a.

Particular interest should focus on substances administered in the context of either breeding of race fillies or the surgery and peri-surgery period. Fillies are commonly bred and continue to race up to

4 months of pregnancy. The scheduling of all breeding associated medications, such as Deslorelin, as S0 would effectively bring this practice to a halt. Many pre-anesthetic, anesthesia induction agents and medications such as reversal agents are in this S0 category. Further, all long-acting sedatives in use to keep horses safe during the peri-surgical period are effectively banned. A simple surgery to remove a chip fracture, usually accompanied by a 6-to-8-week respite from racing, could inadvertently turn into a 14-month ineligibility period because of an innocuous administration of a therapeutic medication, administered for the purpose of maintaining the health and welfare of the animal.

Up to a 14 month period of racing ineligibility for a horse administered any substances in this category is particularly severe, considering that both listed (Animal Drugs, https://ndclist.com/search-animal.php , and human drugs https://www.accessdata.fda.gov/scripts/cder/ndc/index.cfm) as well as compounded medications are in legal use in race horses, in the out of competition period. This provision adversely impacts the health and welfare of the horse, by either preventing the horse from receiving the most appropriate therapy, or preventing a horse from being in training for 14 months after being inadvertently administered one of these common, legal substances. Even if an owner is willing to lay a horse up for 14 months, this time frame will place that horse at higher risk of catastrophic injury. Horses require training to maintain appropriate bone modeling,[1] and 14 months reflects a substantial amount of time during critical growth and development. The pharmacology of these substances in no case justifies a 14-month period of ineligibility to ensure integrity or safety, and this time frame penalizes not only the trainer and owner, but also the breeder, who is completely innocent of any possible wrongdoing.

We urge the HISA Anti-Doping and Medication Committee to consider the placement of FDA approved medications or their metabolites currently categorized as S0 into the S7 category and to further reconsider the 14-month ineligibility period. Unless such a penalty might be reasonable for the use of substances like designer anabolic steroids or EPO (interesting to note: Erythropoietin is actually listed as an S2 substance in the Series 4000, associated with the shorter ineligibility period of 6 months). However, it is inappropriate to include in this S0 category, therapeutic substances whose use is Standard of Veterinary Practice as reflected by their inclusion in common Equine Formularies or a cursory search of the scientific and veterinary literature.

[1] Carrier TK, Estberg L, Stover SM, Gardner IA, Johnson BJ, Read DH, Ardans AA. Association between long periods without high-speed workouts and risk of complete humeral or pelvic fracture in thoroughbred racehorses: 54 cases (1991-1994). J Am Vet Med Assoc. 1998 May 15;212(10):1582-7. PMID: 9604029.

Table 1a: Valid therapeutic uses of FDA approved substances on the HISA S0 list (prohibited at all times). *Indicates a metabolite on the S0 list that is a primary metabolite of an S7 substance.

HISA S0 Substances	Use	Included in Equine Formulary	Reference(s)
Atipamezole	Alpha-2 agonist reversal agent	Yes	Hubbell and Muir 2006
Betaxolol	Beta-agonist ophthalmic for glaucoma		Tolar and Labelle 2013
Buprenorphine	Pre-anesthetic	Yes	Taylor et al 2015
Cannabinoids	Anti-inflammatory		St Blanc et al 2022
Chloral hydrate	Sedative	Yes	Benson and Thurman 1990
Deslorelin	Stimulation of ovulation	Yes	Ganheim et al 1995 (+ many others)
Edrophonium	Reversal of neuromuscular blocking agents during anesthesia	Yes	Martin-Flores et al 2012 (+ many others)
Fluoxetine	Facilitate stall rest	Yes	Fontenot et al 2021 (+ others)
Meprobamate*	Metabolite of Carisoprodol, an S7 substance		Lewandowski 2017
Methazolamide	Glaucoma		Olliver and Monclin 2010
Naltrexone	Opioid antagonist, stimulation follicular development		UCVM Class of 2018 et al 2018 Dodman et al 1987
Nordazepam*	Metabolite of Diazepam, an S7 substance		Schenk et al 2021
Paroxetine	Facilitate stall rest		Nurnberg et al 1997
Perphenazine	Facilitate stall rest Stimulation follicular development		McCrindle et al 1989 Bennett-Winbush et al 1998
Pregabalin	Neurogenic pain	Yes	Mullin et al 2013
Thiopental	Anesthesia	Yes	Wakuno et al 2017 Tokushige et al 2019 (+ many others)
Tolazoline	Reversal of alpha 2 agonists	Yes	Hubbell and Muir 2006
Trazodone	Facilitate stall rest	Yes	Davis et al 2018

Table 1b: Valid therapeutic uses of FDA Listed substances on the HISA S0 list (prohibited at all times).

HISA S0 Substances	Use	Included in Equine Formulary	Reference(s)
Ambroxol	Mucolytic		Dieckmann 1987
Carbazochrome Salicylate	EIPH preventative		Perez-Moreno et al 2009
Buserelin	Ovulation in mares	Yes	Barrier-Battut et al 2001
Dembrexine	Mucolytic	Yes	Matthews et al 1988
Ethamsylate	EIPH preventative		Segura et al 2007
Isoxsuprine	Vasodilator for improved blood flow, laminitis, navicular disease, sesamoiditis	Yes	Belloli et al 2000
Strychnine	Colic, appetite		Homeopathic
Sulpiride	Stimulation of follicular development in mares	Yes	Oberhaus et al 2019
Ethanol	Arthrodesis of distal hock joints		Lamas 2012

Table 1 References:

Barrier-Battut I, Le Poutre N, Trocherie E, Hecht S, Grandchamp des Raux A, Nicaise JL, Vérin X, Bertrand J, Fiéni F, Hoier R, Renault A, Egron L, Tainturier D, Bruyas JF. Use of buserelin to induce ovulation in the cyclic mare. Theriogenology. 2001 May 1;55(8):1679-95. doi: 10.1016/s0093-691x(01)00512-x. PMID: 11393219.

Belloli C, Carcano R, Arioli F, Beretta C. Affinity of isoxsuprine for adrenoreceptors in equine digital artery and implications for vasodilatory action. Equine Vet J. 2000 Mar;32(2):119-24. doi: 10.2746/042516400777591543. PMID: 10743967.

Bennett-Wimbush K, Loch WE, Plata-Madrid H, Evans T. The effects of perphenazine and bromocriptine on follicular dynamics and endocrine profiles in anestrous pony mares. Theriogenology. 1998 Mar;49(4):717-33. doi: 10.1016/S0093-691X(98)00021-1. PMID: 10732080.

Benson GJ, Thurmon JC. Intravenous anesthesia. Vet Clin North Am Equine Pract. 1990 Dec;6(3):513-28. doi: 10.1016/s0749-0739(17)30528-x. PMID: 2282545.

Davis JL, Schirmer J, Medlin E. Pharmacokinetics, pharmacodynamics and clinical use of trazodone and its active metabolite m-chlorophenylpiperazine in the horse. J Vet Pharmacol Ther. 2018 Jun;41(3):393-401. doi: 10.1111/jvp.12477. Epub 2018 Jan 14. PMID: 29333613; PMCID: PMC7167085.

Dieckmann, M.P. (1987) Zur Wirksamkeit von Ambroxolhydrochlorid (Mukovent) bein lungenkranken Pferden-klinische, Funktionelle und zytologische Untersuchungen. Dissertation, Tieraerztliche Hochschule Hannover, Germany.

Dodman NH, Shuster L, Court MH, Dixon R. Investigation into the use of narcotic antagonists in the treatment of a stereotypic behavior pattern (crib-biting) in the horse. Am J Vet Res. 1987 Feb;48(2):311-9. PMID: 3826875.

Fontenot RL, Mochal-King CA, Sprinkle SB, Wills RW, Calder CD. Retrospective Evaluation of Fluoxetine Hydrochloride Use in Horses: 95 Cases (2010-2019). J Equine Vet Sci. 2021 Feb;97:103340. doi: 10.1016/j.jevs.2020.103340. Epub 2020 Dec 4. PMID: 33478760.

Gånheim A, Gånheim A, Jöchle W. Acceleration and timing of fertile ovulation in cyclic mares with a deslorelin implant. Acta Vet Scand. 1995;36(4):393-400. doi: 10.1186/BF03547654. PMID: 8669367; PMCID: PMC8095403.

Gerring EE, Hunt JM. Pathophysiology of equine postoperative ileus: effect of adrenergic blockade, parasympathetic stimulation and metoclopramide in an experimental model. Equine Vet J. 1986 Jul;18(4):249-55. doi: 10.1111/j.2042-3306.1986.tb03618.x. PMID: 3758000.

Hubbell JA, Muir WW. Antagonism of detomidine sedation in the horse using intravenous tolazoline or atipamezole. Equine Vet J. 2006 May;38(3):238-41. doi: 10.2746/042516406776866408. PMID: 16706278.

Table 1 References, continued:

Lamas LP, Edmonds J, Hodge W, Zamora-Vera L, Burford J, Coomer R, Munroe G. Use of ethanol in the treatment of distal tarsal joint osteoarthritis: 24 cases. Equine Vet J. 2012 Jul;44(4):399-403. doi: 10.1111/j.2042-3306.2011.00512.x. Epub 2011 Dec 1. PMID: 22128830.

Lewandowski TA. Pharmacokinetic modeling of carisoprodol and meprobamate disposition in adults. Hum Exp Toxicol. 2017 Aug;36(8):846-853. doi: 10.1177/0960327116672912. Epub 2016 Oct 10. PMID: 27758843.

Loos CMM, Urschel KL, Vanzant ES, Oberhaus EL, Bohannan AD, Klotz JL, McLeod KR. Effects of Bromocriptine on Glucose and Insulin Dynamics in Normal and Insulin Dysregulated Horses. Front Vet Sci. 2022 May 31;9:889888. doi: 10.3389/fvets.2022.889888. PMID: 35711802; PMCID: PMC9194999.

Marti M, Mevissen M, Althaus H, Steiner A. In vitro effects of bethanechol on equine gastrointestinal contractility and functional characterization of involved muscarinic receptor subtypes. J Vet Pharmacol Ther. 2005 Dec;28(6):565-74. doi: 10.1111/j.1365-2885.2005.00693.x. PMID: 16343290.

Martin-Flores M, Pare MD, Adams W, Campoy L, Gleed RD. Observations of the potency and duration of vecuronium in isoflurane-anesthetized horses. Vet Anaesth Analg. 2012 Jul;39(4):385-9. doi: 10.1111/j.1467-2995.2012.00720.x. Epub 2012 May 30. PMID: 22642379.

Matthews AG, Hackett IJ, Lawton WA. The mucolytic effect of Sputolosin in horses with respiratory disease. Vet Rec. 1988 Jan 30;122(5):106-8. doi: 10.1136/vr.122.5.106. PMID: 3363832.

McCrindle CM, Ebedes H, Swan GE. The use of long-acting neuroleptics, perphenazine enanthate and pipothiazine palmitate in two horses. J S Afr Vet Assoc. 1989 Dec;60(4):208-9. PMID: 2577292.

Mullen KR, Schwark W, Divers TJ. Pharmacokinetics of single-dose intragastric and intravenous pregabalin administration in clinically normal horses. Am J Vet Res. 2013 Jul;74(7):1043-8. doi: 10.2460/ajvr.74.7.1043. PMID: 23802677.

Nurnberg HG, Keith SJ, Paxton DM. Consideration of the relevance of ethological animal models for human repetitive behavioral spectrum disorders. Biol Psychiatry. 1997 Jan 15;41(2):226-9. doi: 10.1016/s0006-3223(96)00100-x. PMID: 9018394.

Oberhaus EL, Thompson DL Jr, Foster BA, Pinto CR. Effects of Combined Estradiol-Sulpiride Treatment and Follicle Ablation on Vernal Transition in Mares: Evaluation of Plasma and Follicular Fluid Hormones and Luteinizing Hormone Receptor Gene Expression. J Equine Vet Sci. 2018 May;64:69-76. doi: 10.1016/j.jevs.2018.02.020. Epub 2018 Feb 27. PMID: 30973156.

Ollivier F, Monclin S. 2010. Equine Glaucomas. Equine Vet Educ 2010 June 299-304.
Perez-Moreno CI, Couëtil LL, Pratt SM, Ochoa-Acuña HG, Raskin RE, Russell MA. Effect of furosemide and furosemide-carbazochrome combination on exercise-induced pulmonary hemorrhage in Standardbred racehorses. Can Vet J. 2009 Aug;50(8):821-7. PMID: 19881919; PMCID: PMC2711466.

Table 1 References, continued:

Schenk I, Machnik M, Broussou D, Meuly A, Roques BB, Lallemand E, Düe M, Röttgen H, Lagershausen H, Toutain PL, Thevis M. Kinetic disposition of diazepam and its metabolites after intravenous administration of diazepam in the horse: Relevance for doping control. J Vet Pharmacol Ther. 2021 Sep;44(5):733-744. doi: 10.1111/jvp.12991. Epub 2021 Jun 11. PMID: 34115414.

Segura D, Monreal L, Pérez-Pujol S, Alonso A, Díaz-Ricart M, Brugués R, Ordinas A, Escolar G. Effects of etamsylate on equine platelets: in vitro and in vivo studies. Vet J. 2007 Sep;174(2):325-9. doi: 10.1016/j.tvjl.2006.06.002. Epub 2006 Aug 10. PMID: 16904352.

Taylor PM, Hoare HR, de Vries A, Love EJ, Coumbe KM, White KL, Murrell JC. A multicentre, prospective, randomised, blinded clinical trial to compare some perioperative effects of buprenorphine or butorphanol premedication before equine elective general anaesthesia and surgery. Equine Vet J. 2016 Jul;48(4):442-50. doi: 10.1111/evj.12442. Epub 2015 Jun 10. PMID: 25772950; PMCID: PMC5033022.

Tokushige H, Araki M, Kusano K, Arima D, Ito H, Yamazaki Y, Urayama S, Kambayashi Y, Tateno O, Ohta M. A retrospective comparison of induction with thiopental/guaifenesin and propofol/ketamine in Thoroughbred racehorses anesthetized with sevoflurane and medetomidine during arthroscopic surgery. J Equine Sci. 2019 Jul;30(2):25-31. doi: 10.1294/jes.30.25. Epub 2019 Jul 3. PMID: 31285690; PMCID: PMC6606449.

Tolar EL, Labelle AL. How to diagnose and manage horses with glaucoma. Proc AAEP 2013 59:174-180.

UCVM DVM Class of 2018, Kwong GPS, Klein C. Deslorelin and naltrexone stimulate follicular development in mares during autumn transition and early anestrus. Can Vet J. 2019 Aug;60(8):855-858. PMID: 31391602; PMCID: PMC6625173.

Wakuno A, Aoki M, Kushiro A, Mae N, Kodaira K, Maeda T, Yamazaki Y, Ohta M. Comparison of alfaxalone, ketamine and thiopental for anaesthetic induction and recovery in Thoroughbred horses premedicated with medetomidine and midazolam. Equine Vet J. 2017 Jan;49(1):94-98. doi: 10.1111/evj.12548. Epub 2016 Feb 6. PMID: 26850885.

Zakia LS, Gomez DE, Kenney DG, Arroyo LG. Sabulous cystitis in the horse: 13 cases (2013-2020). Can Vet J. 2021 Jul;62(7):743-750. PMID: 34219784; PMCID: PMC8218954.

Review of Endogenous and Dietary Substances

Review of Endogenous and Dietary Substances:

HISA recognizes the existence of substances that may be present in forage or otherwise may contaminate the environment of the horse, by establishing the category of "Specified Substances." This designation and the characteristics that place a substance into this category is not defined or explained in any approved or draft HISA regulation, but is comprised of substances for which sanctions are "…subject to more flexible sanctions" (**Series 4010**). However, the Federation Equestre Internationale (FEI) defines Specified Substances as "…substances which are more likely to have been ingested by Horses for a purpose other than the enhancement of sport performance, for example, through a contaminated food substance." (https://inside.fei.org/fei/about-fei/nis-sportsforum/2020/equine/overview-5#:~:text=A%20Specified%20Substance%20can%20be,Banned%20Substance%20(Specified%20Substance)., accessed 8/6/2022) and we strongly recommend that this definition also be adopted by HISA.

In a recent meeting on June 20, 2022, at Churchill Downs, Lisa Lazarus, CEO of HISA indicated that, in the case of a Specified Substance, horsemen would have an opportunity to establish the source of a positive, which would then be a mitigating circumstance. Our concern with this approach is that the source of environmental and dietary substances often remains unidentified, despite thorough investigation. Horsemen are typically informed of a positive test weeks after the hay or feed is consumed, making any conclusive investigation of source almost impossible.

Endogenous Substances:

Substances that are both produced by the animal's own body (endogenous) and can be exogenously administered must be regulated by thresholds that are determined by widespread testing of normal populations. One substance included on the S0 Prohibited List and one substance on the S1 Prohibited List are produced by the animal's own body without a listed threshold. One substance on the S0 Prohibited list and three substances included on the Controlled S7 list are produced by the animal's own body and are associated with a threshold, although the scientific data underlying those thresholds are not provided by HISA (Table 2a).

We urge HISA to **remove all endogenous substances** from the S0 category, since these would be expected to be present at some level in all animals. We further urge HISA to adopt science-based screening limits for endogenous substances in order to prevent inappropriate penalties.

Dietary Substances:

Dietary substances are those that can be detected in the animal's blood or urine from its natural presence in hay or feed. There are 13 dietary substances in the HISA S0 category, of which only 2 are associated with screening limits. There are 2 dietary substances in the HISA S1 category. There are 16 dietary substances in the HISA S7 category, of which only 10 are associated with a threshold (Table 2b).

We again urge HISA to adopt screening limits for all dietary substances. Some provisional screening limits can be readily adopted from existing sources. For example, there are in house screening limits for glaucine and lobeline at PETRL in Pennsylvania. Provisional screening limits exist in the scientific literature for others, including aminorex (75 ng/mL Urine),[1] synephrine (50 ng/mL Urine)[2] and cathinone (10 ng/mL urine).[3]

---

[1] Maylin G, Fenger C, Machin J, Kudrimoti S, Eisenberg R, Green J, Tobin T. Aminorex identified in horse urine following consumption of Barbarea vulgaris; a preliminary report. Ir Vet J. 2019 Dec 23;72:15. doi: 10.1186/s13620-019-0153-5. PMID: 31890155; PMCID: PMC6929286.

[2] Brewer K, Machin JJ, Maylin G, Fenger C, Morales-Briceño A, Neidhart MM, Tobin T. Case report: Synephrine, a plant substance yielding classic environmental clusters of hay related identifications in equine urine. Drug Test Anal. 2022 Apr;14(4):774-780. doi: 10.1002/dta.3212. Epub 2022 Jan 28. PMID: 35088566.

[3] Brewer K, Stirling K, Tobin T. World Rules for Equine Drug Testing and Therapeutic Medication Regulations. 2012. Wind Publications.

Table 2: (a) Endogenous Substances

HISA Schedule	Substance	Screening Limit in HISA Technical Document	Reference(s)
S0	Diisopropylamine	No	Liu et al 2018
S0	Dimethyltryptamine (DMT)	Yes	Rodrigues et al 2019
S1	Dihydrotestosterone	No	Hoffman and Landeck 1999
S7	Morphine	Yes	Stefano et al 2012
S7	Hydrocortisone	Yes	Tou et al 2022
S7	Prednisolone	Yes	Fidani et al 2012

Table 2: (b) Dietary Substances

HISA Schedule	Substance	Screening Limit	Source	Reference(s)
S0	Dimethyltryptamine (DMT)	Yes	Reed Canary Grass	Rodrigues et al 2019 Barker 2018
S0	Ergonovine	No	Claviceps fungus (rye)	Canty et al 2014 Meidaner and Geiger 2015
S0	Digitoxin	No	Foxglove	Castello et al 2012 Jamloka et al 2022
S0	Cannabinoids	No	Hemp	ElSohly et al 2017
S0	Paraxanthine	No	Caffeine	Dyke and Sams 1998 Machnik et al 2016
S0	Glaucine	No	Poplar Shavings	Haughn et al 2022
S0	Bufotenine	Yes	Reed Canary Grass	Marten 2015
S0	Dicoumarol	No	Sweet Clover	Blakley 1985 Olsen and Harty 2021
S0	Aminorex	No	Yellow Rocket	Maylin et al 2019
S0	Papaverine	No	Poppies	Davies and Hollman 2002
S0	Lobeline	No	Lobelia spp	Tamboli et al 2012
S0	Demecolcine	No	Autumn Crocus	Yamada et al 1998
S0	Oripavine	No	Poppies	Nielson et al 1983
S1	Zeranol	No	Fusarium fungus (corn)	Hsieh et al 2012
S1	THC	No	Hemp	ElSohly et al 2017
S7	Morphine	Yes	Poppies	Davies and Hollman 2002 Thevis et al 2003
S7	Atropine	Yes	Jimson Weed	Chan 2002
S7	Methylsulfonylmethane (MSM)	Yes	Alfalfa	Sham 2021 Pearson et al 1981
S7	Hordenine	Yes	Barley, Reed Canary Grass	Woods et al 1979
S7	Ergotamine	No	Claviceps fungus (rye)	Canty et al 2014 Meidaner and Geiger 2015
S7	Digoxin	No	Foxglove	Castello et al 2012 Jamloka et al 2022
S7	Capsaicin	No	Pepper	Morrison 2022
S7	Dihydroergotamine	No	Claviceps fungus (rye)	Canty et al 2014 Meidaner and Geiger 2015
S7	Salicylic Acid	Yes	Willow bark, apples, many sources	Vlachojannis et al 2011
S7	Scopolamine	Yes	Jimsonweed	Brewer et al 2014
S7	Synephrine	No	Teff hay	Brewer et al 2022
S7	Thebaine	No	Poppies	Seddigh et al 1982
S7	Arsenic	Yes	Any plant grown in a region with high soil Arsenic	Li et al 2015 Dartmouth Toxic Metals website
S7	Dimethylsulfoxide (DMSO)	Yes	Alfalfa	Sham 2021 Pearson et al 1981
S7	Theobromine	Yes	Chocolate	Dyke and Sams 1998 Machnik et al 2016
S7	Theophylline	Yes	Tea	Dyke and Sams 1998 Machnik et al 2016

Table 2 References:

Barker SA. N, N-Dimethyltryptamine (DMT), an Endogenous Hallucinogen: Past, Present, and Future Research to Determine Its Role and Function. Front Neurosci. 2018 Aug 6;12:536. doi: 10.3389/fnins.2018.00536. PMID: 30127713; PMCID: PMC6088236.

Blakley BR. Moldy sweet clover (dicoumarol) poisoning in Saskatchewan cattle. Can Vet J. 1985 Nov;26(11):357-60. PMID: 17422592; PMCID: PMC1680139.

Brewer K, Dirikolu L, Hughes CG, Tobin T. Scopolamine in racing horses: trace identifications associated with dietary or environmental exposure. Vet J. 2014 Mar;199(3):324-31. doi: 10.1016/j.tvjl.2013.12.013. Epub 2013 Dec 14. PMID: 24440440.

Brewer K, Shults TF, Machin J, Kudrimoti S, Eisenberg RL, Hartman P, Wang C, Fenger C, Beaumier P, Tobin T. A cluster of trace-concentration methamphetamine identifications in racehorses associated with a methamphetamine-contaminated horse trailer: A report and analysis. Can Vet J. 2016 Aug;57(8):860-4. PMID: 27493286; PMCID: PMC4944564.

Canty MJ, Fogarty U, Sheridan MK, Ensley SM, Schrunk DE, More SJ. Ergot alkaloid intoxication in perennial ryegrass (Lolium perenne): an emerging animal health concern in Ireland? Ir Vet J. 2014 Sep 25;67(1):21. doi: 10.1186/2046-0481-67-21. PMID: 25295161; PMCID: PMC4186922.

Castello LM, Negro S, Santi F, Zanotti I, Vidali M, Bagnati M, Bellomo G, Avanzi GC. Accidental digitoxin intoxication: an interplay between laboratory and clinical medicine. Biochem Med (Zagreb). 2012;22(3):380-4. doi: 10.11613/bm.2012.040. PMID: 23092069; PMCID: PMC3900044.

Chan K. Jimson Weed Poisoning—A Case Report. Perm J. 2002 Fall;6(4):28–30. PMCID: PMC6220643.

Dartmouth Toxic Metals “Arsenic in Plants.” sites.dartmouth.edu/toxmetal/research-projects/arsenic-uptake-transport-and-storage-in-plants/read-more-arsenic-in-plants/ accessed 8/6/22

Davies MK, Hollman A. The opium poppy, morphine, and verapamil. Heart vol. 88,1 (2002): 3.

Dyke TM, Sams RA. Detection and determination of theobromine and caffeine in urine after administration of chocolate-coated peanuts to horses. J Anal Toxicol. 1998 Mar-Apr;22(2):112-6. doi: 10.1093/jat/22.2.112. PMID: 9547407.

El Sohly MA, Radwan MM, Gul W, Chandra S, Galal A. Phytochemistry of Cannabis sativa L. Prog Chem Org Nat Prod. 2017;103:1-36. doi: 10.1007/978-3-319-45541-9_1. PMID: 28120229.

Fidani M, Pompa G, Mungiguerra F, Casati A, Fracchiolla ML, Arioli F. Investigation of the presence of endogenous prednisolone in equine urine by high-performance liquid chromatography mass spectrometry and high-resolution mass spectrometry. Rapid Commun Mass Spectrom. 2012 Apr 30;26(8):879-86. doi: 10.1002/rcm.6169. PMID: 22396023.

Haughan JE, Missanelli JR, You Y, Stefanovski D, Soma LR, Robinson MA. Pharmacokinetics of glaucine after intravenous and oral administrations and detection of systemic aporphine alkaloids after ingestion of tulip poplar shavings in horses. J Vet Pharmacol Ther. 2022 May;45(3):273-282. doi: 10.1111/jvp.13057. Epub 2022 Apr 8. PMID: 35394081.

Hoffmann B, Landeck A. Testicular endocrine function, seasonality and semen quality of the stallion. Anim Reprod Sci. 1999 Oct 31;57(1-2):89-98. doi: 10.1016/s0378-4320(99)00050-0. PMID: 10565441.

Hsieh HY, Shyu CL, Liao CW, Lee RJ, Lee MR, Vickroy TW, Chou CC. Liquid chromatography incorporating ultraviolet and electrochemical analyses for dual detection of zeranol and zearalenone metabolites in mouldy grains. J Sci Food Agric. 2012 Apr;92(6):1230-7. doi: 10.1002/jsfa.4687. Epub 2011 Oct 19. PMID: 22012692.

Table 2 References continued:

Jamloki A, Trivedi VL, Nautiyal MC, Semwal P, Cruz-Martins N. Poisonous Plants of the Indian Himalaya: An Overview. Metabolites. 2022 Jun 13;12(6):540. doi: 10.3390/metabo12060540. PMID: 35736473; PMCID: PMC9229149.

Li N, Wang J, Song WY. Arsenic Uptake and Translocation in Plants. Plant Cell Physiol. 2016 Jan;57(1):4-13. doi: 10.1093/pcp/pcv143. Epub 2015 Oct 10. PMID: 26454880.

Liu D, Zhao N, Wang M, Pi X, Feng Y, Wang Y, Tong H, Zhu L, Wang C, Li E. Urine volatile organic compounds as biomarkers for minimal change type nephrotic syndrome. Biochem Biophys Res Commun. 2018 Jan 29;496(1):58-63. doi: 10.1016/j.bbrc.2017.12.164. Epub 2017 Dec 30. PMID: 29291407.

Machin J, Brewer K, Morales-Briceno A, Fenger C, Maylin G, Tobin T. Sporadic worldwide "clusters" of feed driven Zilpaterol identifications in racing horses: a review and analysis. Ir Vet J. 2022 May 14;75(1):11. doi: 10.1186/s13620-022-00215-8. PMID: 35568924; PMCID: PMC9107120.

Machnik M, Kaiser S, Koppe S, Kietzmann M, Schenk I, Düe M, Thevis M, Schänzer W, Toutain PL. Control of methylxanthines in the competition horse: pharmacokinetic/pharmacodynamic studies on caffeine, theobromine and theophylline for the assessment of irrelevant concentrations. Drug Test Anal. 2017 Sep;9(9):1372-1384. doi: 10.1002/dta.2097. Epub 2016 Nov 4. PMID: 27662634.

Marten GC. Alkaloids in Reed Canarygrass. Anti-Quality Components of Forages, 2015, pp. 15–31., doi:10.2135/cssaspecpub4.c2.

Maylin G, Fenger C, Machin J, Kudrimoti S, Eisenberg R, Green J, Tobin T. Aminorex identified in horse urine following consumption of Barbarea vulgaris; a preliminary report. Ir Vet J. 2019 Dec 23;72:15. doi: 10.1186/s13620-019-0153-5. PMID: 31890155; PMCID: PMC6929286.

Miedaner T, Geiger HH. Biology, genetics, and management of ergot (Claviceps spp.) in rye, sorghum, and pearl millet. Toxins (Basel). 2015 Feb 25;7(3):659-78. doi: 10.3390/toxins7030659. PMID: 25723323; PMCID: PMC4379517.

Morrison, J. Hot Topic: Where Are All the Capsaicin Positives Coming from? Canadian Thoroughbred, 6 July 2020, canadianthoroughbred.com/horse-news/hot-topic-where-capsaicin-positives-coming-from/. Accessed 8/7/22

Nielsen B, Röe J, Brochmann-Hanssen E. Oripavine - a new opium alkaloid. Planta Med. 1983 Aug;48(8):205-6. doi: 10.1055/s-2007-969921. PMID: 17404984.

Olson, Ken and Additional Authors: Adele Harty. “Sweet Clover Poisoning.” SDSU Extension, 18 Nov. 2021, extension.sdstate.edu/sweet-clover-poisoning.

Pearson TW, Dawson HJ, Lackey HB. Natural occurring levels of dimethyl sulfoxide in selected fruits, vegetables, grains and beverages. J Agric Food Chem 1981 29:1089-1091.

Rodrigues AV, Almeida FJ, Vieira-Coelho MA. Dimethyltryptamine: Endogenous Role and Therapeutic Potential. J Psychoactive Drugs. 2019 Sep-Oct;51(4):299-310. doi: 10.1080/02791072.2019.1602291. Epub 2019 Apr 25. PMID: 31018803.

Seddigh M, Jolliff GD, Calhoun W et al. Papaver bracteatum, potential commercial source of codeine. Econ Bot 36, 433–441 (1982). https://doi.org/10.1007/BF02862702

Table 2 References continued:

Sham L. DMSO (Dimethyl Sulfoxide) and MSM (Methylsulfonylmethane) Now Have International Residue Limits. National Horseracing Authority, 28 Oct. 2021, www.nhra.co.za/index.php/general-notice/691-dmso-dimethyl-sulfoxide-and-msm-methylsulfonylmethane-now-have-international-residue-limits

Stefano GB, Ptáček R, Kuželová H, Kream RM. Endogenous morphine: up-to-date review 2011. Folia Biol (Praha). 2012;58(2):49-56. PMID: 22578954.

Tamboli AM, Rub RA, Ghosh P, Bodhankar SL. Antiepileptic activity of lobeline isolated from the leaf of Lobelia nicotianaefolia and its effect on brain GABA level in mice. Asian Pac J Trop Biomed. 2012 Jul;2(7):537-42. doi: 10.1016/S2221-1691(12)60092-6. PMID: 23569966; PMCID: PMC3609340.

Thevis M, Opfermann G, Schänzer W. Urinary concentrations of morphine and codeine after consumption of poppy seeds. J Anal Toxicol. 2003 Jan-Feb;27(1):53-6. doi: 10.1093/jat/27.1.53. PMID: 12587685.

Tou K, Cawley A, Bowen C, Sornalingam K, Fu S. Measurements of hydrocortisone and cortisone for longitudinal profiling of equine plasma by liquid chromatography-tandem mass spectrometry. Drug Test Anal. 2022 May;14(5):943-952. doi: 10.1002/dta.3244. Epub 2022 Mar 4. PMID: 35195373.

Vlachojannis J, Magora F, Chrubasik S. Willow species and aspirin: different mechanism of actions. Phytother Res. 2011 Jul;25(7):1102-4. doi: 10.1002/ptr.3386. PMID: 21226125.

Woods DL, Hovin AW, Marten GC. Seasonal variation of hordenine and gramine concentrations and their heritability in reed canarygrass [Phalaris arundinacea]. Crop Science 1979 19(6):853-857.

Yamada M, Nakagawa M, Haritani M, Kobayashi M, Furuoka H, Matsui T. Histopathological study of experimental acute poisoning of cattle by autumn crocus (Colchicum autumnale L.). J Vet Med Sci. 1998 Aug;60(8):949-52. doi: 10.1292/jvms.60.949. PMID: 9764409.

Review of Environmental Substances

Review of Environmental Substances:

Environmental Substances include veterinary pharmaceuticals, human pharmaceuticals, human recreational drugs and even by-products of manufacturing. For drugs or medications taken or administered to humans or animals, substances that are (1) eliminated in the urine at a high level, (2) stable in the environment, and (3) readily absorbed by the mucus membranes or gastrointestinal tract are considered to be Environmental Substances. Additionally, substances found in human or animal topical products, or administered by mouth to horses are highly susceptible to being taken up by horses in trace amounts close to racing, as a result of their presence on feed tubs, hay nets and even the cobwebs of the barn.[1] Again referencing the establishment of the "Specified Substances" category by HISA, it is clear the ADMC committee recognizes inadvertent environmental transfer can and does occur, resulting in positive tests. Some human medications may be identified in ground water at levels in the ng/mL range,[2] exceeding the levels at which a positive may be called in a race horse. Substances meeting these criteria, highly stable in the environment and readily accessible to horses are shown in Tables 3a and 3b. These substances cut across all HISA Schedules (S0-S7), and include equine therapeutics, human therapeutics and human recreational substances.

With the ever-increasing sensitivity of drug testing in horse racing the Environmental Substances that are readily detected in water, reflecting stability in the environment or commonly present in human topical products, should all be included as Specified Substances. Further, in the adjudication resulting from an adverse analytical finding for a Specified Substance, at a level consistent with inadvertent environmental transfer rather than intentional administration should be eligible for a minimal penalty for the trainer and the horse. A preponderance of evidence supports that such adverse analytical findings are randomly occurring, have no impact on the performance of the horse, and serve only to fuel bad publicity for the industry.

Also, we wish to address the concept that the Responsible Person must investigate and provide evidence for the source of Adverse Analytical Findings violates the due process owed American citizens. The Authority investigations of adverse analytical findings should include procedures that provide potentially exculpatory evidence, and be directed at identifying facts and truth, rather than placing the investigatory agency in the direct role of identifying only incriminating evidence. In many cases, the source of the inadvertent environmental exposure cannot be identified. Adverse Analytical Findings may be communicated to Responsible Persons after the last of a batch of hay, straw or feed has been consumed, or employees have moved on.

In a recent interview,[3] Dr. Scott Stanley suggested that a "…*non-prosecutorial "initial review" first take place before any regulatory action occurs, if indeed environmental contamination appears a genuine possibility*," which is the only possible way to address all such adverse analytical findings. In very few cases have stalls been swabbed or tested for contamination with Environmental Substances, a procedure we believe should be conducted in every case in which a positive for an Environmental Substance is identified. Forensic investigation of laboratory findings, such as the identification of the parent esters of substances in the case of steroids, the co-identification of other plant alkaloids in the case of alkaloids identification, and the determination of the presence of both glucuronidated and non-glucuronidated metabolites in urine. Further, drug testing of stable employees of the trainer, and also of the race track and test barn, as well as the swabbing of stalls for drug testing should all be standard

[1] Russell CS, Maynard S. Environmental contamination with Isoxsuprine. In Proceedings of the 13th International Conference of Racing Analysts and Veterinarians, eds RB Williams, E Houghton, JF Wade, pp 381-383.
[2] Patel M, Kumar R, Kishor K, Mlsna T, Pittman CU Jr, Mohan D. Pharmaceuticals of Emerging Concern in Aquatic Systems: Chemistry, Occurrence, Effects, and Removal Methods. Chem Rev. 2019 Mar 27;119(6):3510-3673. doi: 10.1021/acs.chemrev.8b00299. Epub 2019 Mar 4. PMID: 30830758.
[3] Ross D. The Black Eye of contamination, Part two. Thoroughbred Daily News, Nov 23, 2020.

procedures in the investigation of Adverse Analytical Findings. Integrity in Horse racing should not mean a conviction at any cost, but rather a good faith effort to determine the facts and truth of all Adverse Analytical Findings.

Similar to the dietary substances, screening limits consistent with environmental contamination should be considered for Environmental Substances. The Authority can readily adopt interim limits from existing Equine Drug Testing laboratories that have in-house screening limits for some environmental substances. Further, the scientific literature provides screening limit recommendations, including Cocaine (as Benzoylecgonine),[4] methamphetamine,[5] Dextromethorphan (as dextrorphan)[6] and Dexamethasone.[7]

[4] Camargo FC, Hughes C, Lehner AF, Stirling K, Tobin T. "Trace" Benzoylecgonine Identifications in PostRace Urines: Probable Sources and Regulatory Significance of Such Identifications. 2006. AAEP Proceedings 52:331-336.
[5] Brewer K, Shults TF, Machin J, Kudrimoti S, Eisenberg RL, Hartman P, Wang C, Fenger C, Beaumier P, Tobin T. A cluster of trace-concentration methamphetamine identifications in racehorses associated with a methamphetamine-contaminated horse trailer: A report and analysis. Can Vet J. 2016 Aug;57(8):860-4. PMID: 27493286; PMCID: PMC4944564.
[6] Machin J, Shults T, Fenger CK, Tobin T. Inadvertent Environmental Transfer of Dextromethorphan from Groom to Racehorse Results in the Establishment of a Pharmacologically Relevant Cutoff. 2017 ToxTalk 41(2):20-22.
[7] McClure S, Fenger C, Kersh K, Brown B, Maylin G, Duer W, Dirikolu L, Brewer K, Machin J, Tobin T. Dexamethasone serum concentrations after intravenous administration in racing horses during race training. Comparative Exercise Physiology. 2020 17(3):263-272.

Table 3: (a) Environmental Substances: HISA Schedule S0 through S6

HISA Schd	Substance	Screening Limit	Human Recrea.	Human Pharm.	Equine Pharm.	Reference(s)
S0	Cannabinoids	No	Yes	Yes	No	Common ingredient in hand lotions/sanitizers
S0	Paraxanthine	No	No	Yes	No	Bexfield et al 2019
S1	THC	No	Yes	Yes	No	Carmona et al 2014
S0	Trazodone	No	No	Yes	Yes	Pivetta et al 2020
S0	Fluoxetine	No	No	Yes	Yes	Bexfield et al 2019 Bradley et al 2016
S0	3,4-methylenedioxypyrovalerone (MDVP)	No	Yes	No	No	Fenger et al 2018
S0	Acetanilide	No	No	No	No	Stamper et al 1998 EPA 1995
S0	Amphetamine	No	Yes	Yes	No	Bradley et al 2016 Fenger et al 2018 Brewer et al 2016
S0	Cathinone	No	Yes	No	No	Kind et al 2016
S0	Cocaine (as Benzoylecgonine)	No	Yes	No	No	Pal et al 2012 Fenger et al 2018
S0	Codeine	No	Yes	Yes	No	Thurman et al 2018 Bradley et al 2016
S0	Dextropropoxyphene	No	Yes	No	No	Bradley et al 2016
S0	Hydrocodone (dihydrocodienone)	No	Yes	Yes	No	Bradley et al 2016
S0	Isoxsuprine	No	No	No	Yes	Fenger et al 2018
S0	Meprobamate (metabolite of S7 substance Carisoprodol)	No	Yes	Yes	Yes	Bradley et al 2016 Bexfield et al 2019 Fenger et al 2018
S0	Methadone	No	No	Yes	No	Bradley et al 2016 Bexfield et al 2019 Fenger et al 2018
S0	Methamphetamine	No	Yes	Yes	No	Bradley et al 2016 Fenger et al 2018 Brewer et al 2016
S0	Methylphenidate	No	Yes	Yes	No	Fenger et al 2018
S0	Nikethamide	No	Yes	No	No	Fenger et al 2018
S0	Nordazepam	No	Yes	No	No	Bexfield et al 2019
S0	Oxycodone	No	Yes	Yes	No	Thurman et al 2018 Bradley et al 2016 Fenger et al 2018
S0	Sertraline	No	Yes	Yes	No	Bradley 2016
S0	Sildenafil	No	No	Yes	No	Hong et al 2021
S0	Venlafaxine	No	No	Yes	No	Thurman et al 2018 Bradley et al 2016
S0	Muscarine	No	No	No	No	
S1	Norethisterone (norethindrone)	No	No	Yes	No	Bradley et al 2016
S1	Ractopamine	No	No	No	No	Machin et al 2022
S1	Zilpaterol	No	No	No	No	Machin et al 2022
S5	Triamterene	No	No	Yes	No	Bradley et al 2016
S6	Altrenogest	No	No	No	Yes	Golovko et al 2018 Common oral use in fillies is likely to result in environmental transfer to males/geldings

Table 3: (b) Environmental Substances: HISA Schedule S7

HISA Schd	Substance	Screening Limit	Human Recrea.	Human Pharm.	Equine Pharm.	Reference(s)
S7	Carbamazepine	No	Yes	Yes	Yes	Patel et al 2019 Bexfield et al 2019 Bradley et al 2016 Wang et al 2011 Santiago-Martin et al 2020
S7	Acebutolol	No	No	Yes	No	Gabet Giraud et al 2014
S7	Acetaminophen	No	No	Yes	Yes	Santiago-Martin et al 2020
S7	Albuterol	Yes	No	Yes	Yes	Weider et al 2013
S7	Alprazolam	No		Yes		Bradley 2016
S7	Amitriptyline	No		Yes		Bradley 2016
S7	Atenolol	No		Yes		Bradley 2016 Patel 2019 Thurman 2018 Bexfield 2019 Gabet Giraud et al 2014
S7	Benzocaine	No		Yes		Topical
S7	Betamethasone	Yes		Yes		Topical
S7	Bupivacaine	No		Yes		Topical
S7	Bupropion	No		Yes		Bradley 2016 Thurman 2018 Bexfield 2019
S7	Caffeine	Yes		Yes		Barker 2008
S7	Carisoprodol	No		Yes		Bradley 2016 Bexfield 2019
S7	Chlorpheniramine	No		Yes		Bradley 2016
S7	Citalopram	No		Yes		Bradley 2016 Bexfield 2019
S7	Dexamethasone	Yes		Yes		McClure 2021
S7	Dexamethasone sodium phosphate	No		Yes		McClure 2021
S7	Dextromethorphan	No		Yes		Thurman 2018 Bexfield 2019 Bradley 2019 Fenger 2017 (dextrorphan)
S7	Diazepam	No		Yes		Bradley 2016
S7	Diltiazem	No		Yes		Thurman 2018 Bradley 2016
S7	Famotidine	No		Yes		Bradley 2016
S7	Fexofenadine	No		Yes		Bradley 2016
S7	Firocoxib	No		Yes		Fenger 2017
S7	Flunixin	Yes		Yes		Norgren 2000 Popot 2007 Fenger 2017
S7	Gabapentin	No		Yes		Thurman 2018
S7	Glycopyrrolate	No		Yes		Fenger 2017
S7	Guaifenesin (glycerol guiacolate)	Yes		Yes		Fenger 2017
S7	Ketoprofen	Yes		Yes		Fenger 2017
S7	Levamisole	No		No		Mooney et al 2020 Gutierrez et al 2010
S7	Lidocaine	Yes		Yes		Bexfield 2019 Bradley 2016 Martinez Piernas 2021 Fenger 2017 Topical

HISA Schd	Substance	Screening Limit	Human Recrea.	Human Pharm.	Equine Pharm.	Reference(s)
S7	Medroxyprogesterone	No		Yes		Golovko et al 2017
S7	Mepivacaine	Yes		Yes		Martinez Piernas 2021
S7	Metaxalone	No		Yes		Bexfield 2019 Bradley 2016
S7	Metformin	No		Yes		Bexfield 2019 Bradley 2016 Fenger 2017
S7	Methocarbamol	No		Yes		Bexfield 2019 Bradley 2016 Fenger 2017
S7	Methylsalicylate	No		Yes		Carmona et al 2014
S7	Metoprolol	No		Yes		Patel, 2019 Thurman 2018 Bradley 2016 Fenger 2017
S7	Minoxidil	No		Yes	No	Topical
S7	Morphine	Yes	Yes	Yes	Yes	Pal et al 2012
S7	Naproxen	No		Yes		Wennerlund 2000 Fenger 2017
S7	Nifedipine	No		Yes		Bradley 2016
S7	Oxazepam	No		Yes		Kosjek 2011
S7	Pemoline	No				Mooney et al 2020 Gutierrez et al 2010
S7	Pentoxyfylline	No		Yes		Bexfield 2019 Bradley 2016
S7	Phenytoin	No		Yes		Bradley 2016
S7	Pramoxine	No		Yes		Topical
S7	Propranolol	No		Yes		Bradley 2016 Patel 2019
S7	Pseudoephedrine	No		Yes		Bexfield 2019 Bradley 2016
S7	Pyrilamine	No				Thompson and Holder 1984
S7	Temazepam	No		Yes		Bexfield 2019 Bradley 2016
S7	Tramadol	No		Yes		Bradley 2016 Fenger 2017
S7	Verapamil	No		Yes		Bradley 2016
S7	Altrenogest	No				Golovko et al 2018 Common oral use in fillies is likely to result in environmental transfer to males/geldings
S7	Diclofenac	Yes		Yes		Carmona et al 2014 Topical
S7	Lamotrigine	No		Yes		Thurman 2018
S7	Loratidine	No		Yes		Bradley 2016
S7	Acepromazine	Yes				Fenger 2017
S7	Cimetidine	No		Yes		Bexfield 2019 Bradley 2016
S7	Diphenhydramine	No		Yes		Thurman 2018 Bradley 2016
S7	Omeprazole	Yes		Yes		Fenger 2017
S7	Ranitidine	No		Yes		Bradley 2016 Fenger 2017

Table 3 References:

Barker SA. Drug contamination of the equine racetrack environment: a preliminary examination. J Vet Pharmacol Ther. 2008 Oct;31(5):466-71. doi: 10.1111/j.1365-2885.2008.00978.x. PMID: 19000266.

Bexfield LM, Toccalino PL, Belitz K, Foreman WT, Furlong ET. Hormones and Pharmaceuticals in Groundwater Used As a Source of Drinking Water Across the United States. Environ Sci Technol. 2019 Mar 19;53(6):2950-2960. doi: 10.1021/acs.est.8b05592. Epub 2019 Mar 5. PMID: 30834750.

Bradley PM, Journey CA, Button DT, Carlisle DM, Clark JM, Mahler BJ, Nakagaki N, Qi SL, Waite IR, VanMetre PC. Metformin and Other Pharmaceuticals Widespread in Wadeable Streams of the Southeastern United States. Environmental Science & Technology Letters 2016 3 (6), 243-249. DOI: 10.1021/acs.estlett.6b00170

Carmona E, Andreu V, Picó Y. Occurrence of acidic pharmaceuticals and personal care products in Turia River Basin: from waste to drinking water. Sci Total Environ. 2014 Jun 15;484:53-63. doi: 10.1016/j.scitotenv.2014.02.085. Epub 2014 Mar 29. PMID: 24686145.

de Santiago-Martín A, Meffe R, Teijón G, Martínez Hernández V, López-Heras I, Alonso Alonso C, Arenas Romasanta M, de Bustamante I. Pharmaceuticals and trace metals in the surface water used for crop irrigation: Risk to health or natural attenuation? Sci Total Environ. 2020 Feb 25;705:135825. doi: 10.1016/j.scitotenv.2019.135825. Epub 2019 Nov 30. PMID: 31818606.

Fenger CK, Catignani M, Machin J, Tobin T. An in depth look at stall contamination: A total of 28 substances were identified in Charlestown Ship-In stalls as a mix of human medications and recreational substances and some actual equine medications. Horseman's Journal Winter 2017, pp 41 – 44.

Fidani M, Pompa G, Mungiguerra F, Casati A, Fracchiolla ML, Arioli F. Investigation of the presence of endogenous prednisolone in equine urine by high-performance liquid chromatography mass spectrometry and high-resolution mass spectrometry. Rapid Commun Mass Spectrom. 2012 Apr 30;26(8):879-86. doi: 10.1002/rcm.6169. PMID: 22396023.

Gabet Giraud V, Miege C, Jacquet R, Coquery M. Impact of wastewater treatment plants on receiving surface waters and a tentative risk evaluation: the case of estrogens and beta blockers. Environmental Science and Pollution Research, Springer Verlag, 2014, 21 (3), p. 1708 - p. 1722. 10.1007/s11356-013-2037-7. hal-01072988

Golovko O, Šauer P, Fedorova G, Kroupová HK, Grabic R. Determination of progestogens in surface and waste water using SPE extraction and LC-APCI/APPI-HRPS. Sci Total Environ. 2018 Apr 15;621:1066-1073. doi: 10.1016/j.scitotenv.2017.10.120. Epub 2017 Nov 6. PMID: 29102184.

Hong Y, Lee I, Tae B, Lee W, Pan SY, Snyder SW, Kim H. Contribution of sewage to occurrence of phosphodiesterase-5 inhibitors in natural water. Sci Rep. 2021 May 4;11(1):9470. doi: 10.1038/s41598-021-89028-3. PMID: 33947926; PMCID: PMC8096833.

https://www3.epa.gov/pesticides/chem_search/reg_actions/reregistration/fs_PC-108801_1-Apr-95.pdf, accessed 8/8/22

Patel M, Kumar R, Kishor K, Mlsna T, Pittman CU Jr, Mohan D. Pharmaceuticals of Emerging Concern in Aquatic Systems: Chemistry, Occurrence, Effects, and Removal Methods. Chem Rev. 2019 Mar 27;119(6):3510-3673. doi: 10.1021/acs.chemrev.8b00299. Epub 2019 Mar 4. PMID: 30830758.

Pivetta RC, Rodrigues-Silva C, Ribeiro AR, Rath S. Tracking the occurrence of psychotropic pharmaceuticals in Brazilian wastewater treatment plants and surface water, with assessment of environmental risks. Sci Total Environ. 2020 Jul 20;727:138661. doi: 10.1016/j.scitotenv.2020.138661. Epub 2020 Apr 14. PMID: 32334225.

Table 3 References continued:

Russell CS, Maynard S. Environmental contamination with Isoxsuprine. In Proceedings of the 13th International Conference of Racing Analysts and Veterinarians, eds RB Williams, E Houghton, JF Wade, pp 381-383.

Stamper DM, Tuovinen OH. Biodegradation of the acetanilide herbicides alachlor, metolachlor, and propachlor. Crit Rev Microbiol. 1998;24(1):1-22. doi: 10.1080/10408419891294163. PMID: 9561822.

Thompson HC Jr, Holder CL. Trace analysis of the antihistamines methapyrilene hydrochloride, pyrilamine maleate and triprolidine hydrochloride monohydrate in animal feed, human urine and wastewater by high-performance liquid chromatography and gas chromatography with nitrogen-phosphorus detection. J Chromatogr. 1984 Jan 20;283:251-64. doi: 10.1016/s0021-9673(00)96260-5. PMID: 6142898.

Thurman EM, Ferrer I, Zweigenbaum JA. Identification of unknowns in ground and surface water by LC/Q-TOF. Application Note Environmental. Agilent Technologies, Inc.

Wieder ME, Paine SW, Hincks PR, Pearce CM, Scarth J, Hillyer L. Detection and pharmacokinetics of salbutamol in thoroughbred racehorses following inhaled administration. J Vet Pharmacol Ther. 2015 Feb;38(1):41-7. doi: 10.1111/jvp.12150. Epub 2014 Sep 17. PMID: 25229326.

Handling of Therapeutic Medications (S7)

The Prohibited Substances Technical Document handling of therapeutic medications (S7) indicates a clear departure from the original ARCI goal of establishing scientifically based withdrawal times and thresholds for therapeutic medications that would permit their use to protect the health and welfare of the equine athlete. HISA has, instead, determined the regulation of most therapeutic medications is to be at limit of detection. This decision fails to place the health and welfare of the horse first and foremost in the development of its regulations. Most therapeutic medications can be detected well below their Irrelevant Plasma Concentration, owing to prolonged terminal half-lives and modern high-sensitivity drug testing. For example, Aminocaproic Acid, a substance commonly used to prevent EIPH during Workouts, and also used as a life-saving medication in the event of hemorrhage can be identified for at least seven days after administration, which is 6 days beyond any possible effect. Regulation at the limit of detection restricts the use of many therapeutic medications, which endangers the health and welfare of the horse, because many horsemen have no choice but to refuse appropriate care if it might prevent the horse from racing in a reasonable, predictable time frame. Further, limit of detection regulations for therapeutic medications are subject to change at any moment when the technology advances, the very definition of arbitrary and capricious.

The ARCI thresholds have been developed over the course of a number of years, with input from multiple different chemists and scientists, and input from Industry in open meetings. We are disappointed to see that the ARCI thresholds for substances for which no IFHA Screening Limit exists are ignored in the Prohibited Substances Technical Document. The Act requires that Section 1206(b)(1) "…*Covered horses should compete only when they are free from the influence of medications, other foreign substances, and methods that affect their performance*" and Section 1206(g)(2)(A) *"…the baseline antidoping and medication control rules described in this paragraph are …the lists of permitted and prohibited substances…in effect for the International Federation of Horseracing Authorities for urine and …plasma*." Therefore, there was no reason for the Authority to abandon the in-place ARCI thresholds for substances not included in the IFHA screening limits.

The Horseracing Integrity and Safety Act mandates that as a base line, HISA is to rely on the International Federation of Horseracing Authorities (IFHA) International Screening Limits for urine and plasma. Certain screening limits and detection times are set forth in the HISA Technical Document, however it is unclear from the document upon what scientific basis HISA relies for the listed "Detection Times."

In most cases, the detection times appear to have been taken from the European Horserace Scientific Liaison Committee (EHSLC) detection times. A Detection Time is defined as the longest time post administration that the last of a very small group of horses (usually 4 to 6, but as few as 2 in the HISA Technical Document) no longer tests positive for a substance at a level which is not always defined in the Technical Document. Withdrawal periods are estimated as being anywhere between 1.4 to 2 times the length of the Detection Time, although this provides no reliable guidance for the regulated horsemen.[1] Controlled Therapeutic medications have been regulated by the ARCI by establishing a withdrawal period that represents a balance between appropriate care of the equine athlete, and preventing an effect of the medication on the outcome of the race. Thresholds have been developed based on the withdrawal period. While this approach has its own drawbacks, it is significantly more scientifically rigorous than virtually all of the HISA/IFHA therapeutic medication guidelines. Where the

[1] Toutain PL. How to extrapolate a withdrawal time from an EHSLC published detection time: a Monte Carlo simulation appraisal. Equine Vet J. 2010 Apr;42(3):248-54. doi: 10.1111/j.2042-3306.2010.00028.x. PMID: 20486982.

detection times are based on only 2 horses, such as for Hydroxyzine, an actual withdrawal period is essentially impossible to determine.

The limit of detection of one laboratory may be very different than the limit of detection of another. The European Screening limits (and therefore detection times) were established by seeking to achieve "harmonization" between their laboratories.[2] The lowest screening limit **that ALL labs** could achieve for certain substances was accepted even when some labs were capable of much lower limits. This was intended to avoid a positive test in one lab that couldn't be confirmed in another; referred to as "risk management". Generally speaking, U.S. labs are capable of much lower detection limits than their IFHA counterparts, and nothing comparable to the European "harmonization" exists. For example, EHSLC, using IFHA "harmonized" screening limits, lists both clodronate and tiludronate with 30-day detection times. Using higher sensitivity testing methodology,[3] tiludronate can be detected for over three years beyond its last administration. Clearly, the lab and lab methodology determine the detection time, and the EHSLC detections times cannot be relied upon for estimating withdrawal times for therapeutic medications when testing is conducted in U.S. laboratories that may have a higher testing sensitivity. Any publication or use of detection times require studies to be conducted in the laboratories that will be performing the actual drug testing. Otherwise, publication of detection times determined by less sensitive testing methodology as guidance for American horsemen/women is entrapment.

It is also important to note the science behind all of the EHSLC detection times, the limit of detection or screening limit that was used in determining these detection times, is not disclosed. Unlike the European countries from which these limits were taken, in the United States, the 6th Amendment to the Constitution guarantees the right for the accused to see the evidence against them. In this country, penalties cannot be assigned to individuals based on inaccurate and undisclosed scientific bases. As delineated in the footnotes of Table 4, there are a number of outright errors in the Technical Document that are easily identified. While we are appreciative where the adoption of IFHA screening limits provides added protections for horsemen with horses requiring therapeutic medications that were not historically discussed, it is far from being as comprehensive as it should be. It is also concerning that there are likely to be many more errors, were we able to review any actual data.

Finally, we strongly urge HISA to establish a transition period between the existing therapeutic medication regulations and the new IFHA based regulations. Errors are going to occur, and horses requiring medication are not going to be medicated. Unless a transition period is in place to gradually impose the proposed penalties, the upheaval in horse racing will be unsurpassed in history.

[2] Toutain P. Transcript of testimony in NYRA V Baffert

[3] Riggs CM, Thompson SL, So YM, Wong JKY, Wan TSM, Robinson P, Stewart BD, Ho ENM. Tiludronic acid can be detected in blood and urine samples from Thoroughbred racehorses over 3 years after last administration. Equine Vet J. 2021 Nov;53(6):1287-1295. doi: 10.1111/evj.13395. Epub 2020 Dec 23. PMID: 33247964.

Table 4: Selected Therapeutic (S7) Substances comparison to ARCI

Substance	Therapeutic use	Route	HISA Detection Time	HISA SL	ARCI Threshold
Acepromazine	Sedation, tying up	IV oral	48 h IV 72 h oral	10 ng/mL HEPS urine*	10 ng/mL HEPS urine
Acetylcysteine	Mucolytic	Inhaled IV	No	No	No
Acetylsalicylic Acid†	Uveitis Tying Up	Oral	No	750 mcg/mL urine* 6.5 mcg/mL serum*	750 mcg/mL urine 6.5 mcg/mL serum
Albuterol	Inflammatory Airway Disease	Inhaled	72 h	0.5 ng/mL urine*	1 ng/mL urine
Altrenogest	Heat suppression	Oral	No	No	No
Atropine	Mydriasis	Ophth.	No	60 ng/mL urine*	No
Betamethasone	Anti-inflammatory	IA Topical	No	0.2 ng/mL urine*	No
Butorphanol	Sedation	IV IM	72 h	No	300 ng/mLurine 2 ng/mL serum
Ceterizine	Antihistamine	Oral	No	No	6 ng/mL serum
Ciclosenide‡	Inflammatory Airway Disease	Inhaled	?	No	No
Cimetidine	Anti-ulcer	Oral	No	No	400 ng/mL serum
Clenbuterol	Inflammatory Airway Disease	Oral	Minimum Vet's List 21 days	No	140 pg/mL urine
Dantrolene	Tying Up	Oral	48 h	3 ng/mL 5-OH Urine*	100 pg/mL 5-OH Serum
Detomidine	Sedation	IV IM	48 h	2 ng/mL 3-OH Urine*	2 ng/mL COOH Urine 1 ng/mL Serum
Dexamethasone††	Anti-inflammatory	Oral IV IM	72 h	0.2 ng/mL Urine*	No
Dexamethasone Sodium Phosphate††	Anti-Inflammatory	IV	72 h	No	No
Diclofenac	Anti-inflammatory	Topical	No	50 ng/mL Urine*	No
Dimethylsulfoxide	Anti-inflammatory	IV Topical	No	15 mcg/mL Urine* 1 mcg/mL serum*	10 mcg/mL serum
Dipyrone	Anti-inflammatory	IV	72 h	1 mcg/mL urine * (4-methyl metabolite)	No
Firocoxib	Anti-inflammatory	Oral	360 h	No	No
Flunixin	Anti-inflammatory	IV	144 h	100 ng/mL urine*	5 ng/mL serum
		Oral	(no guidance)		

Guaifenesin	Mucolytic	Oral	48 h	12 ng/mL serum	12 ng/mL serum
		IV	(no guidance)		
Hydrocortisone	Anti-inflammatory	Topical IV IM	No guidance	1 mcg/mL urine*	No
Hydroxyzine**	Anti-histamine	Oral	96 h	No	No
Ipratropium	Bronchodilator	Inhaled	120 h	0.25 ng/mL urine*	No
Ketoprofen	Anti-inflammatory	IV IM	96 h	100 ng/mL Urine*	2 ng/mL serum
Lidocaine	Local anesthetic	SQ IA	72 h	10 ng/mL 3-OH Urine*	20 pg/mL 3-OH serum
Medetomidine	Sedation	IV	No	5 ng/mL 3-OH Urine*	No
Mepivacaine	Local anesthetic	SQ IA	No	10 ng/mL 3-OH urine*	10 ng/mL 3-OH urine or LOD serum
Misoprostil	Anti-ulcer	Oral	48 h	No	No
N-Butylscopolammonium	Gas Colic	IV	48 h	25 ng/mL Urine*	No
Omeprazole	Anti-ulcer	Oral	48 h	1 ng/mL Urine unhydrolyzed *	10 ng/ml serum
Phenylbutazone	Anti-inflammatory	Oral IV	168 h	100 ng/mL Urine*	0.3 mcg/ml serum
Prednisolone	Anti-inflammatory	Oral	48 h	10 ng/mL Urine*	No
Romifidine	Sedation	IV	60 h	1 ng/mL Urine*	No
Triamcinolone‡‡	Anti-inflammatory	IA	No	0.5 ng/ml*	No
Xylazine	Sedation	IV	No	10 ng/ml 4-OH Urine*	200 pg/mL serum

*Screening Limit identical to IFHA

†Acetylsalicylic acid is listed in the Technical Document as aspirin, with no threshold indicated, and aminosalicylic acid is listed as salicylate with a threshold. Since aminosalicylic acid does not metabolize to salicylate, we are assuming that this is an error, and the threshold for salicylate was intended to be in the Acetylsalicylic acid row.

‡The Technical Document indicates a dose and dosage recommendation for Ciclosenide in 6 horses, but no actual detection time is listed in the document.

††Dexamethasone Sodium Phosphate is listed separately from Dexamethasone, but Dexamethasone Sodium Phosphate is rapidly hydrolyzed to free dexamethasone, and is never identified in drug testing as its ester. On the other hand, injectable Dexamethasone as the FDA Approved formulation is manufactured with propylene glycol which prolongs its half-life, and represents approximately 25% more dexamethasone than the same mg quantity of dexamethasone sodium phosphate. Since the source of the 72-hour detection time is not disclosed in this document, we have not modified this chart. The original RMTC data used Dexamethasone Sodium Phosphate for both the IM and IV data, and dexamethasone for the oral data. If this is the case, the actual dose of dexamethasone in the IM and IV datasets is closer to 15 mg than 20 mg. The EHLSC detection time for dexamethasone sodium phosphate for this dose is 120 h, not 72 h. Recommendations for this Substance require clarification.

‡‡The Screening Limit appears to be taken from the IFHA Urine screening limit, which lists Triamcinolone Acetonide as the analyte, whereas the Prohibited Substances Technical Document actually lists Triamcinolone. As we are unable to review the actual data underlying this Screening Limit, we presume that this is intended to be triamcinolone acetonide.

**Hydroxyzine is listed with a detection time of 96 h, and Cetirizine is listed with no detection time associated, presumably limit of detection. As Cetirizine is the primary metabolite of hydroxyzine, it is concerning that a positive may arise for Cetirizine when Hydroxyzine is administered, and no Hydroxyzine is detectable.

The National HBPA, Inc.
NATIONAL HEADQUARTERS
www.hbpa.org

3380 Paris Pike • Lexington, KY 40511
(859) 259-0451 – Telephone (859) 259-0452 – Facsimile
Email: racing@hbpa.org

President & Chairman
Dr. Doug Daniels – VA

Chief Executive Officer
Eric J. Hamelback

Regional Vice Presidents
J. Lloyd Yother – AZ
Joe Davis – IN
Rick Hiles – KY
Sandee Martin – PA

Secretary/Treasurer
Lynne Schuller – NE

General Counsel
Peter Ecabert

Federal Trade Commission:

The National Horsemen's Benevolent and Protective Association (NHBPA) asks the Federal Trade Commission and Horseracing Integrity and Safety Authority (Authority) to consider the comments below as important as our specific concerns submitted in the attached PDF materials.

We appreciate the opportunity to review and provide comments on the Anti-Doping and Medication Control Protocols, the Prohibited List, Equine Testing and Investigation Standards for Laboratories and Accreditation and Arbitration Procedures. The NHBPA's position regarding the Horseracing Integrity and Safety Act (HISA) continues to be believe the Horseracing Integrity and Safety Act ("HISA") is an unconstitutional delegation of legislative authority to a private nongovernmental organization-- the Authority. For that reason, among others, the NHBPA and several state affiliates remain committed to our lawsuit, currently in appeal in federal court against the Commission and the Authority seeking to declare HISA unconstitutional and enjoin its enforcement.

The NHBPA has long called for uniformity across all racing jurisdictions that is *soundly based on veterinary science and research*. We have been involved with the model rules process both with the Association of Racing Commissioners International (ARCI) and with a board seat at the Racing Medication & Testing Consortium (RMTC). While we didn't always agree with the majority, we understood it was the industry participants weighing in to construct the rules.

Through that process, the National Uniform Medication Program (NUMP) was born and established. While not all jurisdictions had adopted all four phases of NUMP, there were 12 jurisdictions that had, and the other jurisdictions saw substantial compliance. The cries for uniformity came about under these rules. Not a cry for a changing of the rules and not a cry saying veterinary research on the medication rules we have had in place are not in the best interest of equine health and welfare. Uniformity: that was/is the cry.

In that context, we can't fathom why the members of the Authority and HISA are dead set on dismantling the medication model rules. Why not adopt the process in place now and then begin to work on improvements to the overall program? This would certainly have produced more buy-in by industry participants than the process being put forth by HISA. The model rules are

and have been working for many years. What is needed now is the entity that can unify the model rules across all jurisdictions, not blow up the considerable progress made.

Our attached comments identify a few issues and challenges that would benefit from further discussion with horsemen and horsewomen who are immersed in this profession seven days a week. We hope HISA staff and the Authority members respect the opinions and institutional knowledge that horsemen, horsewomen and veterinarians have gleaned from dealing with these issues and challenges in real time and in real-life settings, in many instances for decades.

Trying to offer constructive criticism on documents of such magnitude as those before us is extremely difficult under the best of circumstances. Compounding that, the time we had to sit down with our committee members to review and formulate comments on the proposed regulations has been limited by the issues we have dealt with during the HISA registration process.

Again, this is too important not to do everything possible to get this program right for the sake of our equine athletes, human participants and the health of our industry. We firmly believe HISA's best chance to succeed and to truly benefit and improve horse racing will come by welcoming dialogue with the country's largest Thoroughbred horsemen's organization.

It is vitally important that HISA understands "doping" does not include the treatment of our equine athletes with therapeutic substances or practices deemed necessary for the best interest of equine health and welfare. With that, we ask HISA and the Authority to substantially incorporate many of the current model rules of racing concerning doping and controlled medication in the hopes this will minimize the issues that will arise from a complete overhaul of our regulations.

While we continue to have questions, we thank HISA for the work done to this point on the medication regulation and respectfully ask for an opportunity to further engage in the near future.

Sincerely,

Eric J. Hamelback
CEO, The National HBPA

RULE SERIES 3000

EQUINE ANTI-DOPING AND CONTROLLED MEDICATION PROTOCOL

(7) sets out uniform rules and procedures for the Agency's management of the results of testing and investigations, and for its prosecution of charges that Covered Persons have violated this Protocol, including incorporating the Arbitration Procedures to ensure the fair adjudication of those charges;

(8) sets out the sanctions that may be applied in case of admitted or proven violations of this Protocol, including Disqualification of results, forfeiture of prizes and purses, fines, and periods of Ineligibility for Covered Horses and/or Covered Persons (Rules 3221 to 3232, and Rules 3341 to 3351); and provides for the Authority, State Racing Commissions, the organizers of Covered Horseraces, and other relevant authorities to recognize and enforce those sanctions within their respective spheres of authority (Rule 3710);

(9) regulates the public reporting of case outcomes, and permits and facilitates statistical reporting to the Authority and to the US Congress, the Commission, State Racing Commissions, and other federal or state governmental bodies or agencies having jurisdiction over the sport of horseracing in the USA (Rules 3630); and

(10) empowers the Agency to undertake and commission education and research activities designed to advance the integrity and safety of horseracing in the USA (Rule 3810).

(g) The Protocol comes into force on the Program Effective Date and will apply in full as from that date. In accordance with section 5(k) of the Act, the Protocol only has prospective effect, i.e., it does not apply to, and does not give the Authority or Agency authority to investigate, prosecute, adjudicate, or penalize conduct that occurs before the Program Effective Date (Rule 3070).

(h) The Protocol incorporates by reference the following supporting rules and documents approved by the Commission and issued by the Authority, including Rule Series 1000 (General Provisions), Rule Series 2000 (Racetrack Safety), Rule Series 4000 (Prohibited List), Rule Series 5000 (Testing and Investigations Standards), Rule Series 6000 (Laboratory Standards), Rule Series 7000 (Arbitration Procedures), Rule Series 8000 (Enforcement Rule), Rule Series 8500 (Methodology for Determining Assessments), and Rule Series 9000 (Registration of Covered Persons and Covered Horses).

(i) In accordance with section 6(c)(4) of the Act, the Authority may issue further rules, protocols, policies, standards, and guidelines to support the implementation of this Protocol (subject to Commission oversight in accordance with section 4 of the Act). These materials shall be developed and recommended (in consultation with the Agency) by the Anti-Doping and Medication Control Standing Committee (**ADMC**) of the Authority.

(j) Nothing in this Protocol or in any of its associated rules, protocols, policies, standards, and guidelines: (a) is intended to constrain or limit in any way the powers of the Authority and/or the Agency under the Act; or (b) shall be interpreted or applied in a manner that has the effect of constraining or limiting those powers in any way.

(k) Unless specified otherwise, words and terms in the Protocol that are capitalized are defined terms that have the meaning given to them in Rule 1010.

(l) The rules of interpretation included at Rule 1020 and Rule 3060 shall be used as an aid to interpretation of this Protocol.

CHAPTER I – THE PURPOSE, SCOPE, AND ORGANIZATION OF THE PROTOCOL

Rule 3020. Application

The Protocol applies to and is binding on:

(a) any horserace involving Covered Horses that has a substantial relation to interstate commerce, including any Thoroughbred horserace that is the subject of interstate off-track or advance deposit wagers (each, a **Covered Horserace**);

(b) any Thoroughbred horse, or any other horse made subject to this Act by election of the applicable State Racing Commission or the breed governing organization for such horse under section 5(k), during the period (A) beginning on the date of the horse's first timed and reported Workout at a Racetrack that participates in Covered Horseraces or at a Training Facility; and (B) ending on the date on which the Authority receives written notice that the horse has been retired (each, a **Covered Horse**); and

suggest inserting: from racing

(c) the following persons (each, a **Covered Person**): means all Trainers, Owners, Breeders, Jockeys, Racetracks, Veterinarians, Persons licensed by a State Racing Commission and the agents, assigns, and employees of such Persons and other horse support personnel who are engaged in the care, training, or racing of Covered Horses. Each person falling within this sub-paragraph is deemed to have agreed, by undertaking the activities that bring them within this sub-paragraph, to be subject to and to comply with this Protocol.

Rule 3030. Responsible Persons

(a) '**Responsible Person**' means:

(1) For a Covered Horse that has not yet participated in its first Workout (or, if earlier, been nominated for entry in or entered in a Covered Horserace), the Responsible Person is the Owner or Trainer of the Covered Horse.

(2) Once a Covered Horse has participated in its first Workout (or, if earlier, been nominated for entry in or entered in in a Covered Horserace), the Responsible Person for the Covered Horse is its Trainer.

(3) If a Covered Horse is claimed in a claiming race, the person designated as the Responsible Person prior to the claiming race shall be liable for any violation resulting from a Sample collected on Race Day to the same extent they would have been liable if the Covered Horse had not been claimed. The person who claims the Covered Horse in the claiming race will not be liable for such violation, unless they were involved in the violation.

(4) If a Covered Horse stops training for a period of time, the Responsible Person designation may be transferred to the Owner.

(5) If the Owner is an entity, the Managing Owner shall be named as the Responsible Person.

(b) In the event that no Responsible Person has been designated with the Authority for a Covered Horse, the Responsible Person shall be the Owner of the Covered Horse.

(c) The Responsible Person designation shall be filed with the Authority and kept up-to-date. The transfer of the Responsible Person designation shall be done with the Authority (in accordance with its published procedures) prior to the effective date of the transfer, except that if a Covered Horse is claimed in a claiming race, the transfer shall be done on the day of the claiming race.

(d) The Responsible Person must be the sole representative for the interests of a Covered Horse for which they are the responsible in any matter arising under the Protocol. The Owner of the Covered Horse (if not the Responsible Person) acknowledges and agrees that the Responsible Person for the Covered Horse will represent the Owners' rights and interests in the adjudication of alleged Anti-Doping and/or Controlled Medication Rule Violations under the Protocol.

Rule 3040. Core responsibilities of Covered Persons

(a) *Responsibilities of all Covered Persons*

It is the personal responsibility of each Covered Person:

(1) to be knowledgeable of and to comply with this Protocol at all times;

(2) not to have in their Possession (unless they are a Veterinarian) and not to Use any hypodermic/injection needle at a Racetrack during the Race Period, unless there is compelling justification (e.g. such Use is required as part of life-saving treatment). Failure to comply may constitute a violation pursuant to Rule 3510(c);

(3) to cooperate promptly and completely with the Authority and the Agency in the discharge of their responsibilities, including:

(i) in relation to the Testing program and in relation to the investigation of potential violations of the EAD Rules and/or the ECM Rules;

(ii) by providing complete and accurate information to the Authority and the Agency in all interactions and filings; and

(iii) on request by the Authority or Agency, (a) making available for inspection any facility, office, stall, equipment, feed, or medicine given to Covered Horses; (b) submitting to under-oath transcribed interviews about their dealings with or in relation to Covered Horses; (c) providing immediate and unfettered access to any and all data, documents, and records related to any Covered Horse (including but not limited to data, documents and records existing in electronic form, e.g., on computers, mobile phones, or other devices); and (d) permitting the Agency to review and/or make and take away copies of such data, documents and records for analysis, investigation, and potential use as evidence of violation of this Protocol by a Covered Person; provided that the Agency will act in accordance with standard operating procedures designed to ensure that it only exercises these powers in a lawful and proportionate manner;

Failure to cooperate with the Authority or Agency may constitute a violation pursuant to Rule 3510(b); and

(4) not to engage in offensive conduct (including improper, insulting, and/or obstructive conduct) towards any Sample Collection Personnel, or any representative of the Agency or the Authority. Failure to comply may constitute a violation pursuant to Rule 3510(a) or potentially Tampering or Attempted Tampering depending on the circumstances of the case;

(b) *Additional responsibilities of Responsible Persons*

In addition to the duties under Rule 3040(a), it is the personal responsibility of each Responsible Person:

(1) to ensure that their Covered Horses (i.e., Covered Horses for which they are the Responsible Person) are made available for Sample collection at any time and any place upon request, whether in or out of competition, and that a Nominated Person who is eighteen or older is present to represent the Responsible Person, and that that Nominated Person provides full cooperation on behalf of the Responsible Person to the Sample Collection Personnel to enable compliance with the applicable Testing procedures;

(2) to ensure that treatments and medications administered to their Covered Horses:

(i) are administered only on the advice of a Veterinarian;

(ii) do not contain a Banned Substance or involve a Banned Method; and

(iii) do not otherwise violate the Protocol;

(3) to inform all Covered Persons, employees, personnel, agents, and other Persons involved in any way with the care, training, and/or treatment of their Covered Horses of their respective obligations under the Protocol (including in particular those specified in Rule 3040(a)), and to accept full responsibility for any violations by such Covered Persons or other Persons of this Protocol;

(4) to adequately supervise all Covered Persons, employees, personnel, agents, and other Persons involved in the care, training, and/or treatment of their Covered Horses, including by (without limitation):

(i) conducting appropriate due diligence in the hiring process before engaging their services;

(ii) creating and maintaining systems to ensure those Persons comply with this Protocol; and

(iii) adequately monitoring and overseeing the care by those Persons of their Covered Horses;

(5) to file and update as necessary with the Authority information identifying what Covered Horses they are the Responsible Person for;

(6) to maintain accurate, complete, and up-to-date treatment records (including without limitation records of medical, therapeutic, and surgical treatments and procedures, including diagnostics) of their Covered Horses in an electronic or other form specified by the Agency, and to provide the Agency with access to those records upon request and without delay so that it may inspect and make and retain copies of them for purposes of monitoring and ensuring compliance with the requirements of this Protocol. The records must include details of all treatments administered to the Responsible Person's Covered Horse(s), detailing in each case the name of the Covered Horse, the date and time of administration, the name of the substance or method, route of administration, amount, duration (if multiple dosing), name of person administering and authorizing administration, the reason for administration, and any other information relevant to the health and welfare of the Covered Horse that is required by the Agency or Authority. The Responsible Person must update the treatment records of their Covered Horses within five (5) working days of administration (or, for records from a veterinary hospital, within five (5) working days of the

Not to be submitted.

In what Provided platform?

To what entity?

Covered Horse's departure from the veterinary hospital) and shall keep them for at least the term determined at the Agency's sole discretion.

(7) at the time of registering a horse with the Authority and prior to such horse competing in any Workout or Covered Horserace, the Responsible Person shall declare in writing to the Agency all administrations of Banned Substances and Banned Methods to the horse since the Responsible Person first owned the horse (or, if not the Owner, since the Owner who owns the horse at the time of registration first owned the horse). On request by the Agency, the Responsible Person shall provide any related treatment records for the horse during that period. Where a Banned Substance or Banned Method has been administered in that period, the Agency may impose a stand down period for the horse of up to the period of Ineligibility that would be applicable for the relevant Banned Substance or Banned Method and require that the Covered Horse provide one or more negative Samples before subsequently being eligible to participate in a Workout or Covered Horserace. Failure by a Responsible Person to comply with this Rule 3040(b)(7) may constitute a violation of Rule 3510(b);

(8) if any Covered Horse is moved from a Racetrack or public Training Facility to a private facility, the Responsible Person shall provide sufficient information about the horse's whereabouts so that the Agency remains able to Test the horse at any time in accordance with the Agency's whereabouts policy. The Responsible Person shall also provide any further information about the whereabouts of a Covered Horse that is specifically requested by the Agency. Failure to do so may constitute a violation of Rule 3510(d);

(9) to notify the Authority in writing within seven (7) days of becoming aware that a Covered Horse for which they are the Responsible Person:

(i) is pregnant;

(ii) was pregnant but has foaled or is no longer pregnant;

(iii) has been castrated; or

(iv) has suffered a fatal condition.

In each case, the Responsible Person must state the name of the Covered Horse, the date of the event triggering the notice, and (for paragraph iv above) a summary explanation regarding the cause of the fatal condition.

(c) *Additional responsibilities of Owners*

In addition to the duties under Rule 3040(a), it is the personal responsibility of an Owner of a Covered Horse:

(1) to ensure that the Agency is notified in writing of the Owner's ownership interest in the Covered Horse, and that the Agency receives prior written notice of any transfer of that ownership interest to a third party (each person with a 3% percent or greater ownership or property interest in a Covered Horse must register with the Authority as an Owner of the Covered Horse); and

This is duplicate with JC registration

(2) if a Covered Horse is owned by multiple Owners, to ensure that the Agency is notified in writing of one (1) Owner of the Covered Horse who is authorized by all of the Owners to act as their representative and to receive communications on their behalf in respect of the Covered Horse.

(d) *Additional responsibilities of Attending Veterinarians*

In addition to the duties under Rule 3040(a), and the further duties and requirements imposed under the Rule Series 2000 (Racetrack Safety), it is the personal responsibility of each Attending Veterinarian to keep updated treatment records (including without limitation records of medical, therapeutic, and surgical treatments and procedures, including diagnostics) in an electronic database designated by the Agency or in any other form designated by the Agency and provide access to the Agency upon request and without delay to and/or copies of such treatment records. The records must include the name of the Covered Horse, and all treatments administered or prescribed to any Covered Horse by the Veterinarian. The records must detail the date and time of administration, the name of the substance, route of administration, amount, duration, name of person administering and authorizing administration, the reason for administration, and any other information prudent to the health and welfare of the Covered Horse or otherwise required by the Agency or Authority.

Provided in what platform?

Submitted how often?

Rule 3050. Retirement and equine fatalities

(a) *Covered Persons*

(1) Each Responsible Person will continue to be bound by and required to comply with the Protocol unless and until they give written notice to the Authority of their retirement from the position that made them a Responsible Person. In each case, the Responsible Person will be deemed to have retired (and to be no longer subject to the Protocol) on the later of (i) the date given in the written notice of retirement and (ii) the date the notice is received.

The Responsible person could and may change often

(2) Any other Covered Person will continue to be bound by and required to comply with the Protocol unless and until their registration with the Authority lapses.

When do registrations lapse?

(3) If a Covered Person retires or ceases to be subject to the Protocol while the Agency is conducting a Results Management process in respect of that person, the Agency retains jurisdiction to complete its Results Management process. If a Covered Person retires or ceases to be subject to the Protocol before any Results Management process has begun, and the Agency had jurisdiction over the Covered Person at the time the anti-doping rule or Controlled Medication Rule Violation was committed, the Agency retains jurisdiction to conduct Results Management in respect of that violation.

Defined?

(4) If a Covered Person retires while subject to a period of Ineligibility, they must give written notice of such retirement to the Authority. The Covered Person may not return to the sport (i.e. carry out any of the activities prohibited under Rules 3229/3329) unless the Covered Person has (i) given six (6) months' prior written notice (or notice equivalent to the period of Ineligibility remaining as of the date the Covered Person retired, if that period was longer than six months) to the Authority of their intent to return to the sport, and (ii) made their Covered Horses available for Testing (including, if requested, by providing whereabouts information) for that notice period.

(5) The Agency may forward notifications of retirement of Covered Persons to Interested Parties.

Defined as who?

(b) *Covered Horses*

I would suggest adding the phrase "from racing." Conflicts with Breed registry

(1) If an Owner wishes to retire a Covered Horse such that it is no longer made available for Testing, the Owner must provide written notice of such retirement to the Agency, in accordance with its published procedures.

(2) A Covered Horse that has been retired in accordance with the previous clause may not participate in a Workout or be entered in a Covered Horserace until the Covered Horse has been made available for Testing at least six (6) months prior to notice being given to the Agency (in accordance with its published procedures) of the intention to unretire the Covered Horse.

(3) If a Covered Horse is retired from horseracing or suffers a fatal condition while the Agency is conducting a Results Management process in respect of it, the Agency retains jurisdiction to complete its Results Management process. If a Covered Horse is retired or suffers a fatal condition before any Results Management process has begun, and the Agency had jurisdiction over the Covered Horse at the time the Anti-Doping or Controlled Medication Rule Violation was committed, the Agency retains jurisdiction to conduct Results Management in respect of that violation.

(4) If a Covered Horse is retired from horseracing while subject to a period of Ineligibility, the Owner must notify the Agency in writing of such retirement. If the Owner wishes that horse to return to participation in Covered Horseraces and/or Workouts, the Owner must first provide the Agency with written notice and make the Covered Horse available for Testing for at least six (6) months prior to such participation or for the remainder of the Covered Horse's period of Ineligibility (whichever is longer).

(5) The Agency may retire a Covered Horse based on inactivity (i.e. where the Covered Horse does not participate in a Workout or Covered Horserace for one (1) or more year, excluding periods of inactivity due to a Provisional Suspension or period of Ineligibility) by sending written notice thereof to the Agency and the Owner in accordance with the Agency's procedures. If the Owner disputes that retirement, while the dispute is pending the Covered Horse may not participate in any Workout or Covered Horserace but must be made available for Testing upon demand. Upon resolution of the dispute, the Authority will notify the Agency whether the horse is retired and therefore no longer subject to Testing. If the Owner wishes to return the Covered Horse to participation in Workouts and/or Covered Horseraces, the Owner must first provide the Agency with written notice and make the Covered Horse available for Testing for at least six (6) months prior to such participation.

(6) The Agency may reduce the six (6) month notice period applicable pursuant to Rule 3050(b)(2) or Rule 3050(b)(4) or Rule 3050(b)(5) to two (2) months if the Owner can establish with supporting evidence including veterinary records that (i) the Covered Horse is infertile or otherwise unsuitable for breeding, and (ii) the Owner made the Covered Horse available for Testing within seven (7) days after learning of the Covered Horse's infertility, and (iii) a Sample collected from the Covered Horse by the Agency and analyzed by a Laboratory was negative for Prohibited Substances. The costs of such Sample collection and analysis must be paid by the Owner.

(7) The Agency may forward notifications of retirement of Covered Horses to Interested Parties.

CHAPTER I – THE PURPOSE, SCOPE, AND ORGANIZATION OF THE PROTOCOL

Rule 3060. Amendment and interpretation of the Protocol

(a) The Authority may amend this Protocol from time to time, as necessary to ensure that it remains fit for purpose, in accordance with section 8(e) of the Act. Unless provided otherwise, any amendments will come into force on the date specified or (if no date is specified) on the date the amendment is approved by the Commission.

(b) Subject to Rule 3060(c), the Protocol shall be interpreted as an independent and autonomous text and not by reference to existing law or statutes.

(c) The Protocol has been adopted pursuant to the Act and shall be interpreted, where applicable, in a manner that is consistent with applicable provisions of the Act and the other rules in Rule Series 1000-9000. In the event of any conflict between the Act and the Protocol, the Act shall prevail. In the event of any conflict between the Protocol and any other rules in Rule Series 1000-9000, the Protocol shall prevail.

(d) Subject to Rule 3060(b), the Protocol is governed by the laws of the Commonwealth of Kentucky. Without prejudice to the jurisdiction conferred on the arbitrator(s), National Stewards Panel, and appeal bodies to hear and determine charges brought for violations of the Protocol and certain related issues, and to any powers of review that may be exercised by the Commission or administrative law judges, any other claims or disputes (contractual or otherwise) relating to or arising out of the Protocol are subject to the exclusive jurisdiction of the Commonwealth of Kentucky state courts.

in every state

Can this be correct?

(e) The World Anti-Doping Code (**Code**), the comments annotating various provisions of the Code, and any case law interpreting and/or applying the Code provisions and/or comments, may be considered by hearing panels adjudicating cases relating to the Protocol where they consider it appropriate.

Rule 3070. Transitional provisions

(a) The Protocol shall not apply retroactively to matters pending before the Program Effective Date.

Which is July 1 2022

(b) A presence violation under Rule 3212 or Rule 3312 that occurs after the Program Effective Date as a result of Use or Administration prior to the Program Effective Date shall not constitute a violation of the Protocol.

(c) The relevant State Racing Commission retains authority (including results management) in relation to any anti-doping or controlled medication matters taking place prior to the Program Effective Date.

(d) Changes to substances on the Prohibited List shall not, unless they specifically provide otherwise, be applied retroactively. However, a Responsible Person or other Person who is serving a period of Ineligibility on account of a formerly Prohibited Substance or Prohibited Method that is subsequently removed from the Prohibited List may apply to the Agency to consider a reduction in the period of Ineligibility in light of that removal.

Rule 3080. Statute of limitations

(a) No charge may be brought against a Covered Person or in relation to a Covered Horse in respect of an Anti-Doping Rule Violation unless the Covered Person or Responsible Person for the Covered Horse has been given the ADRV Notice referenced in Rule 3245, or notification has been reasonably attempted, within ten (10) years of the date the Anti-Doping Rule Violation is asserted to have occurred.

(b) No charge may be brought against a Covered Person or in relation to a Covered Horse in respect of a Controlled Medication Rule Violation unless the Covered Person or Responsible Person for the Covered Horse has been given the ECM Notice referenced in Rule 3345, or notification has been reasonably attempted, within one (1) year of the date the Controlled Medication Rule Violation is asserted to have occurred.

Cite this reference

(c) Any violation of Rule 3229 or 3329 is subject to a ten (10) year limitation period.

DB: The 10-year-period to bring a charge of an Anti-Doping Violation against a Covered Person is quite simply too long. A Covered Person can't be reasonably expected to defend themselves against an allegation of this nature that is 10 years old. This should be changed to a 2-year-period.

(d) Any violation of Rule 3510 is subject to a four (4) year limitation period.

CHAPTER II: PROHIBITED LIST, RULES OF PROOF, AND TESTING & INVESTIGATIONS

3110. THE PROHIBITED LIST

Rule 3111. Prohibited Substances and Prohibited Methods

(a) The Prohibited List identifies Prohibited Substances and Prohibited Methods that are:

(1) prohibited at all times (**Banned Substances** and **Banned Methods**) on the basis of the Agency's determination that medical, veterinary, and/or other scientific evidence or experience supports their actual or potential (i) ability to enhance performance in Covered Horseraces, (ii) masking properties, and/or (iii) detrimental impact on horse welfare; or

(2) prohibited for Use on or Administration to a Covered Horse during the Race Period and prohibited to be present in a Sample collected from a Covered Horse on Race Day, except as otherwise specified in the Prohibited List (**Controlled Medication Substances** and **Controlled Medication Methods**).

(b) The Prohibited List also designates certain Prohibited Substances as **Specified Substances**. Specified Substances are subject to more flexible sanctions under this Protocol.

(c) Prohibited Substances and Prohibited Methods may be included in the Prohibited List by general category (e.g. anabolic steroids) or by specific reference to a particular substance or method.

Rule 3112. Review and publication of the Prohibited List

The Prohibited List will be published at least annually on the website(s) of the Authority and/or Agency, following an opportunity for stakeholder comment. Each new version of the Prohibited List will also be sent to the State Racing Commissions.

The Authority (on recommendation of the ADMC, in consultation with the Agency) may revise the Prohibited List from time to time subject to approval by the Commission. Revisions to the Prohibited List will go into effect on the date specified in the revised Prohibited List (which will not be any earlier than ninety (90) days following its publication). All Covered Persons shall be bound by the Prohibited List, and any revisions thereto, from the date they go into effect, without further formality. It is the responsibility of all Covered Persons to familiarize themselves with the most up-to-date version of the Prohibited List and all revisions thereto.

Rule 3113. Validity of the Prohibited List

Does this imply that no mitigating circumstances to be allowed?

The following decisions are final and shall not be subject to any challenge by any Covered Person or other Person on any basis, including any challenge based on an argument that the substance or method is not a masking agent or does not have the potential to enhance performance in future Covered Horseraces or have a detrimental impact on the horse's welfare: (i) the Authority's determination of the Prohibited Substances and Prohibited Methods that are (or will be) included on the Prohibited List; (ii) the Commission's approval of the Prohibited List; (iii) the classification of substances and methods into categories on the Prohibited List; (iv) the classification of a

DB: 3113 and 3122- Not allowing any challenges to analytical methods, screening limits, decision limits and assuming they are scientifically valid is simply wrong whether they are for Prohibited Substances of Controlled Medications. If these methods and limits are scientifically valid they will stand up to legal challenges, conversely if they are scientifically flawed then a horsemen should not be held responsible for meeting them and they should be allowed to be challenged and subsequently changed.

substance or method as a Banned Substance or Banned Method as opposed to a Controlled Medication Substance or Controlled Medication Method; (v) the periods during which certain Prohibited Substances are prohibited; (vi) the establishment of a threshold for a Prohibited Substance and/or the quantitative amount of such threshold; and (vii) the classification of Prohibited Substances as either Specified Substances or non-Specified Substances.

Rule 3114. Monitoring Program

The Agency may approve a monitoring program regarding substances that are not on the Prohibited List, but that the Agency wishes to research or monitor, including to identify potential patterns of misuse in horseracing. Laboratories will report the instances of reported Use or detected presence of monitored substances to the Agency, but the results of any such analyses shall not constitute an Anti-Doping or Controlled Medication Rule Violation. Nothing in this Rule 3114 or elsewhere in the Protocol prevents a Laboratory from sharing information with the Agency for any anti-doping or controlled medication purpose or other purpose authorized by the Act. The list of substances in the monitoring program will be reviewed annually.

3120. PROOF OF VIOLATIONS

Rule 3121. Burden and standard of proof

(a) The Agency shall have the burden of establishing that a violation of the Protocol has occurred to the comfortable satisfaction of the hearing panel, bearing in mind the seriousness of the allegation that is made. This standard of proof in all cases is greater than a mere balance of probability (aka preponderance of the evidence) but less than clear and convincing evidence or proof beyond a reasonable doubt.

(b) Where the Protocol places the burden of proof on a Covered Person to rebut a presumption or establish specified facts or circumstances, the standard of proof shall be by a balance of probability (aka preponderance of the evidence), except as provided in Rules 3122(c) and 3122(d).

Rule 3122. Methods of establishing facts and presumptions

Facts related to violations may be established by any reliable means, including admissions. The following rules of proof shall apply:

(a) Analytical methods, Minimum Reporting Levels, Thresholds, Screening Limits, Decision Limits, and any other Laboratory reporting requirements approved by the Commission are presumed to be scientifically valid and shall not be subject to challenge.

(b) Compliance with the Standards (as opposed to an alternative standard, practice, or procedure) will be sufficient to conclude that the procedures addressed by those Standards were performed properly.

(c) Laboratories are presumed to have conducted Sample analysis and custodial procedures in accordance with the Laboratory Standards. A Covered Person who is alleged to have committed a violation may rebut this presumption by establishing that a departure from the Laboratory Standards occurred that could reasonably have caused the Adverse Analytical Finding or other factual basis for any other violation asserted. Where the presumption is rebutted, the Agency shall have the

(b) In accordance with Rule 3040(b)(1), Responsible Persons are responsible for ensuring that their Covered Horses are available for Sample collection at any time and any place upon request, and that all Sampling procedure requirements are complied with. A Responsible Person may delegate the submission and supervision of the Covered Horse to a third party, but the Responsible Person remains responsible for the Covered Horse throughout the Sample collection process, the acts and omissions of their delegate are imputed to them, and therefore they are deemed liable for their delegate's evasion of Sample collection; refusal or failure without compelling justification to submit the Covered Horse to Sample collection; and/or refusal or failure to comply with any of the sampling procedure requirements.

(c) No violation occurs where a Covered Horse is made available for Sample collection but a Sample is not collected because the Covered Horse is intractable.

Rule 3216. Other Anti-Doping Rule Violations

The following acts and omissions constitute Anti-Doping Rule Violations by the Covered Person(s) in question:

(a) Tampering or Attempted Tampering by a Covered Person with any part of Doping Control or Medication Control;

(b) a Covered Person assisting, encouraging, aiding, abetting, conspiring, covering up, or engaging in any other type of intentional complicity or Attempted complicity (i) in an Anti-Doping Rule Violation committed by another Person, or (ii) in relation to a violation of Rule 3229 by another Person.

(c) Prohibited Association:

(1) Association by a Covered Person in a professional or sport-related capacity with any Person who:

(i) is serving a period of Ineligibility; or

(ii) has been found in a criminal, disciplinary or professional proceeding to have engaged in conduct that would have constituted a violation of the Protocol if it had been applicable to such Person at the relevant time. The disqualifying status of such Person shall last for the longer of (A) six (6) years from the criminal, professional, or disciplinary decision; and (B) the duration of the criminal, disciplinary, or professional sanction imposed; or

(iii) is serving as a front or intermediary for an individual falling within Rule 3216(c)(1)(i) or (ii).

(2) To establish a violation of Rule 3216(c), the Agency must establish that the Covered Person knew at the relevant time of the Person's disqualifying status. It is presumed that any association with the Person described in Rules 3216(c)(1)(i) and (ii) above is in a professional or sport-related capacity, and the burden shall be on the Covered Person to rebut that presumption.

(3) It shall be a defense to a charge of violation of Rule 3216 if the Covered Person establishes that the association with the Person could not have been reasonably avoided.

(d) Acts by a Covered Person to discourage or retaliate against reporting to authorities.

(1) Where such conduct does not otherwise constitute a violation under Rule 3216(a) (Tampering or Attempted Tampering):

(i) Any act that threatens or seeks to intimidate another Person with the intent of discouraging that Person from the good faith reporting of information that relates to an alleged Anti-Doping Rule Violation or other alleged non-compliance with the Protocol to the Agency or other appropriate Person.

(ii) Retaliation against a Person who, in good faith, has provided evidence or information that relates to an alleged Anti-Doping Rule Violation or other alleged non-compliance with the Protocol to the Agency or other appropriate entity or Person.

(2) For purposes of Rule 3216(d), retaliation, threatening, and intimidation include an act taken against such Person that lacks a good faith basis or is a disproportionate response.

3220. SANCTIONS

Rule 3221. Disqualification of the Covered Horse's results

(a) *Automatic Disqualification of Race Day results*

(1) An Anti-Doping Rule Violation that arises from a Race Day Test, or that occurs during the Race Period, automatically leads to Disqualification of the results of the Covered Horse obtained on the Race Day(s) that fall(s) within the Race Period, even if any other sanction for the violation is reduced or eliminated under Rules 3224 to 3226.

(2) In circumstances where (i) an ADRV Notice has been sent as required under Rule 3245, and (ii) the B Sample analysis confirms the A Sample analysis, or the right to request the analysis of the B Sample is waived, the Agency and/or the Responsible Person and/or Owner of the Covered Horse in question may ask the arbitrator(s) to apply Rule 3221 immediately, i.e., prior to adjudication of any other issue.

DB: 3221 (b) Any Covered Horse which was claimed from the race in which the Anti-Doping Violation occurred and changed ownership and subsequently raced for the new ownership should specifically be excluded from this provision.

(b) *Disqualification of subsequent results*

In addition to the automatic Disqualification of results under Rule 3221(a), any other results that the Covered Horse obtained from the date the Anti-Doping Rule Violation first occurred, as well as during any retroactive Ineligibility period applied pursuant to Rule 3248(d), shall be Disqualified, unless it is established that fairness requires otherwise.

(c) *Consequence of Disqualification of results*

If a Covered Horse has results Disqualified under the Protocol, all purses and other compensation, prizes, trophies, points, and rankings are forfeited and must be repaid or surrendered (as applicable) to the race organizer, and the results of the other Covered Horses in the race(s) in question must be adjusted accordingly. Purses, prizes, trophies, and other compensation will (where possible) be withheld for the Covered Horse in issue pending resolution of the relevant charge.

Rule 3222. Ineligibility for Covered Horses

(a) For a violation of Rule 3212 (presence) or 3213 (Use or Attempted Use), the Covered Horse involved shall be Ineligible for the time designated for the particular substance or category of substance in the Prohibited List.

(b) For a violation of Rule 3215 (evading, refusing, or failing to submit to Sample collection), the Covered Horse involved shall be Ineligible for eighteen (18) months.

(c) Rule 3228 on increased periods of Ineligibility for repeat offenders does not apply to Covered Horses.

(d) The Ineligibility period for a Covered Horse shall be deemed to commence on the date that the violation occurred (which, in the case of a Rule 3212 violation, shall be the date that the positive Sample was collected, even if the Covered Horse has participated in Workouts or Covered Races after that date).

(e) A Covered Horse will be reinstated once its period of Ineligibility ends, provided that (i) the Ineligibility has been respected in full throughout that period in accordance with Rule 3229, and (ii) the Covered Horse has been made available for Testing during that period in accordance with Rule 3132(c). However, such reinstatement is without prejudice to any rest or stand down period that may be imposed on the Covered Horse (e.g. due to injuries), and any requirements for release from the Veterinarians' List, pursuant to the Racetrack Safety Program.

Rule 3223. Ineligibility and financial penalties for Covered Persons

(a) *General*

(1) The periods of Ineligibility set out in this Rule 3223 apply to the Covered Person's first doping offense. Where an offense is not the Covered Person's first doping offense, Rule 3228 applies.

(2) Unless specified otherwise, the periods of Ineligibility set out in this Rule 3223 are subject to potential elimination, reduction, or suspension pursuant to Rules 3224 to 3226 or potential increase pursuant to Rule 3227.

(3) Unless Rule 3230(b)(1) applies, the periods of Ineligibility set out in this Rule 3223 shall be reduced by any period of Provisional Suspension served by the Covered Person in accordance with Rule 3247.

(b) *Sanctions*

(1) For a violation of Rule 3212 (presence), 3213 (Use or Attempted Use), 3214(a) (Possession), or 3214(c) (Administration or Attempted Administration), the period of Ineligibility shall be two (2) years. The Covered Person may also be required to pay a fine of up to USD 15,000 or 10% of the gross purse (whichever is greater) and some or all of the Agency's legal costs.

(2) For a violation of Rule 3214(b) (Trafficking or Attempted Trafficking), the period of Ineligibility shall be a minimum of four (4) years up to lifetime Ineligibility, depending on the seriousness of the violation. The Covered Person may also be required to pay a fine of

up to USD 25,000 or 25% of the gross purse (whichever is greater) and some or all of the Agency's legal costs.

(i) A Rule 3214(b) violation involving a Minor shall be considered a particularly serious violation and shall result in lifetime Ineligibility for the Covered Person who commits it.

(ii) Violations of Rule 3214(b) that may also violate non-sporting laws and regulations shall be reported to the competent administrative, professional, or judicial authorities.

(3) For a violation of Rule 3215 (evading, refusing, or failing to submit to Sample collection) or 3216(a) (Tampering or Attempted Tampering), the period of Ineligibility shall be four (4) years, except:

DB:3223 (b) (3) (i) If a Covered Person established that the failure to submit a sample was not intentional why would there be an automatic 2- year period of Ineligibility. This is far beyond what fairness calls for and should be lowered greatly or at a minimum the adjudicating body should have the option to lower greatly based upon the circumstances.

(i) in the case of failing to submit to Sample collection, if the Covered Person can establish that the failure was not intentional, the period of Ineligibility will be two (2) years;

(ii) in all other cases, if the Covered Person can establish exceptional circumstances that justify a reduction of the period of Ineligibility, the period of Ineligibility will be in a range from two (2) years to four years, depending on their degree of fault.

The Covered Person may also be required to pay a fine of up to USD 15,000 or 10% of the gross purse (whichever is greater) and some or all of the Agency's legal costs.

(4) For a violation of Rule 3216(b) (complicity or Attempted complicity), the period of Ineligibility shall be up to two (2) years, depending on the seriousness of the violation. The Covered Person may also be required to pay a fine of up to USD 15,000 or 10% of the gross purse (whichever is greater) and some or all of the Agency's legal costs.

(5) For a violation of Rule 3216(c) (Prohibited Association), the period of Ineligibility shall be two (2) years, subject to a reduction down to a minimum of one (1) year, depending on the Covered Person's degree of Fault and other circumstances of the case. The Covered Person may also be required to pay a fine of up to USD 15,000 or 10% of the gross purse (whichever is greater) and some or all of the Agency's legal costs.

(6) For a violation of Rule 3216(d) (acts to discourage or retaliate against reporting), the period of Ineligibility shall be a minimum of two (2) years up to lifetime Ineligibility, depending on the seriousness of the violation. The Covered Person may also be required to pay a fine of up to USD 25,000 or 25% of the gross purse (whichever is greater) and some or all of the Agency's legal costs.

(7) For a violation of Rule 3229 (violation of the prohibition against participation during Provisional Suspension or Ineligibility), or complicity or Attempted complicity in such violation, the Consequences set out at Rule 3230 shall apply.

(c) *Commencement of the period of Ineligibility for a Covered Person*

(1) Except as otherwise provided in this Rule 3223, the period of Ineligibility imposed on any Covered Person shall start on the date the period of Ineligibility is accepted or

otherwise imposed in accordance with the Protocol.

(2) Where a Covered Person is already serving a period of Ineligibility for another violation of the Protocol, any new period of Ineligibility will start to run the day after the original period of Ineligibility ends.

(3) Where there have been substantial delays in the adjudication process or other aspects of Doping Control that go well beyond the standard timeframes for Laboratory analyses and Results Management, and the Covered Person can establish that such delays are not attributable to them, the start date of the period of Ineligibility may be deemed back-dated to reflect such delays, but in no event may it be deemed back-dated to a date before the Anti-Doping Rule Violation last occurred. All competitive results achieved during the period of Ineligibility by the Covered Person and/or Covered Horse in issue, including retroactive Ineligibility, shall be Disqualified, unless fairness requires otherwise.

DB: 3224. the requirement that a Covered Person must establish how the prohibited substance entered the Covered Horse's system is too stringent. The Covered Person should only have to establish the most likely cause as to how a prohibited substance entered the Covered Horse's system.

Rule 3224. Elimination of the period of Ineligibility where there is No Fault or Negligence

(a) If a Covered Person establishes in an individual case that they bear No Fault or Negligence for the Anti-Doping Rule Violation(s) charged, the otherwise applicable period of Ineligibility and other Consequences for such Covered Person shall be eliminated (except for those set out in Rule 3221(a) and Rule 3620). When the violation is of Rule 3212 (presence of a Banned Substance), the Covered Person must also establish how the Banned Substance entered the Covered Horse's system as a pre-condition to application of this Rule 3244(a). In the event the period of Ineligibility otherwise applicable is eliminated pursuant to this Rule 3224, the Anti-Doping Rule Violation shall not be considered a prior violation for the purpose of Rule 3228.

(b) Rule 3224 only applies in exceptional circumstances. In particular, it will not apply where the Banned Substance found to be present in a Sample (i) came from a mislabelled or contaminated supplement; or (ii) was administered to the Covered Horse by veterinary or other support personnel without the knowledge of the Responsible Person.

(c) A finding that the Covered Person bears No Fault or Negligence for an Anti-Doping Rule Violation shall not affect the Consequences of that violation that apply to the Covered Horse (i.e., Ineligibility in accordance with Rule 3222(a) and Disqualification of results in accordance with Rule 3221).

Rule 3225. Reduction of the period of Ineligibility where there is No Significant Fault or Negligence

Reductions under this Rule 3225 are mutually exclusive and not cumulative, i.e., no more than one of them may be applied in a particular case.

(a) *General rule*

Where the Covered Person establishes that they bear No Significant Fault or Negligence for the Anti-Doping Rule Violation in question, the period of Ineligibility shall be fixed between three (3) months and two (2) years, depending on the Covered Person's degree of Fault, unless Rule 3225(b) or 3225(c) applies.

RULE SERIES 4000

PROHIBITED LIST

4000. PROHIBITED LIST.

4010. Purpose.

In accordance with Rule 3111, the Prohibited List identifies substances and methods that are prohibited at all times (**Banned Substances and Banned Methods**) and those that are prohibited for Use on or Administration to a Covered Horse during the Race Period and prohibited to be present in a Sample collected from a Covered Horse on Race Day, except as otherwise specified in the Prohibited List (**Controlled Medication Substances or Controlled Medication Methods**). The Prohibited List also designates certain Prohibited Substances as **Specified Substances**, which are subject to more flexible sanctions (see Rule 4400). In accordance with the definition of 'Race Period' (see Rule 1010) the Prohibited List may specify that for certain specified Controlled Medication Substances and Controlled Medication Methods the Race Period shall be shorter or longer in duration.

4100. Banned Substances and Banned Methods

4110. Banned Substances.

4111. S0 Non-approved Substances.

Any pharmacological substance that is not addressed by Rules 4112 through 4117 and with no current approval by any governmental regulatory health authority for veterinary or human therapeutic use or any substance not universally recognized by veterinary regulatory authorities as a valid veterinary therapeutic Treatment is prohibited at all times.

DB: 4111- This proposed regulation will have unintended consequences. Common products for use in horses, including Guaifenesin, lidocaine and all vitamins except E/Se are FDA-listed and NOT FDA-approved. Additionally, no compounded medications could be used under this regulation. Veterinarians simply won't be able to properly treat horses if this regulation is not altered.

4112. S1 Anabolic Agents.

The following substances, and other substances with similar chemical structure or similar biological effect(s), are prohibited at all times:

(a) Anabolic Androgenic Steroids when administered exogenously.

(b) Other Anabolic Agents, including but not limited to:

(1) Selective androgen receptor modulators (SARMs);

(2) Zeranol;

(3) Zilpaterol; and

(4) Ractopamine.

DR CF***: 4111 -****Non-approved substances are banned at all times in all Thoroughbreds from their first Official Workout until retirement.*

FDA approval indicates a marketing status (whether they can market the product with a claim). Listed products are drug products manufactured at an FDA registered facility that are manufactured according to GMP standards and practices (identity, strength, *quality*, *purity*, and *potency), but marketed with no label claim*. No medical practitioner, human or animal, can appropriately treat their patients without non-FDA approved products. Common products for use in horses, including Guaifenesin, lidocaine and all vitamins except E/Se are FDA-listed and NOT FDA-approved. Further, the FDA On April 14, 2022, FDA issued Guidance for Industry #256, entitled "Compounding Animal Drugs from Bulk Drug Substances." The GFI describes the agency's approach to situations where veterinarians need access to these unapproved drugs to provide appropriate care for the medical needs of the diverse species they treat. In particular, when an FDA approved drug is on manufacturer backorder, or the only formulation of the product that is FDA approved is not suitable for use (eg only tablets are available and intravenous is required), compounding is the only means by which a veterinarian can appropriately treat the animal.

4113. S2 Peptide Hormones, Growth Factors, Related Substances, a

The following substances, and other substances with similar chemic effect(s), are prohibited at all times:

(a) Erythropoietins (EPO) and Agents affecting erythropoiesis, including but not limited to:

(1) Erythropoietin-Receptor Agonists;

(2) Hypoxia-Inducible Factor (HIF) Activating Agents;

DR CF: 4111 Continued- Restricting the use of drugs to only those that can be marketed for a specific purpose prevents horses from receiving appropriate veterinary care. This regulation should read:

"Any pharmacological substance that is not FDA approved, FDA Listed or compounded according to FDA Guidance #256 "Compounding Animal Drugs from Bulk Drug Substances" or any substance not universally recognized by veterinarians as a valid veterinary therapeutic Treatment is prohibited at all times.

DR CF: **4113. S2 Peptide Hormones, Growth Factors, Related Substances, and Mimetics.** ACTH is commonly used to prevent heat stroke. There is literally zero scientific evidence that ACTH impacts performance.

(3) GATA (Erythroid Transcription Factor) Inhibitors;

(4) Transforming Growth Factor-beta (TGF-β) signaling inhibitors; and

(5) Innate Repair Receptor Agonists.

(b) Peptide Hormones and their Releasing Factors, including but not limited to:

(1) Chorionic Gonadotrophin (CG) and Luteinizing Hormone (LH) and their Releasing Factors in stallions, ridglings, and geldings;

(2) Corticotrophins and their Releasing Factors;

(3) Growth Hormone (GH), its analogues and fragments; and

(4) Growth hormone releasing factors.

(c) Growth factors and growth factor modulators and other growth factors or growth factor modulators affecting muscle, tendon, or ligament protein synthesis/degradation, vascularization, energy utilization, regenerative capacity or fiber type switching.

4114. S3 Beta-2 Agonists.

The following substances, and other substances with similar chemical structure or similar biological effect(s), are prohibited at all times:

All selective and non-selective beta-2 agonists, including all optical isomers.

Notwithstanding the above, the following are permitted: (a) inhaled beta-2 agonists e.g., albuterol (salbutamol) when prescribed by a Veterinarian as a bronchodilator, and (b) clenbuterol when prescribed by a Veterinarian for a duration not to exceed thirty (30) days in a six (6) month period and provided that following administration of clenbuterol the Covered Horse shall not be eligible to participate in any Workout or Covered Horserace until a urine and a blood Sample have been collected from it by or on behalf of the Agency, and analysis by a Laboratory of those Samples does not detect the presence of clenbuterol or its Metabolites or Markers.

4115. S4 Hormone and Metabolic Modulators.

The following substances, and other substances with similar chemical structure or similar biological effect(s), are prohibited at all times:

(a) Aromatase Inhibitors;

(b) Anti-estrogenic substances, anti-estrogens, and selective estrogen receptor modulators (SERMS), Agents preventing activin receptor IIB activation:

(c) Myostatin inhibitors;

(d) Metabolic modulators including but not limited to:

DB: 4115- Thyroid medications such as Thyro-L have been proven to be beneficial to horses with low t3 and t4 counts. Whether these counts are caused by an actual thyroid condition or the environment we place horses in isn't particularly relevant this regulation takes away a valuable medication and will take horses out of the racing population costing owners revenue.

(1) Insulins and Insulin-Mimetics;

(2) Meldonium; and

(3) Trimetazidinet; and

(e) Thyroid hormone and thyroid hormone modulators.

DR CF: **4115. S4 Hormone and Metabolic Modulators. Continued:** The reason for this ban is a recent paper showing an increased rate of arrhythmias in horses receiving 125 mg per day of thyroxine (10 scoops, or 10 times the usual dose). Horses receiving 50 mg (just over 4 scoops) did NOT exhibit arrhythmias. A separate study showed that theses high levels of supplementation actually increased the resting thyroxine level above the normal range. In human sports, studies have shown that thyroxine supplementation into the abnormally high range detracts from athletic performance. So, the usual veterinary practice of testing thyroxine levels after instituting treatment to make sure supplementation is not excessive is sufficient to protect against this risk.
o, in order to prevent arrhythmia-related sudden death, despite no evidence that any current level of supplementation is inappropriate (doesn't approach the 10x dose studied), HISA would risk breaking off their legs?
Úny regulation of thyroxine should be restricted to a requirement for testing to insure that any supplementation does not exceed the normal range, thereby putting the horse at risk of cardiac arrhythmia.

4116. S5 Diuretics and Masking Agents.

(a) Diuretics and masking agents, and other substances with a similar chemical structure or similar biological effect(s), are prohibited at all times.

(b) Notwithstanding the above, the following are permitted:

(1) Drospirenone, pamabrom, and topical ophthalmic administration of carbonic anhydrase inhibitors (e.g. dorzolamide, brinzolamide);

(2) Trichlormethiazide for treatment of edema; and

(3) Plasma expanders for life-saving procedures.

4117. S6 Miscellaneous Substances.

The following substances, and other substances with similar chemical structure or similar biological effect(s), are prohibited at all times:

(a) Bisphosphonates (except that bisphosphonates may be administered for the purpose of diagnostic imaging, i.e. gamma scintigraphy);

(b) Toxins (e.g. botulinum toxin, botox);

(c) Venoms of any species, their synthetic analogs, or derivatives thereof;

(d) Altrenogest in stallions, ridglings, or geldings; and

(e) Pitcher plant extract (Sarapin).

DB: 4117- Sarapin is effectively used by vets to treat a number of conditions without incident and has never been banned before. Why is it being proposed to be banned now?

DR CF: 4117. S6 Miscellaneous Substances. P-Bloc and Sarapin have clearly been shown to benefit "wind-up" pain and NOT pain from pre-existing injury or inflammation. "Blocking" with these products does not block nerve impulses, and therefore cannot possibly put horses at any kind of risk of injury. Certain types of chronic pain, specifically suspensory origin pain (compartmental syndrome) and foot pain from chronically training on a very hard surface, a loose track or without traction devices cause "wind-up" pain and there are not alternative therapeutics. Because this type of chronic pain is unassociated with inflammation, the typical approaches to decrease inflammation (non-steroidals and rest) do not work. Removing these products from the veterinary practitioner's arsenal of therapeutics damages rather than benefits the integrity of racing.

4120. Banned Methods.

4121. M1 Manipulation of Blood and Blood Components.

(a) The Administration or reintroduction of any quantity of autologous, allogenic (homologous), or heterologous blood or red blood cell products of any origin into the circulatory system.

(b) Artificially enhancing the uptake, transport, or delivery of oxygen, including, but not limited to: Perfluorochemicals, efaproxiral (RSR13), and modified haemoglobin products, e.g. haemoglobin-based blood substitutes and microencapsulated haemoglobin products, excluding supplemental oxygen by inhalation.

(c) Any form of intravascular manipulation of the blood or blood components by physical or chemical means.

(d) Withdrawal of blood for any purpose other than for diagnostic/Laboratory Testing procedures.

(e) Notwithstanding the above, manipulation of blood or blood components is permitted for:

(1) Procedures performed for life-saving purposes; and

(2) Use of veterinary regenerative therapies (autologous conditioned serum or platelet-rich plasma) for the treatment of musculoskeletal injury or disease.

4122. M2 Chemical and Physical Manipulation.

(a) Use of chemical castration or immunocastration. In case of chemical castration or immunocastration, the horse shall remain designated as an intact male.

4123. M3 Gene and Cell Doping.

The following, which have the potential to enhance performance or modify the heritable genome, are prohibited at all times:

(a) The use of nucleic acids or nucleic acid analogues that may alter genome sequences and/or alter gene expression by any mechanism. This includes but is not limited to gene editing, gene silencing, and gene transfer technologies;

(b) The use of normal or genetically modified cells; and

(c) Modification of the heritable genome.

4200. Controlled Medication Substances and Controlled Medication Methods.

(a) Medications administered by Regulatory Veterinarians or Attending Veterinarians providing emergency medical care to a Covered Horse as a result of an injury sustained or other adverse health event during an Official Workout or Covered Horserace are not prohibited.

(b) Unless specified otherwise in the Prohibited List, Controlled Medication Substances and Controlled Medication Methods are prohibited for Use on or Administration to a Covered Horse during the Race Period and prohibited to be present in a Sample collected from a Covered Horse on Race Day.

DB: 4200- Race period also covers the period within 48 of an official workout unless the official workout is to get off of the vet's list the use of Controlled Medications should be permissible.

4210. Controlled Medication Substance(s).

Except as otherwise provided in Rule 4211, the following shall be prohibited on Race Day and during the Race Period:

(a) S7 Medications, supplements, nutraceuticals, feed additives, and substances capable at any time of causing an action or effect, or both an action and effect, within one or more of the following mammalian body systems:

(1) the blood system;

(2) the urinary system;

(3) the cardiovascular system;

DR CF: **4210. Controlled Medication Substance(s).** All feed, hay and water components are capable at any time of causing an action or effect or both on any or all of the systems listed above. Further, all hay, feed and water lack current approval by any governmental regulatory health authority. This regulation is overbroad, and reflects the haste and lack of careful thought evidenced by much of the HISA regulations to date. "If we don't know what to do about it, just ban it."

DR CF: **4200. Controlled Medication Substances and Controlled Medication Methods.** Many therapeutic medications can be identified in a drug test for days to even weeks beyond any pharmacologic effect. The restriction of all medications and their metabolites in horses on Race Day is excessive. We have worked for years to achieve reasonable thresholds for many therapeutics. This rule pulls us into the dark ages. Further, many horsemen and veterinarians double or triple the withdrawal times for racing to be even safer (which is not necessarily in the best interest of the horse). However, restricting medications in the same way for workouts is beyond excessive. It essentially makes most therapeutic medications completely illegal. For example, Xylazine is a tranquilizer that has an effect for about 1.5 hours. However, it can be detected for at least 4 days. Aminocaproic acid is a valuable anti-bleeding medication. It currently tests for at least 8 days. It is commonly used in horses for workouts for the purpose of preventing pulmonary hemorrhage. This regulation prevents the safe use of this valuable therapeutic. This rule should revisit what can and can not be used in horses for published workouts. Specifically, restricting the use of non-steroidals and local anethestics is appropriate, but not restricting the use of most other therapeutics. Further, thresholds should continue to be used for other therapeutics for the actual post-race testing to permit their use for the health and welfare of the horse.

(4) the digestive system;

(5) the endocrine system;

(6) the immune system;

(7) the musculoskeletal system;

(8) the nervous system;

(9) the reproductive system; and/or

(10) the respiratory system.

(b) All substances, including all optical isomers, e.g., d- and l- where relevant; and

(c) Metabolites, artifacts, and isomers of S7 substances.

S7 substances exclude those (i) lacking current approval by any governmental regulatory health authority for veterinary or human therapeutic use (e.g. drugs under pre-clinical or clinical development or designer drugs), and (ii) any substance not universally recognized by veterinary regulatory authorities as a valid veterinary therapeutic treatment that falls under section S0. Such substances are Banned Substances.

4211. Exceptions to Rule 4210.

(a) Notwithstanding the provisions of Rule 4210, the following may be administered up to twenty four (24) hours prior to the Race Day in which a Covered Horse participates or is entered (the start of the 'Race Period' shall be modified accordingly for these substances):

(1) Orally administered vitamins;

DR CF: **4211. Exceptions to Rule 4210.**

Feed, Hay and water are not included as exceptions to rule 4210.

(2) Ranitidine;

(3) Licensed vaccines against infectious agents;

(4) Unsupplemented, isotonic electrolyte solutions;

(5) Altrenogest in female horses;

(6) Antimicrobials (antibiotics) and other anti-infective agents, excluding procaine penicillin or other antimicrobial/anti-infective agents containing or metabolizing to Controlled Medication Substances;

(7) Antiparasitic/anthelmintics approved and registered for use in horses, excluding levamisole or other antiparasitic/anthelmintics metabolizing to and/or containing other Controlled Medication Substances;

(8) Cimetidine; and

(9) Omeprazole.

(b) Notwithstanding the provisions of Rule 4210:

(1) Furosemide (aka Lasix or Salix) is permitted during Workouts and Official Workouts;

(2) Furosemide (aka Lasix or Salix) may be administered during the Race Period in connection with a Covered Horserace in accordance with specific provisions of the Act and any guidance or exceptions approved by the Authority;

(b) Notwithstanding the foregoing, the presence of the following Controlled Medication Substances is prohibited in Covered Horses performing Workouts:

(1) Analgesics;

(2) Nonsteroidal anti-inflammatory drugs; (NSAIDs)

(3) Local anesthetics; and

(4) Corticosteroids.

4220. Controlled Medication Method(s).

In addition to any prohibited practices set forth in the Rule 2000 Series, and except as may otherwise be provided in Rule 4211:

(a) M4 Alkalinization shall be prohibited on Race Day and during Official Workouts.

(b) M5 Intra-articular injections shall be prohibited on Race Day and within the fourteen (14) days preceding Race Day. The Covered Horse is not eligible to race for fourteen (14) days from the date on which such Covered Horse received the administration of the intra-articular injection.

(c) M6 The use of a nasogastric tube is prohibited within twenty-four (24) hours preceding Race Day for any Covered Horserace in which the Covered Horse is entered.

(d) M7 Intra-articular injections of polyacrylamide hydrogels shall be prohibited within one hundred and eighty (180) days preceding Race Day.

The start of the 'Race Period' shall be modified for each of the methods above (i.e. each of M4-M7) based on the time period specified for such method (e.g. the Race Period for M5 shall start fourteen (14) days prior to Race Day).

4300. Ineligibility Periods for Covered Horse.

(a) *Prohibited Substances.* The period of Ineligibility of a Covered Horse resulting from a violation of this Rule 4000 Series involving a Prohibited Substance shall be as set forth in Table 1 to this Rule 4300.

TABLE 1

Violation	**Ineligibility Period**
S0 BANNED Substances-Non-approved substances	14 months
S1 BANNED Substances-Anabolic Agents	14 months
S2 BANNED Substances-Peptide Hormones	6 months
S3 BANNED Substances-Beta-2 Agonists	14 months
S4 BANNED Substances-Hormone and Metabolic Modulators	3 months
S5 BANNED Substances-Diuretics and Masking Agents	0 months
S6 BANNED Substances-Miscellaneous Substances	—
(1) Bisphosphonates	Life
(2) All other S6 Miscellaneous Substances	0 months
S7 CONTROLLED Substances-Medications, supplements and feed additives – Covered Horserace	0 months
S7-CONTROLLED substances-Medications, supplements, nutraceuticals, and feed additives-Official Workout	The horse is not released from the Vets' List and a subsequent Official Workout must be scheduled.

(b) *Prohibited Methods.* The period of Ineligibility of a Covered Horse resulting from a violation of this Rule 4000 Series involving a Prohibited Method shall be as set forth in Table 2 to this Rule 4300.

TABLE 2

Violation	**Ineligibility Period**
M1 Manipulation of Blood and Blood Components	6 months
M2 Chemical and Physical Manipulation	0 months
M3 Gene and Cell Doping	Life
M4 Alkalinization	0 months
M5 Intra-articular injection within 14 days of a Covered Horserace	1 month
M6 Use of a nasogastric tube within 24 hours of a Covered Horserace	0 months
M7 Intra-articular injection of polyacrylamide hydrogel within 180 days of a Covered Horserace	12 months

4400. Specified Substances.

The following substances shall be categorized as Specified Substances:

DR CF: 4400. Specified Substances.

Specified substances are defined as substances subjected more flexible sanctions, however, the subsets of BANNED vs CONTROLLED are not defined or explained.

CATEGORY	SUBSTANCE	ACTIVITY
BANNED	Arsenic	Stimulant/toxic
CONTROLLED	Atropine	Anticholinergic
BANNED	Bufotenine	Naturally occurring hallucinogen
CONTROLLED	Caffeine	Central nervous system stimulant
BANNED	Natural Cannabinoids, synthetic cannabinoids and other cannabimimetics	Psychotropic
CONTROLLED	Cannabidiol (CBD; CBDA)	Psychotropic
BANNED	CBD (Cannabidiol; CBDA)	Psychotropic
BANNED	CBDA (Cannabidiol; CBD)	Psychotropic
CONTROLLED	Codeine (Specified Substance when detected as a metabolite of morphine)	Analgesic
BANNED	Colchicine	Rheumatic treatment/anti-cancer
BANNED	Demecolcine	Rheumatic treatment/anti-cancer
BANNED	Dimethyltryptamine (DMT)	Psychedelic
BANNED	DMT (Dimethyltryptamine)	Psychedelic
BANNED	Ergonovine	Vasoconstrictor
BANNED	Ergotamine	Plant alkaloid
CONTROLLED	Hordenine	Norepinephrine stimulant
CONTROLLED	Hyoscine (Scopolamine)	Parasympathetic
BANNED	Meconine	Opioid
CONTROLLED	Morphine	Opioid analgesic
BANNED	Muscarine	Parasympathomimetic
BANNED	Oripavine	Opioid analgesic
BANNED	Papaverine	Opiate - muscle spasm treatment
CONTROLED	Paraxanthine	Stimulant
CONTROLLED	Scopolamine (Hyoscine)	Parasympathetic
BANNED	Sparteine	Anti-arrhythmic
BANNED	Synephrine	Stimulant
BANNED	Thebaine	Opioid alkaloid
CONTROLLED	Theobromine	Vasodilator
CONTROLLED	Theophylline	Bronchodilator

DB: The listing of substances into either a banned or controlled category has several issues.
Cannabidiol, CBD and CBDA are listed as both controlled and banned in different boxes.
While substances such as caffeine and morphine are rightly on the controlled list to the possibility of environmental contamination synephrine which has been found in hay is listed as a banned substance.