

CALIFORNIA HORSE RACING BOARD

1010 Hurley Way, Suite 300
Sacramento, CA 95825
www.chrb.ca.gov
(916) 263-6000 Fax (916) 263-6042



REGULAR MEETING

of the **California Horse Racing Board** will be held on **Thursday, March 19, 2015**, commencing at **10:00 a.m.**, in the **Clubhouse at the California Exposition and State Fair Grandstand, 1600 Exposition Boulevard, Sacramento, California**. The audio portion only of the California Horse Racing Board regular meeting will be available online through a link at the CHRB website (www.chrb.ca.gov) under "Webcasts."

AGENDA

Action Items:

1. **Approval of the minutes of February 18, 2015.**
2. **Executive Director's Report.**
3. **Public Comment:** Communications, reports, requests for future actions of the Board. **Note:** Persons addressing the Board under this item will be restricted to **three (3) minutes** for their presentations.
4. Discussion and action by the Board regarding the **proposed amendment to CHRB Rule 1588, Horse Ineligible to Start in a Race**, to provide that a horse is ineligible to start in any race in California if it is on the veterinarian's list in another racing jurisdiction, unless with prior approval of the stewards.
5. Discussion and action by the Board regarding the **proposed amendment to CHRB Rule 1843.2, Classification of Drug Substances**, to add cobalt to the CHRB Penalty Categories Listing by Classification, thereby establishing the violation and penalty guidelines for the presence of cobalt in an official blood sample.
6. Discussion and action by the Board regarding a **report from Golden Gate Fields on the status of its marketing efforts for rebranding racing at Golden Gate Fields for the future, as noted in its race meet application for license.**
7. Discussion and action by the Board regarding **adoption of the proposed criteria to evaluate the rehabilitation of a person when considering denial of a license pursuant to Business and Professions Code section 480 and considering suspension or revocation of a license pursuant to Business and Professions Code section 490.**
8. Discussion and action by the Board regarding **the proposed adjustment of the 2015 Southern California racing calendar, to allocate September 26th and September 27th from Santa Anita to Fairplex, at Los Alamitos.**

9. Discussion and action by the Board regarding **the proposed adjustment of the 2015 Northern California racing calendar to modify the allocated Fresno October 1, 2015 starting date to October 8, 2015.**
10. **Closed Session:** For the purpose of receiving advice from counsel, considering pending litigation, reaching decisions on administrative licensing and disciplinary hearings, and personnel matters, as authorized by section 11126 of the Government Code.
 - A. The Board may convene a Closed Session to confer with and receive advice from its legal counsel regarding the pending litigation described in the attachment to this agenda captioned "Pending Litigation," as authorized by Government Code section 11126(e).
 - B. The Board may convene a Closed Session to confer with and receive advice from its legal counsel regarding the pending administrative licensing or disciplinary matters described in the attachment to this agenda captioned "Pending Administrative Adjudications," as authorized by Government Code section 11126(e).
 - C. The Board may convene a Closed Session for the purposes of considering personnel matters as authorized by Government Code section 11126, (a).

Additional information regarding this meeting may be obtained from the CHRB Administrative Office, 1010 Hurley Way, Suite 300, Sacramento, CA 95825; telephone (916) 263-6000; fax (916) 263-6042. This notice is located on the CHRB website at www.chrb.ca.gov. *Information for requesting disability related accommodation for persons with a disability who require aid or services in order to participate in this public meeting, should contact Jacqueline Wagner.

CALIFORNIA HORSE RACING BOARD

Chuck Winner, Chairman
Bo Derek, 1st Vice Chairman
Richard Rosenberg, 2nd Vice Chairman
Steve Beneto, Member
Jesse H. Choper, Member
George Krikorian, Member
Madeline Auerbach, Member
Rick Baedeker, Executive Director
Jacqueline Wagner, Assistant Executive Director

CALIFORNIA HORSE RACING BOARD
1010 HURLEY WAY, SUITE 300
SACRAMENTO, CA 95825
(916) 263-6000
FAX (916) 263-6042



**PENDING LITIGATION
MARCH 2015**

COURT LITIGATION

- A. Jeff Mullins vs. CHRB, et al**
Superior Court of California, County of San Diego, Case No. 37-2010-00092212
- B. Morteza Atashkar vs. CHRB**
Superior Court of California, County of Sacramento, Case No. 34-2008-00024426
Court of Appeal, Third Appellate District, C074852
- C. San Luis Rey Racing, Inc., vs. CHRB, et al**
Superior Court of California, County of San Diego, Case No. 37-2011-00096586
- D. Donald Lockwood vs. CHRB**
Superior Court of California, County of Los Angeles, Case No. BS147701
- E. Jose DeLaTorre vs. CHRB**
Superior Court of California, County of Los Angeles, Case No. BS152795
- F. Eloy Navarro vs. CHRB**
Superior Court of California, County of Los Angeles, Case No. BS153348

CALIFORNIA HORSE RACING BOARD
1010 HURLEY WAY, SUITE 300
SACRAMENTO, CA 95825
(916) 263-6000
FAX (916) 263-6042



**PENDING ADMINISTRATIVE ADJUDICATIONS
MARCH 2015**

CASE

- A. Proposed Decision After Remand**
Donald Lockwood vs. California Horse Racing Board
Case Number: SAC 13-0017, Superior Court Case No. BS147701

PROCEEDINGS of the Regular Meeting of the **California Horse Racing Board** held at the **Santa Anita Park Race Track, Baldwin Terrace Room**, 285 West Huntington Drive, Arcadia, California, on **February 18, 2015**.

Present: Chuck Winner, Chairman
 Richard Rosenberg, 2nd Vice-Chairman
 Madeline Auerbach, Member
 Steve Beneto, Member
 Jesse H. Choper, Member
 George Krikorian, Member
 Rick Baedeker, Executive Director
 Jacqueline Wagner, Assistant Executive Director
 Robert Miller, General Counsel

APPROVAL OF THE MINUTES OF JANUARY 15, 2015

Chairman Winner asked for approval of the minutes of the Regular Meeting of January 15, 2015.

Chairman Winner **motioned** to approve the minutes. Commissioner Krikorian **seconded** the motion, which was **unanimously carried**.

EXECUTIVE DIRECTOR'S REPORT.

Executive Director Rick Baedeker introduced Philip Laird, the new California Horse Racing Board (CHRB) staff counsel. He stated Mr. Laird would work with CHRB law enforcement, licensing, policy, regulations, and legislation. Executive Director Baedeker stated the microchip program was scheduled to begin on April 1, 2015, at Golden Gate Fields (GGF). He said CHRB safety stewards met with three trainers who would be participating in the program and everyone was supportive. The California Thoroughbred Trainers and management at GGF had been helpful and supportive of the project, which was appreciated by the Board. Executive Director Baedeker stated the California Department of Food and Agriculture provided six microchip scanners for the program, which was appreciated as well. Executive Director Baedeker stated

regulating the use of cobalt would be presented at the February 2015 Regular Board meeting. He said the Medication Committee approved the proposed threshold of 25 parts per billion. He stated even though cobalt was a natural mineral, and found in vitamin B12, if administered in higher doses it could be a performance enhancer, and in very high doses could be toxic to a horse. Executive Director Baedeker stated Galway Downs was in compliance with all CHRB regulations. He said Galway Downs met all of its conditions and horses were shipped in. Executive Director Baedeker reported on Advance Deposit Wagering (ADW) distributions. He stated John Bucalo, of the Barona Casino, asked about the percentage that went to satellites from ADW. Executive Director Baedeker said a thorough understanding of how the percentage was derived and figures were provided to the Board by Bernie Thurman of Southern California Off Track Wagering, Incorporated (SCOTWINC). He stated distributions were paid to the following: the host, ADW company, retirement fund, Workers' Compensation, equine fund, Public Employment Board, backstretch fund, satellites, expense fund, stabling and vanning, breeder awards, purses and track commissions. He said distributions could change depending on who made the wager, on which track, and on what breed. He stated, for example, ADW wagers placed by Southern California residents on cards hosted by Santa Anita would be distributed as follows: 79.87 percent back to bettors; 4.91 percent hub fee paid to ADW; 1.89 percent to the various funds mentioned; 1.97 percent to brick-and-mortar satellites. He said the 1.97 percent would be placed in a pool and distributed according to the level of business done by the individual satellite the previous year; 2.9 percent to the expense fund; 5.12 percent to purses; and 3.35 percent to tracks. He stated Barona handled \$12,207,000 in 2014; it received \$248,000 in brick-and-mortar commissions, plus \$183,000 from the ADW share. He said added together this resulted in 3.54 percent of business done at Barona. Executive Director Baedeker stated the

financials for the month were good; business from daytime meets was up one percent and business for night meets was up 27.82 percent. He said the night meets were up due to a significant increase in ADW, two more racing days, and days where harness and quarter horses did not run against each other. He stated business was up just under 3.4 percent for the month. Chairman Winner asked Kip Levin of TVG and Keith Brackpool of the Stronach Group to report on HRTV and TVG. Mr. Brackpool stated the purchase of HRTV by TVG was announced, and the parties wanted to provide the Board with background on the transaction. He stated people wondered why they had two networks competing with other sports TV. He said the biggest issue facing horse racing was carrier distribution. He stated there had been a consolidation of main carriers of satellite and cable television with a fractured distribution depending on where someone lived in the country; you got one or nothing – not both. He said it was difficult to get both with California being an example. He stated he was introduced to Mr. Levin, CEO of TVG, and they began dialogue on merging the two companies. He said the transaction had closed and they were very excited. He stated it would have a positive effect on California racing because Santa Anita and Golden Gate would be on the main HD channel with licensed rights to show other Stronach Group tracks around the country. Mr. Levin stated TVG invested in building an amazing TV product and platform to represent the racing industry. TVG was building a new studio and upgrading its HD signal. He said TVG's plan was to continue to operate the two networks in unison. He stated the strategy was to shine a nation-wide spotlight on all premium races in California and to show more racing on TV. Chairman Winner asked when HRTV and TVG would be relicensed under the new agreement. Mr. Brackpool stated the ADW providers had not merged; just the television companies. He said Xpressbet was still owned 100% percent by the Stronach Group. Commissioner Auerbach asked Mr. Brackpool if

TVG was assuming control immediately; would the Board see TVG from Santa Anita, live onsite? Mr. Brackpool said yes; it would be seen immediately. He stated any issues that arose due to the purchase of HRTV would be worked through within one to two weeks and the entities would be smoothly integrated within 30 to 45 days. Mr. Levin stated there would be two television networks that would work in tandem/unison with each other. Mr. Brackpool gave the Board an example of Santa Anita; the race meeting would be shown on both networks and only certain races would be shown on one network. He said the intent was to have a main HD channel that would feature the premium racing, and other racing would be shown at a faster rate on the second channel. Commissioner Auerbach asked if the signal would be merged with the TVG signal and would the HRTV signal become superfluous. Mr. Brackpool stated TVG intended to keep the two channels operating. The branding issue would be discussed over time. Mr. Levin said the programming would allow the two channels to work in tandem rather than compete with each other. He used a stakes race at Santa Anita broadcast by HRTV as an example. As the race closed, instead of cutting over to another race, HRTV would show the winner's circle. Customers interested in watching a race starting at another race location would be told to turn to TVG. Chairman Winner asked if replays would be eliminated. Mr. Levin stated there would be time to show the replays for premium races. Chairman Winner asked if certain races shown on tape delay could be eliminated. Mr. Levin stated hundreds of races every year were shown on tape delay due to content commitments. He said tape delay would give TVG more time to figure out how to place a bigger spotlight on the premium content in California, while also meeting the needs of other content commitments. 2nd Vice-Chairman Rosenberg asked if the Stronach Group would have control of TVG going forward. Mr. Brackpool stated TVG acquired HRTV as part of the asset; however, the Stronach Group was

concurrently licensed to show Stronach Group racing around the country to the new entity. He said there was a TV board made up of himself, Mr. Levin, Scott Daruty, and others from TVG, as well as a combined TV board. Commissioner Auerbach asked if the CHRB was unhappy that TVG was not showing Golden Gate; could the CHRB lobby TVG. Mr. Levin stated TVG signed a contract commitment to show Golden Gate. Executive Director Baedeker asked if the existing HRTV channel would be converted to a second TVG channel; would both channels always be available? Mr. Levin said that would be dependent on the TV distributors, but they would promote both channels across each other; the hope was to get broader distribution for the second network. Commissioner Krikorian asked if TVG had a plan in place to expand high definition. Mr. Levin said both networks would broadcast out of TVG's HD studio and HRTV would move under the same technology platform. He stated TVG would have a conversation with the satellite companies and distributors to ensure they would broadcast the signal in HD. Commissioner Choper asked about potential antitrust implications. Mr. Brackpool stated they did not believe they had violated any antitrust regulations. Commissioner Beneto asked if the different race tracks would be on different channels. Mr. Levin stated races would all be on TVG and the premium network. Chairman Winner asked if the names HRTV and TVG would remain. Mr. Levin stated the immediate plan was to keep the name HRTV. Mr. Levin asked Mr. Brackpool if there was a TV board, a board within the company that would operate the TV side of the business. Mr. Brackpool stated there was such a board. Representatives from the Stronach Group and TVG were on the board. 2nd Vice-Chairman Rosenberg asked if the television broadcast arrangement had something to do with Xpressbet being a part of one of the networks. Mr. Brackpool said "no". Chairman Winner asked if Xpressbet and TVG would continue to operate separately. Mr. Levin stated that was correct. Chairman Winner said he

understood HRTV was being retained as the brand. He asked if Xpressbet and HRTV would promote each other on their ADW platforms. Mr. Brackpool stated HRTV did not have a wagering site and Xpressbet was a different unit of The Stronach Group. Chairman Winner stated since Xpressbet was not merging with TVG, and the platform of the ADW remained the same, Xpressbet did not have to reapply for a license.

PUBLIC COMMENT

There were no public comments.

DISCUSSION AND ACTION BY THE BOARD ON THE REQUEST FROM THE DEL MAR THOROUGHBRED CLUB TO ENACT CHRB RULE 1406, SUSPENSION OF RULE, TO WAIVE THE PROVISIONS OF CHRB RULE 1433(B), APPLICATION FOR LICENSE TO CONDUCT A HORSE RACING MEETING, TO FACILITATE THE INSTALLATION OF A DIRT RACE TRACK AT DEL MAR.

Josh Rubenstein, Del Mar Thoroughbred Club (DMTC), stated DMTC was returning to a natural dirt surface beginning with its 2015 summer meet. He said it requested a waiver to Rule 1433, subsection (b) of Application for License to Operate a Race Meeting. Subsection 1433(b) mandated a synthetic surface at race tracks that operate four weeks or more of continuous thoroughbred racing in a calendar year. Executive Director Baedeker informed the Board this issue had been administratively handled based on the Board's previous action to amend Rule 1433 to delete the requirement for a synthetic surface. He said based on the Board's intent to amend Rule 1433, staff determined it was appropriate and prudent for Del Mar to begin the process. Chairman Winner **motioned** to approve the request from DMTC to waive the provisions of Rule 1433(b) to facilitate the installation of a dirt racetrack at DMTC. Commissioner Krikorian **seconded** the motion, which was **unanimously carried**.

DISCUSSION AND ACTION BY THE BOARD REGARDING THE PROPOSED AMENDMENT TO CHRB RULE 1658, VESTING OF TITLE TO CLAIMED HORSE, TO PROVIDE THAT A CLAIM SHALL BE VOIDED BY THE STEWARDS IF THE RACING OR OFFICIAL VETERINARIAN DETERMINES THE HORSE WILL BE PLACED ON THE VETERINARIAN'S LIST AS "BLED".

Dr. Rick Arthur, CHRB Equine Medical Director, stated the original version of Rule 1658, Vesting of Title to Claimed Horse, voided claims when the horse bled. However, in subsequent years the provision was eliminated and the regulation only dealt with soundness issues. He said California Thoroughbred Trainers (CTT) and official veterinarians requested that Rule 1658 be amended to include horses that bled. He stated a horse could be claimed as sound, but would go on the Veterinarian's List as bled. He said "bled" was defined in Rule 1845, Authorized Bleeder Medication, as horses that bleed from the nostrils, had epistaxis, appeared as exercise-induced pulmonary hemorrhage. He stated under the proposed amendment, claims would be voided if the claimed horse was placed on the Vet's List as bled. Chairman Winner stated the primary reason for amending Rule 1658 was to discourage the entry of horses for the purpose of offloading them; a deterrent to those who tried to enter a horse in a race that was unsound. He said often a trainer did not know a horse had a bleeding problem until it raced. He stated if the purpose of the proposed amendment was not to discourage placing a damaged horse in a claiming race, then he did not believe it was consistent with the intent of the rule. Dr. Arthur said 60 percent of horses treated with Lasix had exercise-induced pulmonary hemorrhage. He said soundness health and respiratory health were the two issues race track veterinarians dealt with. He stated he believed the proposed amendment to Rule 1658 would protect horses. Commissioner Auerbach asked if the Board wanted to keep amending Rule 1658 when it appeared the proposals were not in line with the original intent of the regulation. Chairman Winner stated he did not want the Board to over-regulate. He said the Board was trying to do

what was right for the industry, the horses, and the riders. He stated a horse would not go down for bleeding, causing damage to other horses, or the rider; however, a horse would more likely go down if there was preexisting skeletal or soft tissue damage. Dr. Arthur stated there were one to four sudden deaths a year related to exercise pulmonary hemorrhage; it was not a big problem. He stated, in terms of protecting the welfare of the horse, the proposed amendment was a reasonable step. Dr. Arthur said if it was known that a horse bled, the horse would go on the Vet's List, and could not race for 15 days. He stated the primary definition for a regulatory action was epistaxis, or blood at the nose, not endoscopic which was internal bleeding. Commissioner Krikorian asked if it was possible for a horse to bleed through the nostrils one time, and not the next time it ran a race. Dr. Arthur stated that was possible. Commissioner Krikorian asked if a horse that bled multiple times could be designated differently than one that had a few drops of blood after a race. Dr. Arthur stated as the regulatory agency, the Board only monitored blood at the nostrils; the Board did not perform endoscopic examinations. Commissioner Krikorian stated he had the same concerns as Chairman Winner and Commissioner Auerbach about the proposed amendment. Commissioner Choper said the purpose of the item was to put the proposed amendment forward for 45 day notice. Jim Cassidy, President, stated CTT was concerned about the welfare of the horse. Chairman Winner asked if a claim would be voided if a horse that never bled before bled once through the nostrils or would a pattern of bleeding be more reason to void a claim? He asked if the proposed amendment was written so if the horse bled through the nostril more than once the claim would be voided. Dr. Arthur stated a horse that bled through the nose would be observed by the official or track veterinarian and would go on the Vet's List for 15 days the first time it bled. Commissioner Choper asked if bleeding during training was included under the proposed amendment. Dr.

Arthur stated the rule did not include training. Commissioner Choper asked if horses that were not claimed would be observed by the track veterinarian as much as the horses that were claimed. Dr. Arthur stated no. He said horses that won were observed for an hour after the race. Commissioner Choper stated he believed claimed horses went on the Vet's List immediately. Dr. Arthur said no, if the horse was claimed it was examined by the official veterinarian at the test barn, and the horse was either released as sound, and the claim stood, or the horse was released as unsound, and the claim voided. Chairman Winner asked if all trainers, even those who opposed the rule initially, supported the proposed amendment. Mr. Cassidy said he believed horsemen thought the rule was working out well. He stated the proposed amendment would help those who claimed a horse but had no idea the horse bled in the past. Commissioner Krikorian asked why the wagering public was not informed about a horse that bled. Dr. Arthur stated the Vet's List was a public document; an individual could look up a horse to see if it had bled. Alan Balch, of the CTT, stated the proposal had to do with fairness. He said the issue arose when a claim was not voided for a horse that bled for the third time and then the horse was out. He stated that was not fair for the claiming owner or the claiming trainer. He said the claiming rule should be consistent and fair for everyone. 2nd Vice Chairman Rosenberg **motioned** to direct staff to initiate a 45-day public comment period for the proposed amendment to Rule 1658. Commissioner Choper **seconded** the motion, which was **unanimously carried**.

DISCUSSION BY THE BOARD REGARDING THE PROPOSED AMENDMENT TO CHRB RULE 1699, RIDING RULES, AS IT PERTAINS TO THE CRITERIA FOR DISQUALIFICATION IN A HORSE RACE.

Executive Director Rick Baedeker stated the Board proposed language for an amendment to Rule 1699, Riding Rules, at the November 2014 Steward's Committee meeting. He said the language

went to the Regulatory and Legislative Committee for further review. He stated there were still issues with the proposed language and he recommended the Board postpone further action until a final text was approved. Chairman Winner stated the Board wanted the proposed amendment to be as clear and consistent as possible for the industry and to the wagering public. Executive Director Baedeker stated the issues with Rule 1699 did not originate with the controversial call in the Breeders' Cup Classic; the item was already on the agenda for the Stewards' Committee meeting prior to the Classic. He said he recognized the rule was interpreted differently in the North than the South. He stated the goal of the proposed amendment was to achieve more precise wording. He said when the Stewards' met in November 2014 they supported the change. Chairman Winner stated the Board looked at other racing jurisdictions, and discovered there was not a lot of difference between California and other jurisdictions' rules. He said at the conclusion of the Stewards' Committee meeting in November 2014, it was agreed that a change to Rule 1699 was necessary, and the draft language presented was well received. Commissioner Auerbach stated she agreed with the Stewards that the language should not be changed. She said the language was not the problem; the problem was lack of leadership. She stated it was up to the Board to set the tone for how its rules should be interpreted. The first priority should be safety of the riders, as well as the safety of the horse. She stated if the Board made rulings based on those two priorities it would see statewide alignment of rulings in California. Chairman Winner stated he believed the Stewards understood the priority to ensure the safety of horse and rider. He said he believed California's Stewards understood the Board provided them with guidance. He stated he watched the race in question 50 times, and based on the current version of Rule 1699 he agreed with the decision not to disqualify the horse. He said biggest problem, besides safety, was inconsistency between North and South, and within the same jurisdictions.

He stated the Stewards did the best they could and strove to make the right decisions. He said the Board could help the Stewards by clarifying the regulation. Commissioner Auerbach stated she did not object to clear language. She said she was concerned about young, inexperienced jockeys who did not know what to do. Chairman Winner asked Steward Scott Chaney why the Stewards changed their position regarding the proposed text. Mr. Chaney stated at the November 2014 Stewards Committee meeting the Stewards had the impression a rule change would occur regardless. He said a second conference call was held and the Stewards had the opportunity to express their opinions. He stated in close cases, ones in which the Stewards were not sure about, some Stewards believed the order of finish should be left alone, and that was the difference between North and South. He said there were more disqualifications in Northern California than in the South. He stated consistency was important and suggested taking a horse down in close cases would create more disqualifications in Southern California, but it may align Northern and Southern California. He said he was not opposed to making Rule 1699 clearer, either through a language change, or direction from the Board. Chairman Winner asked if suspending the rider would be more appropriate than taking a horse down if it was not clear that it affected the outcome of the race. Mr. Chaney stated suspending the jockey was more appropriate. Chairman Winner stated another alternative to consider was increasing the number of suspension days for riders. Commissioner Choper stated if the Board wanted consistency, it could be achieved by reducing the discretion of the decision maker. He said Rule 1699 could be amended to punish the jockey and not take the horse down. 2nd Vice Chairman Rosenberg stated versions two and three of the draft language were an attempt to distinguish between a foul at the start of a race and after the start of a race. That did not mean there was a disqualification; the language defined interference in each case. Executive Director Baedeker stated the difference

was severely bumping or severely impeding relative to the start, versus the definition of interference after the start. Mr. Chaney asked if the language of the proposed amendment changed what constitutes the collectively agreed upon meaning of interference. He said the subjective part was: did the interference cost the horse the opportunity of a better placing? 2nd Vice Chairman Rosenberg stated that was two separate issues. He said the problem with the language was the definition of when interference occurred, or disqualification. Mr. Chaney stated an example was the Breeders' Cup Classic. He said everyone agreed it was interference, but even if interference was defined, it would not have changed the analysis. He stated it would have still been called interference, and the Stewards would have been burdened with whether or not it cost the horse the opportunity of a better placing. Mr. Chaney said the blimp shot showed interference, but it was not severe. 2nd Vice Chairman Rosenberg stated a clear definition of interference would result in more consistent rulings. He asked how to interpret "a horse shall not cause interference in a part of the race where the horse loses the opportunity to place where it might be reasonably expected to finish." Mr. Chaney said in California that had always been interpreted as the next immediate place; whether it cost a horse a head, or if the horse was six lengths back, one had to decide whether it cost the horse six lengths to be in the immediate place ahead. Chairman Winner stated there should be greater discretion, not just verbal direction; the rule could be improved to ensure more consistency and guidance. Mr. Chaney said Rule 1699 should not be used to punish the jockey; its purpose was to get the correct order of finish. Commissioner Krikorian stated he agreed with Commissioner Choper that discretion needed moderation. He said the proposed language was going in the right direction and could be improved by reducing the discretion of the stewards. Chairman Winner stated it was a difficult issue and what was important was safety, clarity for the wagering public, and consistency. He

suggested the Board refer the issue to the next Stewards Committee meeting. Commissioner Auerbach requested a meeting with the Stewards and the jockeys. Chairman Winner stated the Stewards' Committee meeting was only for Stewards; however, an ad hoc meeting could work. He said he would work with staff to schedule a meeting with the Stewards and Jockeys. 2nd Vice Chairman Rosenberg suggested the Stewards form a subcommittee to draft language to either present at the Stewards' Committee meeting or before the Board. Chairman Winner stated the Board would proceed on the two issues.

DISCUSSION AND ACTION BY THE BOARD REGARDING THE PROPOSED AMENDMENT TO CHRB RULE 1844, AUTHORIZED MEDICATION, TO 1) LOWER THE AMOUNT OF KETOPROFEN THAT CAN BE PRESENT IN A TEST SAMPLE FROM 10 NANOGRAMS PER MILLILITER OF BLOOD PLASMA OR SERUM TO 2 NANOGRAMS PER MILLILITER OF BLOOD PLASMA OR SERUM; AND 2) TO ADD ISOFLUPRODONE AND ITS SPECIFIED AUTHORIZED LEVEL TO THE LIST OF CALIFORNIA'S AUTHORIZED MEDICATION.

Dr. Rick Arthur, CHRB Equine Medical Director, stated the proposed amendment to Rule 1844, Authorized Medications, would bring California in line with the National Uniform Medication Testing Program for Therapeutic Medications. He said the proposed amendment would add corticosteroid and isofluprodone to the list of authorized medications under Rule 1844, and would reduce the permitted non-steroidal anti-inflammatory drug substance levels from 10 nanograms to 2 nanograms. Commissioner Beneto **motioned** to direct staff to initiate a 45-day public comment period regarding the proposed amendment to Rule 1844. Commissioner Choper **seconded** the motion, which was **unanimously carried**.

DISCUSSION AND ACTION BY THE BOARD REGARDING THE **PROPOSED AMENDMENT TO CHRB RULE 1845, AUTHORIZED BLEEDER MEDICATION, TO REQUIRE THAT AUTHORIZED BLEEDER MEDICATION BE ADMINISTERED BY INDEPENDENT, THIRD PARTY VETERINARIANS.**

Executive Director Rick Baedeker stated the Board was aware the language for the proposed amendment of Rule 1845, Authorized Bleeder Medication, had been opposed by the California Veterinarian Board (Vet Board) because it claimed the veterinarian-patient-client relationship would be violated. He said the Board worked with Agency and the Vet Board over the last few months to develop new language. He stated the new language was presented to the Vet Board, and the issue was resolved. Dr. Rick Arthur, CHRB Equine Medical Director, stated the new language would accomplish third-party Lasix administration as part of the National Uniform Medication Program. 2nd Vice Chairman Rosenberg asked who would be responsible for checking on the business relationship of the third party veterinarian, or medical technicians. Dr. Arthur said it was the responsibility of the official veterinarian who designates the person administering the Lasix. Vice Chairman Rosenberg stated the track veterinarian did not examine horses during a workout; however, the proposed language includes "workout." Dr. Arthur said including the term "workout" would give the official veterinarian or track veterinarian the option to place a horse on the bleeder's list. Robert Miller, CHRB Staff Counsel, asked Dr. Arthur to specify the changes he wanted made to the CHRB 194 form. Dr. Arthur stated on the CHRB 194 form the title would be "Authorized Bleeder Medication Request and Medication History" and a space should be included on the form for the veterinarian to list medical history regarding authorized bleeder medication administration. Chairman Winner **motioned** to direct staff to initiate a 45-day public comment period for the proposed amendment of Rule 1845. Commissioner Choper **seconded** the motion, which was **unanimously carried**.

DISCUSSION AND ACTION BY THE BOARD REGARDING THE **PROPOSED AMENDMENT TO CHRB RULE 1887, TRAINER TO INSURE CONDITION OF HORSE, TO ADD OWNERS OF A SHIP-IN HORSE AS EQUALLY RESPONSIBLE FOR THE CONDITION OF A HORSE.**

Executive Director Rick Baedeker stated the proposed amendment to Rule 1887, Trainer to Insure Condition of Horse, would affect owners that train a horse outside of a CHRB licensed facility, and then bring a horse in to race under another trainer's name. He said incidents occurred where a horse that was brought in to race had a positive test result and the trainer was held responsible as the absolute insurer. He stated the proposed amendment to Rule 1887 would require a ship-in horse to be under the care of a licensed trainer for at least seven calendar days prior to the race; if not, then the owner would be considered the joint absolute insurer. 2nd Vice Chairman asked how long a foreign horse that would be flown in to race had to remain in quarantine? Dr. Rick Arthur, CHRB Equine Medical Director, stated a horse from Europe would remain in quarantine for a minimum of 72 hours. 2nd Vice Chairman asked if a quarantine facility would fall within the enclosure. Dr. Arthur stated not within the enclosure at every race track but the horse would still be under the control of the trainer. Executive Director Baedeker stated the horse must be under the care of a licensed trainer whether in a national or internationally racing jurisdiction. Commissioner Beneto asked if a ship-in horse could be brought in to race with no works. Executive Director Baedeker stated a horse that never raced was required to have a published workout. Chairman Winner **motioned** to direct staff to initiate a 45-day public comment period for the proposed amendment of Rule 1887. Commissioner Auerbach **seconded** the motion, which was **unanimously carried**.

DISCUSSION AND ACTION BY THE BOARD REGARDING THE REQUEST FOR APPROVAL OF THE CONTINUATION OF THE 0.50% DISTRIBUTION TO THE SOUTHERN CALIFORNIA STABLING AND VANNING FUND FROM ADVANCE DEPOSIT WAGERING (ADW) HOSTED BY THOROUGHBRED RACING ASSOCIATIONS AND RACING FAIRS CONDUCTING RACING IN THE CENTRAL AND SOUTHERN ZONES FOR THE PERIOD COMMENCING MARCH 1, 2015 THROUGH FEBRUARY 29, 2016 AS PERMITTED UNDER BUSINESS AND PROFESSIONS CODE SECTION 19604(F)(5)(E).

Joe Morris, of the Thoroughbred Owners of California and the Southern California Stabling and Vanning Committee, stated the funding mechanism was in place March 2014 through the end of February 2015. He asked for a one year extension of the 0.50% distribution to help fund Stabling and Vanning in the South. Commissioner Choper asked if the industry was in agreement. Mr. Morris stated yes; all parties had agreed. Commissioner Krikorian stated a request was previously made for an additional percentage for Southern California Off Track Wagering, Incorporated (SCOTWINC). Mr. Morris stated that request was for the funding of SCOTWINC. He said the current request was for Stabling and Vanning. The funds would pay for auxiliary offsite stabling. Commissioner Krikorian stated there was a shortage in Stabling and Vanning and asked for the number. Mr. Morris said at the end of 2014 the shortage was just shy of \$4.4 million. Chairman Winner asked how the cost of stabling at Galway had improved the situation. Mr. Morris stated it improved greatly. Commissioner Beneto asked how the funds was handling the parties it owed money. Mr. Morris stated the fund had accounts receivable that went out six to seven months. Chairman Auerbach **motioned** to approve the continuation of the 0.50% distribution to the Southern California Stabling and Vanning fund. 2nd Vice-Chairman Rosenberg **seconded** the motion, which was **unanimously carried**.

DISCUSSION BY THE BOARD REGARDING THE OPERATION AND FINANCIAL STATUS OF SOUTHERN CALIFORNIA OFF TRACK WAGERING, INCORPORATED (SCOTWINC) AND NORTHERN CALIFORNIA OFF TRACK WAGERING (NOTWINC), AND THE AWARDING OF THE CONTRACT TO AMTOTE, TO PROVIDE CALIFORNIA'S WAGERING SERVICES AND THE IMPACT THIS MAY HAVE ON CALIFORNIA RACING.

Executive Director Rick Baedeker stated the Board had questions about the operational structure, the financial performance of Southern California Off Track Wagering, Incorporated (SCOTWINC) and Northern California Off Track Wagering (NOTWINC), the procedures used to award the new totalizator contract, and concerns about the number of entities owned or operated all or in part by the Stronach Group. George Haines, SCOTWINC, stated the process started in 2014 and SCOTWINC was in the process to sign a contract with AmTote as the selected vendor. Chris Korby, California Authority of Racing Fairs, stated the contract for the Totalizator System was a statewide contract. 2nd Vice Chairman Rosenberg stated a letter from Sportech sent to SCOTWINC indicated the bidding process was unfair and the Board did not receive the response from SCOTWINC until a couple of days before the Board meeting. He said the response letter from SCOTWINC stated Sportech presented first, with a representative from the Stronach Group present, and AmTote presented a day later. He stated the question was whether AmTote had the opportunity to adjust its proposal after it saw Sportech's proposal. Chairman Winner asked if it would be fair to say AmTote had an opportunity to adjust its presentation in the 24-hour period. Mr. Haines stated that was correct; it had the opportunity. Commissioner Krikorian asked Mr. Haines to explain the Request for Proposal (RFP) process. Chris Korby stated the RFP was a two-step process. He said SCOTWINC first sent out a document called Request for Information. The purpose of the document was to notify interested companies an RFP was forthcoming, and to solicit information from the companies regarding items they thought should be included in the RFP. He said responses were received from several

companies which helped SCOTWINC finalize the RFP. Commissioner Krikorian asked what was submitted by the companies that made proposals; what numbers were submitted and what was discussed? Mr. Korby stated the RFP required a technical proposal that described the services and equipment, and a cost proposal that was submitted in a separate sealed envelope. He said the RFP also required an oral presentation subsequent to submission of the written presentation and cost proposal. He said SCOTWINC allowed both companies to make a written clarification to their cost proposals. Chairman Winner asked if AmTote's cost proposal changed. Mr. Haines stated both companies cost proposals changed. 2nd Vice Chairman Rosenberg asked at what point were the companies allowed to make a change to their cost proposals; was it at the oral presentation? Mr. Korby stated it was after the oral presentation. Mr. Morris stated after SCOTWINC reviewed the proposals SCOTWINC had a few areas that needed clarification because SCOTWINC wanted new equipment. He said SCOTWINC wanted new equipment and the Sportech bid included used equipment. He stated SCOTWINC sent out letters to both companies seeking clarification. In the letter the bidding companies had the opportunity to tweak the cost proposals. Both of the bidding companies lowered their prices. Chairman Winner asked if the members of the Stronach Group who were present at the Sportech presentation knew Sportech's number? Mr. Morris stated the presentation were on technology and not costs; there was no discussion of costs. Chairman Winner asked if AmTote would have seen Sportech's written proposal. Mr. Morris stated possibly. He said the Tote committee did not include Stronach managers. He stated the Tote committee reported to NOTWINC and SCOTWINC at the board level. 2nd Vice Chairman Rosenberg asked when the Tote committee met. Mr. Morris stated the Tote Committee made its recommendation to the full boards at the joint SCOTWINC-NOTWINC meeting and the boards voted at that time. Commissioner Choper

commented the Board should look at anti-trust laws regarding the Stronach Group's involvements throughout the racing industry. Mr. Morris stated the RFP process followed a very diligent process by forming a Tote committee, sending out a Request for Information to identify potential bidders. He said they formed a Tote Committee with no Stronach representatives, required technology presentations, and gave the tote companies an opportunity to make clarifications and tweak numbers. Commissioner Choper stated it would have been better if the process was presented in a general record open to everyone. Commissioner Krikorian said Sportech's letter stated it was not invited to participate in AmTote's presentation, and that no other financial costs were presented after the initial cost submittal. Chairman Winner stated it may have been better if Sportech presented first. Mr. Morris stated Sportech had the option to go first but it chose otherwise. Commissioner Krikorian asked if Sportech put a hold on opening minisatellite facilities. Mr. Morris stated that was correct and he should know in several weeks if Sportech planned to move forward or not. He said if Sportech decided not to move forward he would have a plan B in place. 2nd Vice Chairman Rosenberg asked what would happen to totalizator equipment that was in the minisatellites? Mr. Morris stated initially the two contracts were together but over the last year they had separated the tote contracts from the audio-visual contracts. He said just tote machines would be removed. Commissioner Krikorian stated Sportech representatives should attend the next Regular Board meeting; the Board should give Sportech the opportunity to speak before making a decision to license. Mr. Bucalo asked if there would be downtime when the new equipment was installed, and would there be a loss in revenue during installation. Mr. Haines stated there would be no downtime. 2nd Vice Chairman Rosenberg suggested the report detailing SCTOWINC and NOTWINC financial and corporate

structure be referred to committee for further review. Chairman Winner stated the materials would be referred to committee.

MEETING ADJOURNED AT 12:42 P.M.

A full and complete transcript of the aforesaid proceedings are on file at the office of the California Horse Racing Board, 1010 Hurley Way, Suite 300, Sacramento, California, and therefore made a part hereof.

Chairman

Executive Director

CALIFORNIA HORSE RACING BOARD

MARCH 19, 2015
REGULAR BOARD MEETING

There is no board package material for Item 2

CALIFORNIA HORSE RACING BOARD

MARCH 19, 2015
REGULAR BOARD MEETING

There is no board package material for Item 3

STAFF ANALYSIS
DISCUSSION AND ACTION BY THE BOARD REGARDING THE PROPOSED
AMENDMENT TO CHRB RULE 1588, HORSE INELIGIBLE TO START IN A RACE,
TO PROVIDE THAT A HORSE IS INELIGIBLE TO START IN ANY RACE IN
CALIFORNIA IF IT IS ON THE VETERINARIAN'S LIST IN ANOTHER RACING
JURISDICTION, UNLESS WITH PRIOR APPROVAL OF THE STEWARDS

Regular Board Meeting
March 19, 2015

ISSUE

In December 2014 the proposed amendment to Board Rule 1588, Horse Ineligible to Start in a Race, was submitted to the Office of Administrative Law (OAL) for review. The proposed amendment provided that a horse would be ineligible to start in any race in California if it was on the Veterinarian's List in another racing jurisdiction, unless with prior approval of the stewards. The OAL disapproved the rulemaking action based on the Clarity standard of Government Code section 11349.1. The OAL disapproval stated the rulemaking record implied that the stewards would be responsible for conducting an investigation to determine whether adequate cause existed to allow a horse to race, and the steward approval clause (subsection "j" of the proposed text) was to be used as a mechanism to correct racing eligibility errors that were identified. However, the proposed subsection 1588(j), which delegated unlimited approval power to the stewards, failed to align with the concept. The text of the regulation has been modified to address OAL's concerns. New subsections (j)(1) through (j)(3) define what may constitute "good cause" when the stewards make a determination regarding a horse's eligibility to race. A 15-day public comment period is required before the file can be resubmitted to OAL.

ANALYSIS

California does not have an official Veterinarian's List reciprocity policy for horses on the Veterinarian's List in other states. This potentially allows compromised horses to avoid official veterinary scrutiny by moving to other racing jurisdictions which do not always monitor or recognize out-of-state Veterinarian's Lists. The proposed amendment to Board Rule 1588 prohibits any horse on the Veterinarian's List in another jurisdiction from entering a race in California without the prior approval of the stewards. The 1588 rulemaking file was submitted to OAL for review in December 2014. The file was disapproved based on the Clarity standard, as OAL did not believe the text of the proposed subsection 1588(j), which delegated unlimited approval power to the stewards, aligned with the concept. OAL stated it appeared the Board intended for the stewards to take specific steps to determine whether a horse should be allowed to race, including consultation with the official veterinarian and with racing officials in other racing jurisdictions. OAL declared that those standards of general application should be promulgated in Rule 1588 and adequately explained in the rulemaking record. To address the OAL's concerns, the proposed text of subsection 1588(j) has been modified to provide that the stewards must have "good cause" to approve the entry of a horse that is on another racing jurisdiction's Veterinarian's List. Subsections 1588(j)(1) through (j)(3) have been added to define what such "good cause" may include: 1) unforeseen administrative issues in removing the horse from the other racing jurisdiction's Veterinarian's List; 2) the location of the horse

preventing it from being evaluated by the official veterinarian of another jurisdiction and cleared from that jurisdiction's Veterinarian's List; and 3) another unforeseen event or reason that would prevent the horse from being cleared from another racing jurisdiction's Veterinarian's List.

BACKGROUND

Business and Professions Code section 19440 provides that the Board shall have all powers necessary and proper for it to carry out fully and effectually the purposes of this chapter. Responsibilities of the Board shall include adopting rules and regulations for the protection of the public and the control of horse racing and pari-mutuel wagering. Business and Professions Code section 19562 provides that the Board may prescribe rules, regulations and conditions under which all horse races with wagering on their results shall be conducted in this State.

Board Rule 1866, Veterinarians List, states the official veterinarian shall maintain a Veterinarian's List of those horses determined to be unfit to compete in a race due to physical distress, unsoundness, or infirmity. Subsection 1866(c) provides that a horse placed on the Veterinarian's List shall be removed from the list only after having established or demonstrated to the satisfaction of the official veterinarian or the racing veterinarian that the horse is then sound and in fit physical condition to exert its best effort in a race. The proposed amendment to Rule 1588 specifies that a horse is ineligible to start in any race in California if it is on the Veterinarian's List in another racing jurisdiction, unless with prior approval of the stewards. The proposed amendment to Rule 1588 was submitted to the OAL for review in December 2014. In January 2015, the OAL disapproved the regulatory action based on the Clarity standard of Government Code section 11349.1. The text of the proposed amendment has been modified to address the OAL's concerns. A 15-day public comment period is required before the file can be resubmitted to OAL.

RECOMMENDATION

This item is presented for Board discussion and action. Staff recommends the Board direct staff to initiate a 15-day renotece period.

CALIFORNIA HORSE RACING BOARD
 TITLE 4. CALIFORNIA CODE OF REGULATIONS
 ARTICLE 6. ENTRIES AND DECLARATIONS
 1588. HORSE INELIGIBLE TO START IN A RACE.

Regular Board Meeting
 March 19, 2015

Single underlined text represents the original language noticed to the public from September 5, 2014 to October 20, 2014.

Deletions to the original noticed text appear as ~~double strikethrough~~ and new and revised text appears as double underlined.

1588. Horse Ineligible to Start in a Race.

In addition to any other valid ground or reason, a horse is ineligible to start in any race-if:

(a) if ~~S~~such horse is not registered by the Jockey Club if a thoroughbred, the United States Trotting Association if a standardbred, the American Quarter Horse Association if a quarter horse, the Appaloosa Horse Club if an appaloosa horse, the Arabian Horse Registry of America if an Arabian horse, or the American Paint Horse Association if a paint horse-;

(b) if ~~T~~the parentage verification to both the sire and the dam of all horses foaled in 1992 and thereafter has not been certified by the Jockey Club if a thoroughbred, the United States Trotting Association if a standardbred, the American Quarter Horse Association if a quarter horse, the Appaloosa Horse Club if an appaloosa horse, the Arabian Horse Registry of America if an Arabian horse, or the American Paint Horse Association if a paint horse-;

(c) if, ~~U~~unless the stewards permit otherwise, the certificate of foal registration, eligibility papers, or other registration issued by the official registry for such horse is not on file with the racing secretary at the time of entry;

(d) if ~~S~~such horse has been entered or raced at any recognized race meeting under any name or designation other than the name or designation duly assigned by and registered with the official registry;

(e) ~~if~~ the certificate of foal registration, eligibility papers or other registration issued by the official registry has been altered, erased, or forged;

(f) ~~if~~ the identification markings of the horse do not agree with the identification markings as set forth in the registration of such horse;

(g) ~~Unless~~ he is eligible to enter said race and is duly entered for such race;

(h) ~~When~~ such horse is owned in whole or in part by an unlicensed person or is in the care of an unlicensed trainer;

(i) ~~When~~ such horse is on the Steward's List, the Starter's List or the Veterinarian's List;

(j) when, except with prior approval of the stewards for good cause, such horse is on the Veterinarian's List in another racing jurisdiction, or. Good cause includes:

(1) unforeseen administrative issues in removing the horse from the Veterinarian's List of another racing jurisdiction;

(2) the location of the horse prevents it from being evaluated by the official veterinarian of another racing jurisdiction and cleared from that jurisdiction's Veterinarian's List, and the horse is approved to race by a California official veterinarian; or

(3) any other unforeseen event or reason that would prevent a horse that would otherwise not be on a Veterinarian's List from being cleared from the Veterinarian's List of another racing jurisdiction.

(k) ~~When~~ when, except with prior approval of the stewards, such horse has not been on the grounds of the association or its approved auxiliary stable area for at least 24 hours prior to the time the race is to be run.

Authority: Sections 19440 and 19562,
Business and Professions Code.

Reference: Sections 19440 and 19562,
Business and Professions Code.

STAFF ANALYSIS
DISCUSSION AND ACTION BY THE BOARD REGARDING
THE PROPOSED AMENDMENT TO
CHRB RULE 1843.2. CLASSIFICATION OF DRUG SUBSTANCES
TO ADD COBALT TO THE
CHRB PENALTY CATEGORIES LISTING BY CLASSIFICATION
THEREBY ESTABLISHING THE VIOLATION AND PENALTY
GUIDELINES FOR THE PRESENCE OF COBALT
IN AN OFFICIAL BLOOD SAMPLE

Regular Board Meeting
March 19, 2015

ISSUE

Cobalt is a naturally occurring trace element that may be present in horses at very low levels, as well as a normal dietary substance due to the ingestion of feedstuffs that contain it in trace amounts. Cobalt is also present in vitamin B12. Cobalt can be administered to horses in various forms, including feed supplements or injections. Although cobalt is a naturally existing and necessary dietary mineral for the horse, there is evidence it is being administered in very high doses. High doses of cobalt containing products are used to increase erythropoiesis, the process which produces red blood cells. This may allow a horse to oxygenate better than it would in its normal state; a form of "blood doping". Due to concerns regarding the illicit use of cobalt in horse racing, the Board has determined a threshold must be set to differentiate samples collected from a horse that was normally fed and supplemented from a horse administered an extremely high dose of cobalt to enhance performance. This may be accomplished by amending Board Rule 1843.2, Classification of Drug Substances, to add cobalt to the California Horse Racing Board (CHRB) Penalty Categories Listing by Classification (Revised 02/13).

ANALYSIS

The proposed amendment to Rule 1843.2 will add cobalt to the California Horse Racing Board (CHRB) Penalty Categories Listing by Classification (Revised 02/13), which is incorporated by reference in Rule 1843.2. Cobalt will be listed as:

- 1). A Class 4 drug violation with a Category C penalty for cobalt in blood above 25ng/ml (over 25ng/ml but under 50ng/ml). This would result in a fine and/or short suspension without revocation of purse; and
- 2). A Class 3 drug violation with a Category B penalty for cobalt in blood above 50ng/ml. This would result in purse redistribution, a fine of between \$500 to \$10,000 and a minimum 30 day suspension.

BACKGROUND

Business and Professions Code section 19580 provides that the Board shall adopt regulations to establish policies, guidelines and penalties relating to equine medication to preserve and enhance the integrity of horse racing in this state. Section 19581 of the Business and Professions Code states that no substance of any kind shall be administered by any means to a horse after it has been entered to race in a horse race, unless the Board has, by regulation, specifically authorized the use of the substance and the quantity and composition thereof. Business and Professions Code section 19582 provides that violations of Business and Professions Code section 19581, as determined by the Board, are punishable in regulations adopted by the Board, and that the Board may classify violations based upon each class of prohibited drug substances, prior violations within the previous three years and prior violations within the violator's lifetime. Board Rule 1843, Medication, Drugs and Other Substances, provides that no horse participating in a race shall carry in its body any drug substance or its metabolites or analogues, foreign to the horse except as hereinafter expressly provided. No drug substance shall be administered to a horse which is entered to compete in a race to be run in this state except for approved and authorized drug substances as provided in these rules.

RECOMMENDATION

This item is presented for Board discussion and action. Staff recommends the Board direct staff to initiate a 45-day public comment period regarding the proposed amendment of Rule 1843.2.

CALIFORNIA HORSE RACING BOARD
TITLE 4. CALIFORNIA CODE OF REGULATIONS
ARTICLE 15. VETERINARY PRACTICES
PROPOSED AMENDMENT OF
RULE 1843.2. CLASSIFICATION OF DRUG SUBSTANCES.

Regular Board Meeting
March 19, 2015

1843.2. Classification of Drug Substances.

The Board, the board of stewards, the hearing officer, or the administrative law judge, when adjudicating a hearing for a violation of Business and Professions Code section 19581, shall consider the classification of the substance as referenced in the California Horse Racing Board (CHRB) Penalty Categories Listing by Classification (Revised ~~02/13~~03/15), hereby incorporated by reference, which is based on the Association of Racing Commissioners International (ARCI) Uniform Classification Guidelines for Foreign Substances (~~12/11~~12/14), as modified by the Board.

Authority: Sections 19580, 19581 and 19582,
Business and Professions Code.

Reference: Sections 19580, 19581 and 19582,
Business and Professions Code.

California Horse Racing Board (CHRB) Penalty Categories Listing by Classification

Class 1: Stimulant and depressant drugs that have the highest potential to affect performance and that have no generally accepted medical use in the racing horse. Many of these agents are Drug Enforcement Agency (DEA) schedule II substances. These include the following drugs and their metabolites: Opiates, opium derivatives, synthetic opioids and psychoactive drugs, amphetamines and amphetamine-like drugs as well as related drugs, including but not limited to apomorphine, nikethamide, mazindol, pemoline, and pentylenetetrazol.

Drug	Trade Name	Drug Class	Penalty Class
3, 4-methylenedioxypyrovalerone	MCVP, "BATH Salts"	1	A
Alfentanil	Alfenta	1	A
Amphetamine		1	A
Anileridine	Leritine	1	A
Apomorphine		1	A
Benzylpiperazine (BZP)		1	A
Carfentanil		1	A
Cathinone	Khat	1	A
α -Cobratoxin	Cobra Venom	1	A
Cocaine		1	B
Codeine		1	A
Darbepoetin	Aranesp	1	A
Darb-erythropoetin		1	A
Dermorphin	Frog Venom	1	A
Drug Enforcement Administration (DEA) Class 1 (all)		1	A
Dextromoramide	Palfium, Narcolo	1	A
Diamorphine		1	A
Donepezil	Aricept	1	A
Endorphins		1	A
Enkephalins		1	A
Erythropoietin (EPO)	Procrit, Epogen	1	A
Ethylmorphine	Dionin	1	A
Etorphine HCl	M99	1	A
Fentanyl	Sublimaze	1	A
Heroin		1	A
Hydrocodone (dihydrocodeinone)		1	A
Hydromorphone	Dilaudid	1	A

Listing by Classification

Class 1: Stimulant and depressant drugs that have the highest potential to affect performance and that have no generally accepted medical use in the racing horse. Many of these agents are Drug Enforcement Agency (DEA) schedule II substances. These include the following drugs and their metabolites: Opiates, opium derivatives, synthetic opioids and psychoactive drugs, amphetamines and amphetamine-like drugs as well as related drugs, including but not limited to apomorphine, nikethamide, mazindol, pemoline, and pentylenetetrazol.

Drug	Trade Name	Drug Class	Penalty Class
Hydroxyamphetamine	Paradrine	1	A
ITPP (myo-inositol trispyrophosphate)		1	A
Levorphanol	Levo-Dremoran	1	A
Lofentanil		1	A
Mazindol	Sanorex	1	A
Meperidine	Demerol	1	A
Mephentermine		1	A
Metaraminol	Aramine	1	A
Methadone	Dolophine	1	A
Methamphetamine	Desoxyn	1	A
Methaqualone	Quaalude	1	A
Methcathinone		1	A
Methylhexanamine	Geranamine	1	A
Methylphenidate	Ritalin	1	A
Metopon (methyldihydromorphinone)		1	A
Morphine		1	B
Nikethamide	Coramine	1	A
Oxycodone	Percodan	1	A
Oxymorphone	Numorphan	1	A
Pemoline	Cylert	1	A
Pentylenetetrazol	Metrazol, Nioric	1	A
Phenazocine	Narphen	1	A
Phencyclidine (PCP)	Sernylan	1	A
Phendimetrazine	Bontril, etc.	1	A
Phenmetrazine	Preludin	1	A
Picrotoxin		1	A
Piritramide		1	A
Recombinant Growth Hormones		1	A

Listing by Classification

Class 1: Stimulant and depressant drugs that have the highest potential to affect performance and that have no generally accepted medical use in the racing horse. Many of these agents are Drug Enforcement Agency (DEA) schedule II substances. These include the following drugs and their metabolites: Opiates, opium derivatives, synthetic opioids and psychoactive drugs, amphetamines and amphetamine-like drugs as well as related drugs, including but not limited to apomorphine, nikethamide, mazindol, pemoline, and pentylentetrazol.

Drug	Trade Name	Drug Class	Penalty Class
Remifentanil	Ultiva	1	A
Recombinant Erythropoiesis Stimulating Agents		1	A
Snake Venoms		1	A
Strychnine		1	B
Somatrem	Protropin	1	A
Somatropin	Nutropin	1	A
Sufentanil	Sufenta	1	A
Synthetic cannabis	Spice, K2, Kronic	1	A
Venoms Not Otherwise		1	A
Ziconotide	Cone Snail Venom	1	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	Drug Class	Penalty Class
Acecarbromal		2	A
Acetophenazine	Tindal	2	A
Adinazolam		2	A
Alclofenac		2	B
Alcuronium	Alloferin	2	A
Alphaprodine	Nisentil	2	A
Alpidem	Anaxyl	2	A
Alprazolam	Xanax	2	A
Althesin	Saffan	2	A
Amisulpride	Solian	2	A
Amitriptyline	Elavil, Amitril, Endep	2	A
Amobarbital	Amytal	2	A
Amoxapine	Asendin	2	A
Amperozide		2	A
Anilopam	Anisine	2	A
Aprobarbital	Alurate	2	A
Articaine	Septocaine, Ultracaine, etc.	2	A
Atomoxetine	Strattera	2	A
Atracurium	Tracrium	2	A
Azacyclonol	Frenque	2	A
Azaperone	Stresnil, Suicalm, Fentaz (with Fentanyl)	2	A
Barbital	Veronal	2	A
Barbiturates	Benzo, BZD	2	A
Bemegride	Megimide, Mikedimide	2	A
Benoxaprofen		2	B
Benperidol		2	A
Bentazepam	Tiadipona	2	A
Benzactizine	Deprol, Bronchodiletten	2	A
Benzocetamine		2	A
Benzonatate		2	A
Benzphetamine	Didrex	2	A
Benztropine	Cogentin	2	A
Biriperone		2	A
Brimonidine	Alphagan	2	A
Bromazepam	Lexotan, Lectopam	2	A
Bromisovalum	Diffucord, etc.	2	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	Drug Class	Penalty Class
Bromocriptine	Parlodel	2	A
Bromperidol	Bromidol	2	A
Brotizolam	Brotocol	2	A
Bupivacaine	Marcaine	2	A
Buprenorphine	Temgesic	2	A
Buspirone	Buspar	2	A
Buspropion	Wellbutrin	2	A
Butabarbital (Secbutobarbitone)	Butacaps, Butasol, etc.	2	A
Butalbital (Talbutal)	Fiorinal	2	A
Butanilcaine	Hostacain	2	A
Butaperazine	Repoise	2	A
Butoctamide	Listomin	2	A
Caffeine		2	B
Camazepam	Paxor	2	A
Captodiamine	Covatine	2	A
Carbidopa + levodopa	Sinemet	2	A
Carbromol	Mifudorm	2	A
Carisoprodol	Soma, Rela	2	B
Carphenazine	Proketazine	2	A
Carpipramine	Prazinil	2	A
Carticaine	Ultracain	2	A
Chloralose (Alpha-Chloralose)		2	A
Chloral betaine	Beta-Chlor	2	A
Chloral hydrate	Nactec, Oridrate, etc.	2	A
Chloraldehyde (chloral)		2	A
Chlordiazepoxide	Librium	2	A
Chlormezanone	Trancopal	2	A
Chloroform		2	A
Chlorhexidol		2	A
Chloroprocaine	Nesacaine	2	A
Chlorproethazine	Newiplege	2	A
Chlorpromazine	Thorazine, Largactil	2	A
Chlorprothixene	Taractan	2	A
Citalopram	Celex	2	A
Clobazam	Urbanyl	2	A
Clocapramine		2	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	DrugClass	Penalty Class
Clomethiazole		2	A
Clomipramine	Anafranil	2	A
Clonazepam	Klonopin	2	A
Clorazepate	Tranxene	2	A
Clothiapine	Entermin	2	A
Clotiazepam	Trecalmo, Rize	2	A
Cloxazolam	Enadel, Sepazon, Tolestan	2	A
Clozapine	Clozaril, Leponex	2	A
Codeine		2	B
Conorphone		2	A
Corticaine	Ultracain	2	A
Crotetamide		2	A
Cyamemazine	Tercian	2	A
Cyclobarbital	Phanodorm	2	A
Decamethonium	Syncurine	2	A
Demoxepam		2	A
Desipramine	Norpromine, Pertofrane	2	A
Dezocine	Dalgan®	2	A
Diazepam	Valium	2	B
Dichloralphenazone	Febenol, Isocom	2	A
Diethylpropion	Tepanil, etc.	2	A
Diethylthiambutene	Themalon	2	A
Dihydrocodeine	Parcodin	2	A
Dilorazepam	Briantum	2	A
Diprenorphine	M50/50	2	A
Dixyrazine	Esucos	2	A
Dopamine	Intropin	2	A
Doxacurium	Nuromax	2	A
Doxapram	Dopram	2	A
Doxefazepam	Doxans	2	A
Doxepin	Adapin, Sinequan	2	A
Droperidol	Inapsine, Droleptan, Innovar-Vet (with Fentanyl)	2	A
Duloxetine	Cymbalta, Ariclam	2	A
Enciprazine		2	A
Ephedrine		2	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	DrugClass	Penalty Class
Epibatidine		2	A
Epinephrine		2	A
Ergoloid Mesylates (dihydroergocornine mesylate, dihydroergocristine mesylate and dihydroergocryptine mesylate)	Hydergine	2	A
Estazolam	Domnamid, Eurodin, Nuctalon	2	A
Ethamivan		2	A
Ethanol		2	A
Ethchlorvynol	Placidyl	2	A
Ethinamate	Valmid	2	A
Ethopropazine	Parsidol	2	A
Ethylisobutrazine	Diquel	2	A
Etidocaine	Duranest	2	A
Etifoxin	Stresam	2	A
Etizolam	Depas, Pasaden	2	A
Etodroxizine	Indunox	2	A
Etomidate		2	A
Fenarbamate	Tymium	2	A
Fenclozic acid	Myalex	2	B
Fenfluramine	Pondimin	2	A
Fluanisone	Sedalande	2	A
Fludiazepam	Erispam	2	A
Flunitrazepam	Rohypnol, Narcozep, Darkene, Hypnodorm	2	A
Fluopromazine	Psyquil, Siquil		
Fluoresone	Caducid	2	A
Fluoxetine	Prozac	2	A
Flupenthixol	Depixol, Fluaxol	2	A
Fluphenazine	Prolixin, Permitil, Anatsol	2	A
Flurazepam	Dalmane	2	B
Fluspirilene	Imap, Redeptin	2	A
Flutoprazepam	Restas	2	A
Fluvoxamine	Dumirox, Faverin, etc.	2	A
Galantamine	Reminyl	2	A
Gallamine	Flaxedil	2	A
Gepirone		2	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	DrugClass	Penalty Class
Glutethimide	Doriden	2	A
Halazepam	Paxipam	2	A
Haloperidol	Haldol	2	A
Haloxazolam	Somelin	2	A
Hemoglobin glutamers	Oxyglobin, Hemopure	2	A
Hexafluorenum	Myalexen	2	A
Hexobarbital	Evipal	2	A
Homophenazine	Pelvichthol	2	A
Hydrocodone (dihydrocodeinone)	Hycodan	2	A
Hydroxyzine	Atarax	2	B
Ibomal	Noctal	2	A
Imipramine	Imavate, Presamine, Tofranil	2	A
Isapirone		2	A
Isocarboxazid	Marplan	2	A
Isomethadone		2	A
Isoproterenol	Isoprel	2	A
Isoxicam	Maxicam	2	B
Ketamine	Ketalar, Ketaset, Vetalar	2	B
Ketazolam	Anxon, Laftram, Solatran, Loftran	2	A
Lenperone	Elanone-V	2	A
Levamisole	Ergamisol	2	B
Levomethorphan		2	A
Lidocaine	Xylocaine	2	B
Lithium	Lithizine, Duralith, etc.	2	A
Lobeline		2	A
Loflazepate, Ethyl	Victan	2	A
Loperamide	Imodium	2	B
Loprazolam	Dormonort, Havlane	2	A
Lorazepam	Ativan	2	A
Lormetazepam	Noctamid	2	A
Loxapine	Laxitane	2	A
Maprotiline	Ludiomil	2	A
Mebutamate	Axiten, Dormate, Capla	2	A
Meclofenoxate	Lucidril, etc.	2	A
Medazepam	Nobrium, etc.	2	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	DrugClass	Penalty Class
Melperone	Eunerpan	2	A
Memantine	Akatinol, Namenda, Ebixa	2	A
Meparfynol	Oblivon	2	A
Mepazine	Pacatal	2	A
Mephenoxalone	Control, etc.	2	A
Mephentyoin	Mesantoin	2	A
Mephobarbital (Methylphenobarbital)	Mebaral	2	A
Mepivacaine	Carbocaine	2	B
Meprobamate	Equanil, Miltown	2	B
Mesoridazine	Serentil	2	A
Metaclazepam	Talis	2	A
Metazocine		2	A
Metharbital	Gemonil	2	A
Methohexital	Brevital	2	A
Methotrimeprazine	Levoprome, Neurocil, etc.	2	A
Methyprylon	Noludar	2	A
Metocurine	Metubine	2	A
Metomidate	Hypnodil	2	A
Mexazolam	Melex	2	A
Midazolam	Versed	2	A
Mirtazepine	Remeron	2	A
Modafinil	Provigil	2	A
Molindone	Moban	2	A
Moperone	Luvatren	2	A
Mosaprimine		2	A
Nalbuphine	Nubain	2	A
Nalorphine	Nalline, Lethidrone	2	A
Nefazodone	Serzone	2	A
Nimetazepam	Erimin	2	A
Nitrazepam	Mogadon	2	A
Nordiazepam	Calmday, Nordaz, etc.	2	A
Norepinephrine		2	A
Nortriptyline	Aventyl, Pamelor	2	A
Olanzapine	Zyprexa	2	A
Oxazepam	Serax	2	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	DrugClass	Penalty Class
Oxazolam	Serenal	2	A
Oxilofrine (hydroxyephedrine)		2	A
Oxyperitine	Forit, Integrin	2	A
Paliperidone	Invega	2	A
Pancuronium	Pavulon	2	A
Paraldehyde	Paral	2	A
Paroxetine	Paxil, Seroxat	2	A
Penfluridol	Cyperon	2	A
Pentobarbital	Nembutal	2	A
Perazine	Taxilan	2	A
Perfluorodecalin		2	A
Perfluoro decahydronaphthalen		2	A
Perfluorooctylbromide		2	A
Perfluorotripropylamine		2	A
Perfluorocarbons		2	A
Periciazine	Alodept, etc.	2	A
Perlazine	Hypnodin	2	A
Perphenazine	Trilafon	2	A
Phenaglycodol	Acalo, Alcamid, etc.	2	A
Phenelzine	Nardelzine, Nardil	2	A
Phenobarbital	Luminal	2	A
Phentermine	Iomamin	2	A
Piminodine	Alvodine, Cimadon	2	A
Pimozide	Orap	2	A
Pinazepam	Domar	2	A
Pipamperone	Dipiperon	2	A
Pipecuronium	Arduan	2	A
Pipequaline		2	A
Piperacetazine	Psymod, Quide	2	A
Piperocaine	Metycaine	2	A
Pipotiazine	Lonseren, Piportil	2	A
Pipradrol	Dataril, Gerondyl, etc.	2	A
Piquindone		2	A
Prazepam	Verstran, Centrax	2	A
Prilocaine	Citanest	2	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	DrugClass	Penalty Class
Prochlorperazine	Darbazine, Compazine	2	A
Propanidid		2	A
Propiomazine	Largon	2	A
Propionylpromazine	Tranvet	2	B
Propiram		2	A
Propofol	Diprivan, Disoprivan	2	A
Propoxycaine	Ravocaine	2	A
Prothipendyl	Dominal	2	A
Protriptyline	Concordin, Triptil	2	A
Proxibarbitol	Axeen, Centralgol	2	A
Pyridithione	Hybersulfan, Sonodor	2	A
Quazipam	Doral	2	A
Quetiapine	Seroquel	2	A
Racemethorphan		2	A
Racemorphan		2	A
Raclopride		2	A
Ractopamine	Raylean	2	A
Remoxipride	Roxiam	2	A
Reserpine	Serpasil	2	B
Rilmazafone		2	A
Risperidone		2	A
Ritanserin		2	A
Rivastigmine	Exelon	2	A
Rocuronium	Zemuron	2	A
Rofecoxib	Vioxx	2	B
Romifidine	Sedivet	2	B
Ropivacaine	Naropin	2	A
Secobarbital (Quinalbarbitone)	Seconal	2	A
Selegiline	Eldepryl, Jumex	2	A
Sertraline	Lustral, Zoloft	2	A
Spiclomazine		2	A
Spiperone		2	A
Succinylcholine	Sucostrin, Quelin, etc.	2	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	DrugClass	Penalty Class
Sulfondiethylmethane		2	A
Sulfonmethane		2	A
Sulforidazine	Inofal	2	A
Sulpiride	Aiglonyl, Sulpitol	2	A
Sultopride	Barnetil	2	A
Talbutal	Lotusate	2	A
Tandospirone		2	A
Temazepam	Restoril	2	A
Tetrabenazine	Nitoman	2	A
Tetracaine	Pontocaine	2	B
Tetrazeepam	Musaril, Myolastin	2	A
Thebaine		2	A
Thialbarbital	Kemithal	2	A
Thiamylal	Surital	2	A
Thiethylperazine	Torecan	2	A
Thiopental	Pentothal	2	A
Thiopropazate	Dartal	2	A
Thiopropazine	Majeptil	2	A
Thioridazine	Mellaril	2	A
Thiothixene	Navane	2	A
Tiapride	Italprid, Luxoben, etc.	2	A
Tiletamine	Component of Telazol	2	A
Timiperone	Tolopelon	2	A
Tofisopam	Grandaxain, Seriel	2	A
Topirimate	Topamax	2	A
Tramadol	Ultram	2	A
Tranylcypromine	Parnate	2	A
Trazodone	Desyrel	2	A
Tretoquinol	Inolin	2	A
Triazolam	Halcion	2	A
Tribromethanol		2	A
Tricaine methanesulfonate	Finquel	2	A
Trichloroethanol		2	A
Trichloroethylene	Trilene, Trimar	2	A
Triclofos	Triclos	2	A

Listing by Classification

Class 2: Drugs that have a high potential to affect performance, but less of a potential than Class 1. These drugs are 1) not generally accepted as therapeutic agents in racing horses, or 2) they are therapeutic agents that have a high potential for abuse.

Drug	Trade Name	DrugClass	Penalty Class
Trifluomeprazine	Nortran	2	A
Trifluoperazine	Stelazine	2	A
Trifluoperidol	Triperidol	2	A
Triflupromazine	Vetame, Vesprin	2	A
Trimipramine	Surmontil	2	A
Tubocurarine (Curare)	Metubin	2	A
Tybamate	Benvil, Nospan, etc.	2	A
Urethane		2	A
Valdecoxib		2	B
Valnoctamide	Nirvanyl	2	A
Venlafaxine	Efflexor	2	A
Veralipride	Accional, Veralipril	2	A
Vercuronium	Norcuron	2	A
Viloxazine	Catatrol, Vivalan, etc.	2	A
Vinbarbital	Delvinol	2	A
Vinylbital	Optanox, Speda	2	A
Yohimbine		2	A
Zaleplon	Sonata	2	A
Zilpaterol	Zilmax	2	A
Zolazepam		2	A
Zolpidem	Ambien, Stilnox	2	A
Zomepirac	Zomax	2	B
Zopiclone	Imovan	2	A
Zotepine	Lodopin	2	A
Zuclopenthixol	Ciatyl, Cesordinol	2	A

Listing by Classification

Class 3: Drugs that may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class 2.

Drug	Trade Name	DrugClass	Penalty Class
19-Norandrostenediol		3	B
19-Norandrostenedione		3	B
4-Hydroxytestosterone		3	B
Acebutolol	Sectral	3	B
Acepromazine	Atrovet, Notensil, PromAce®	3	B
Albuterol (Salbutamol)	Proventil, Ventolin	3	B
Almotriptan	Axert	3	A
Alprenolol		3	A
Ambenonium	Mytelase, Myeuran	3	B
Aminophylline	Aminophyllin, etc.	3	B
Amitraz	Mitaban	3	A
Amlodipine	Norvasc	3	A
Amyl nitrite		3	A
Arecoline		3	A
Arformeterol	Brovana	3	A
Atenolol	Tenormin	3	B
Atropine		3	B
Benazepril	Lotensin	3	A
Betaxolol	Kerlone	3	B
Bethanidine	Esbatal	3	A
Biperiden	Akineton	3	A
Bisoprolol	Zebeta, Bisobloc, etc.	3	B
Bitolterol	Effectin	3	B
Bolasterone		3	B
Boldenone	Equipoise	3	B
Boldione		3	B
Bretylium	Bretylol	3	B
Brimonidine	Alphagan	3	B
Bromfenac	Duract	3	A
Bromodiphenhydramine		3	B
Bufexamac		3	B
Bumetanide	Bumex	3	B
Butorphanol	Stadol, Torbugesic	3	B
N-Butylscopolamine	Bucospan	3	B
Candesartan	Atacand	3	B
Captopril	Capolen	3	B
Carazolol	Carbacel, Conductor	3	A

Listing by Classification

Class 3: Drugs that may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class 2.

Drug	Trade Name	DrugClass	Penalty Class
Carbachol	Lentin, Doryl	3	B
Carbamezapine	Tegretol	3	B
Carbinoxamine	Clistin	3	B
Carteolol	Cartrol	3	B
Carvedilol	Coreg	3	B
Celecoxib	Celebrex	3	B
Cimeterol		3	A
Clausterone	Methosorb	3	B
Clemastine	Tavist	3	B
Clenbuterol	Ventipulmin	3	B
Clidinium	Quarezan, Clindex	3	B
Clonidine	Catapres	3	B
Clostebol		3	B
Cobalt (>50ng/ml in blood)		3	B
Cyclandelate	Cyclospasmol	3	A
Cycrimine	Pagitane	3	B
Danazol	Danocrine	3	B
Dehydrochloromethyl- testosterone Dehydrochloromethyltestosterone		3	B
Deracoxib ²	Deremaxx	3	GB
Desoxymethyl-testosterone		3	B
Detomidine	Dormosedan	3	B
Dextropropoxyphene	Darvon	3	B
Diazoxide	Proglycem	3	B
Diflunisal		3	C
Dimefline		3	A
Diphenhydramine	Benadryl	3	B
Dipyridamole	Persantine	3	B
Divalproex	Depakote	3	A
Dobutamine	Dobutrex	3	B
Doxazosin	Cardura	3	A
Doxylamine	Decapryn	3	B
Dromostanolone	Drolban	3	B
Dyphylline		3	B
Edrophonium	Tensilon	3	B
Eletriptan	Relpax	3	A
Enalapril (metabolite enalaprilat)	Vasotec	3	B

Listing by Classification

Class 3: Drugs that may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class 2.

Drug	Trade Name	DrugClass	Penalty Class
Erthryl tetranitrate	Cardilate	3	A
Esmolol	Brevibloc	3	B
Etamiphylline	Millophylline V	3	B
Ethacrynic acid	Edecrin	3	B
Ethosuximide	Zarontin	3	A
Ethylestrenol	Maxibolin, Organon	3	B
Ethylnorepinephrine	Bronkephrine	3	A
Etodolac	Lodine	3	C
Felbamate	Felbatol	3	A
Fenbufen	Gincopal	3	B
Fenoldopam	Corlopam	3	B
Fenoprofen	Nalfon	3	B
Fenoterol	Berotec	3	B
Fenspiride	Respiride, Respan, etc	3	B
Fentiazac		3	B
Flufenamic acid		3	B
Fluoxymesterone	Halotestin	3	B
Flupirtine	Katadolone	3	A
Flurbiprofen	Froben	3	B
Formebolone		3	B
Formoterol	Altram	3	B
Fosinopril	Monopril	3	A
Fosphenytoin	Cerebyx	3	B
Furazabol		3	B
Gabapentin	Neurontin	3	B
Gestrinone		3	B
Glycopyrrolate	Robinul	3	B
Guanadrel	Hylorel	3	A
Guanethidine	Ismelin	3	A
Guanabenz	Wytensin	3	B
Heptaminol	Corofundol	3	B
Homatropine	Homapin	3	B
Hydralazine	Apresoline	3	B
Indomethacin	Indocin	3	B
Ipratropium		3	B

Listing by Classification

Class 3: Drugs that may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class 2.

Drug	Trade Name	DrugClass	Penalty Class
Irbesarten	Avapro	3	A
Ibutilide	Corvert	3	B
Iloprost	Ventavis	3	A
Isoetharine	Bronkosol	3	B
Isosorbide dinitrate	Isordil	3	B
Kebuzone		3	B
Ketorolac	Toradol	3	B
Labetalol	Normodyne	3	B
Lamotrigine	Lamictal	3	A
Levobunolol	Betagan	3	B
Lisinopril	Prinivil, Zestril	3	A
Losartan	Hyzaar	3	B
Mabuterol		3	A
Mecamylamine	Inversine	3	B
Medetomidine	Domitor	3	B
Mefenamic acid	Ponstel	3	B
Mestanolone		3	B
Mesterolone		3	B
Metaproterenol	Alupent, Metaprel	3	B
Metenolone		3	B
Methacholine		3	A
Methandienone		3	B
Methandriol	Probolc	3	B
Methandrostenolone	Dianabol	3	A
Methantheline	Banthine	3	B
Methasterone		3	B
Methixene	Trest	3	A
Methoxamine	Vasoxyl	3	A
Methoxyphenamine	Orthoxide	3	A
Methsuximide	Celontin	3	A
Methyl-1-testosterone		3	B
Methylatropine		3	B
Methyldienolone		3	B
Methyldopa	Aldomet	3	A
Methylnortestosterone		3	B
Methyltestosterone	Metandren	3	B
Metolazone		3	B

(Revised 02/13 03/15)

Listing by Classification

Class 3: Drugs that may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class 2.

Drug	Trade Name	DrugClass	Penalty Class
Metoprolol	Lopressor	3	B
Mibefradil	Posicor	3	B
Mibolerone		3	B
Midodrine	Pro-Amiline	3	B
Minoxidil	Loniten	3	B
Moexipril (metabolite moexiprilat)	Uniretic	3	B
Muscarine		3	A
Nabumetone	Anthraxan, Relafen, Relifex	3	B
Nadol	Corgard	3	B
Naloxone	Narcan	3	A
Naltrexone	Revia	3	A
Naratriptan	Amerge	3	B
Nandrolone	Nandrolin, Laurabolin, Durabolin	3	B
Nebivolol		3	A
Nefopam		3	A
Neostigmine	Prostigmine	3	B
Niflumic acid	Nifluril	3	B
Nimesulide		3	B
Nitroglycerin		3	B
Norbolethone		3	B
Norclostebol		3	B
Norethandrolone		3	B
Nylidrin	Arlidin	3	A
Olmesartan	Benicar	3	A
Oxabolone		3	B
Oxandrolone	Anavar	3	B
Oxprenolol	Trasicor	3	B
Oxymesterone		3	B
Oxymetholone	Adroyd, Andarol	3	B
Papaverine	Pavagen, etc.	3	A
Paramethadione	Paradione	3	A
Pargyline	Eutonyl	3	A
Penbutolol	Levator	3	B
Pentaerythritol tetranitrate	Duotrate	3	A
Pentazocine	Talwin	3	B
Pergolide		3	B

Perindopril

Biprel

3

A

Listing by Classification

Class 3: Drugs that may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class 2.

Drug	Trade Name	DrugClass	Penalty Class
Phenoxybenzamine	Dibenzyline	3	B
Phentolamine	Regitine	3	B
Phenylephrine	Isophrin, Neo-Synephrine	3	B
Phenylpropanolamine	Propadrine	3	B
Physostigmine	Eserine	3	A
Pindolol	Viskin	3	B
Pirbuterol	Maxair	3	B
Piretanide	Arelix, Tauliz	3	B
Piroxicam	Feldene	3	B
Prazosin	Minipress	3	B
Primidone	Mysoline	3	B
Procaine		3	B
Procatamol	Pro Air	3	A
Procyclidine	Kemadrin	3	B
Promazine	Sparine	3	B
Promethazine	Phenergan	3	B
Propantheline	Pro-Banthine	3	A
Propentophylline	Karsivan	3	B
Propranolol	Inderal	3	B
Prostanazol		3	B
Protokylol	Ventaire	3	A
Pseudoephedrine	Cenafed, Novafed	3	B
Pyridostigmine	Mestinon, Regonol	3	B
Pyrilamine	Neoantergan, Equihist	3	B
Quinapril	Accupril	3	A
Quinbolone		3	B
Ractopamine	Raylean	3	B
Ramipril	Altace	3	A
Ritodrine	Yutopar	3	B
Rizatriptan	Maxalt	3	B
Salmeterol		3	B
Scopolamine (Hyoscine)	Triptone	3	B
Sibutramine	Meridia	3	B
Sildenafil	Viagra	3	A
Sotalol	Betapace, Sotacor	3	B
Spirapril, Spiraprilat	Renormax	3	A

Listing by Classification

Class 3: Drugs that may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class 2.

Drug	Trade Name	DrugClass	Penalty Class
Stanazolol	Winstrol-V	3	B
Stenbolone		3	B
Sulindac	Clinoril	3	B
Sumatriptan	Imitrex	3	B
Tadalafil	Cialis	3	A
Telmisartin	Micardis	3	B
Tenoxicam	Alganex, etc.	3	B
Tepoxalin		3	C
Terazosin	Hytrin	3	A
Terbutaline	Brethine, Bricanyl	3	B
Testolactone	Teslac	3	B
Testosterone		3	B
Tetrahydrogestrinone		3	B
Theophylline	Aqualphyllin, etc.	3	B
Tiaprofenic acid	Surgam	3	B
Timolol	Blocardrin	3	B
Tolazoline	Priscoline	3	B
Tolmetin	Tolectin	3	B
Torsemide (Torasemide)	Demadex	3	B
Trandolapril (and metabolite, Trandolaprilat)	Tarka	3	B
Trenbolone	Finoplix	3	B
Trihexylphenidyl	Artane	3	A
Trimethadione	Tridione	3	B
Trimethaphan	Arfonad	3	A
Tripelennamine	PBZ	3	B
Valerenic acid		3	C
Valsartan	Diovan	3	B
Vardenafil	Levitra	3	A
Xylazine	Rompun, Bay Va 1470	3	B
Zolmitriptan	Zomig	3	B
Δ -1-androstene-3,17-diol		3	B
Δ -1-androstene-3,17-dione		3	B
Δ -1-dihydrotestosterone		3	B
Zilpaterol	Zilmax	3	A
Zonisamide	Zonegran	3	B

Listing by Classification

Class 4: This class includes therapeutic medications that would be expected to have less potential to affect performance than those in Class 3.

Drug	Trade Name	DrugClass	Penalty Class
Acetaminophen (Paracetamol)	Tylenol, Tempra, etc.	4	C
Acetanilid		4	B
Acetazolamide	Diamox, Vetamox	4	B
Acetophenetidin (Phenacetin)		4	B
Acetylsalicylic acid (Aspirin)		4	C
Aclomethasone Alclomethasone	Aclovate	4	C
Adrenochrome monosemicarbazone salicylate		4	B
Aldosterone	Aldocortin, Electro cortin	4	B
Ambroxol	Ambril, etc.	4	BC
Amcinonide	Cyclocort	4	C
Amiloride	Moduretic, Midamor	4	B
Aminocaproic acid	Amicar, Caprocid	4	C
Aminodarone		4	B
2-Aminoheptaine 2-Aminoheptane	Tuamine	4	B
Aminopyrine		4	B
Amiodarone		4	B
Amisometradine	Rolictron	4	B
Amlodipine	Norvasc, Ammivin	4	B
Amrinone		4	B
Anisotropine	Valpin	4	B
Antipyrine		4	B
Apazone (Azapropazone)	Rheumox	4	B
Aprindine		4	B
Baclofen	Lioresal	4	B
Beclomethasone	Propaderm	4	C
Benazepril	Lotrel	4	B
Bendroflumethiazide	Naturetin	4	B
Benoxinate	Dorsacaine	4	C
Benzocaine		4	C
Benzthiazide		4	B
Bepridil	Bepadin	4	B
Betamethasone	Betasone, etc.	4	C
Bethanechol	Urecholine, Duvoid	4	C
Bromhexine	Oletor, etc.	4	C
Brompheniramine	Dimetane, Disomer	4	B
Budesonide	Pulmacort, Rhinocort	4	C

Listing by Classification

Class 4: This class includes therapeutic medications that would be expected to have less potential to affect performance than those in Class 3.

Drug	Trade Name	Drug Class	Penalty Class
Butacaine	Butyn	4	B
Butamben (butyl aminobenzoate)	Butesin	4	C
Butoxycaine	Stadacain	4	B
Camphor		4	C
Carbazochrome		4	C
Carprofen	Rimadyl	4	B
Certirizine	Zyrtec	4	B
Chlormerodrin	Neohydrin	4	B
Chlorophenesin	Maolate	4	C
Chloroquine	Avloclor	4	C
Chlorothiazide	Diuril	4	B
Chlorpheniramine	Chlortriemton, etc.	4	B
Chlorthalidone	Hydroton	4	B
Chlorzoxazone	Paraflex	4	B
Ciclesonide	Alvesco, Omnaris, Omniair	4	B
Cinchocaine	Nupercaine	4	C
Clanobutin		4	C
Clibucaine	Batrax	4	C
Clidinium	Quarezan, Clindex, etc.	4	B
Clobetasol	Temovate	4	C
Clocortolone	Cloderm	4	C
Clofenamide		4	B
Clormecaine	Placacid	4	C
Cobalt (>25ng/ml in blood)		4	C
Colchicine		4	B
Cortisone	Cortone, etc.	4	C
Cyclizine	Merazine	4	B
Cyclobenzaprine	Flexeril	4	B
Cyclomethylcaine	Surfacaine	4	C
Cyclothiazide	Anhydron, Renazide	4	B
Cyproheptadine	Periactin	4	C
Dantrolene	Dantrium	4	C
Dembroxol (Dembrexine)	Sputolysin	4	C
Deoxycorticosterone	Percortin, DOCA, Descotone, Dorcostrin	4	C
Desonite	Des Owen	4	C
Desoximetasone	Topicort	4	C

Listing by Classification

Class 4: This class includes therapeutic medications that would be expected to have less potential to affect performance than those in Class 3.

Drug	Trade Name	Drug Class	Penalty Class
Dexamethasone	Azium, etc.	4	C
Dextromethorphan		4	C
Dibucaine	Nupercainal, Cinchocaine	4	C
Dichlorphenamide	Daramide	4	C
Diclofenac	Voltaren, Voltarol	4	C
Diflorasone	Florone, Maxiflor	4	C
Diflucortolone	Flu-Cortinest, etc.	4	C
Digitoxin	Crystodigin	4	B
Digoxin	Lanoxin	4	B
Dihydroergotamine		4	C
Diltiazem	Cardizem	4	B
Dimethisoquin	Quotane	4	B
Dimethylsulfoxide (DMSO) (>1 ug/ml in blood or >10ug/ml in urine)	Domoso	4	C
Diphenoxylate	Difenoxin, Lomotil	4	B
Dipyrrone	Novin, Methampyrone	4	C
Disopyramide	Norpace	4	B
Dromostanolone	Drolban	4	C
Dyclonine	Dyclone	4	C
Eltenac		4	C
Ergonovine	Ergotrate	4	C
Ergotamine	Gynergen, Cafergot, etc.	4	C
Etanercept	Enbrel	4	B
Ethoheptazine	Zactane	4	B
Ethosuximide	Zarontin	4	B
Ethotoin	Peganone	4	B
Ethoxzolamide	Cardrase, Ethamide	4	C
Ethylaminobenzoate (Benzocaine)	Semets, etc.	4	C
Felodipine	Plendil	4	B
Fexofenadine	Allegra	4	C
Firocoxib		4	C
Flecainide	Idalon	4	B
Floctafenine	Idalon, Idarac	4	B
Flucinolone	Synalar, etc.	4	C
Fludrocortisone	Alforone, etc.	4	C
Flumethasone	Flucort, etc.	4	C

Listing by Classification

Class 4: This class includes therapeutic medications that would be expected to have less potential to affect performance than those in Class 3.

Drug	Trade Name	Drug Class	Penalty Class
Flumethiazide	Ademol	4	B
Flunarizine	Sibelium	4	B
Flunisolide	Bronilide, etc.	4	C
Flunixin	Banamine	4	C
Fluocinolone	Synalar	4	C
Fluocinonide	Licon, Lidex	4	C
Fluoroprednisolone	Predef-2X	4	C
Fluprednisolone	Alphadrol	4	C
Flurandrenolide	Cordran	4	C
Flurometholone	FML, Flarex	4	B
Fluticasone	Flixonase, Flutide	4	C
Guaifenesin (glycerol guaiacolate)	Geolate	4	C
Halcinonide	Halog	4	C
Halobetasol	Ultravate	4	C
Hexocyclium	Tral	4	B
Hexylcaine	Cyclaine	4	C
Hydrochlorthiazide	Hydrodiuril	4	C
Hydrocortisone (Cortisol)	Cortef, etc.	4	C
Hydroflumethiazide	Saluron	4	B
Ibuprofen	Motrin, Advil, Nurpin, etc.	4	B or C
Infliximab	Remicade	4	B
Isoflupredone	Predef	4	C
Isometheptene	Octin, Octon	4	B
Isopropamide	Darbid	4	B
Isoxsuprine	Vasodilan	4	C
Isradipine	DynaCirc	4	B
Ketoprofen	Orudis	4	C
Letosteine	Viscotiol, Visiotal	4	C
Loratidine	Claritin	4	B
Meclizine	Antivert, Bonine	4	B
Meclofenamic acid	Arquel	4	C
Medrysone	Medriusar, etc.	4	C
Meloxicam	Mobic	4	C
Mepenzolate	Cantil	4	B
Mephènesin	Tolserol	4	B

Listing by Classification

Class 4: This class includes therapeutic medications that would be expected to have less potential to affect performance than those in Class 3.

Drug	Trade Name	Drug Class	Penalty Class
Meralluride	Mercurydrin	4	B
Merbaphen	Novasural	4	B
Mercaptomerin	Thiomerin	4	B
Mercumalilin	Cumertilin	4	B
Mersalyl	Salyrgan	4	B
Metaxalone	Skelaxin	4	B
Methandrostenolone	Dianabol	4	C
Methantheline	Banthine	4	B
Methapyrilene	Histadyl, etc.	4	B
Methazolamide	Naptazane	4	C
Methdilazine	Tacaryl	4	B
Methocarbamol	Robaxin	4	C
Methotrexate	Folex, Nexate, etc.	4	B
Methscopolamine	Pamine	4	B
Methsuximide	Celontin	4	B
Methylchlorthiazide	Enduron	4	B
Methandrostenolone	Dianabol	4	C
Methylergonovine	Methergine	4	C
Methylprednisolone	Medrol	4	C
Methysergide	Sansert	4	B
Metiamide		4	B
Metoclopramide	Reglan	4	C
Mexilitine	Mexilil	4	B
Milrinone		4	B
Mometasone	Elocon	4	C
Montelukast	Singulair	4	C
Naepaine	Amylsine	4	C
Naphazoline	Privine	4	B
Naproxen	Equiproxen, Naprosyn	4	C
Nicardipine	Cardine	4	B
Nifedipine	Procardia	4	B
Nimodipine	Nemotop	4	B
Norethandrone		4	C
Nortestosterone		4	C
Olsalazine	Dipentum	4	B

Listing by Classification

Class 4: This class includes therapeutic medications that would be expected to have less potential to affect performance than those in Class 3.

Drug	Trade Name	Drug Class	Penalty Class
Orphenadrine	Norflex	4	B
Oxaprozin	Daypro, Deflam	4	C
Oxymetazoline	Afrin	4	B
Oxyphenbutazone	Tandearil	4	C
Oxyphencyclimine	Daricon	4	B
Oxyphenonium	Antrenyl	4	B
Paramethasone	Haldrone	4	C
Pentoxifylline	Trental, Vazofirin	4	C
Phenacetamide	Phenurone	4	B
Phensuximide	Milontin	4	B
Phenylbutazone		4	C
Phenytoin	Dilantin	4	B
Polythiazide	Renese	4	B
Pramoxine	Tronothaine	4	C
Prednisolone	Delta-Cortef, etc.	4	C
Prednisone	Meticorten, etc.	4	C
Probenecid		4	C
Procainamide	Pronestyl	4	B
Propafenone	Rythmol	4	B
Propantheline	Pro-Banthine	4	B
Proparacaine	Ophthaine	4	C
Propylhexedrine	Benzedrex	4	B
Quinidine	Quinidex, Quinocardine	4	B
Salicylamide		4	C
Salicylate		4	C
Spironolactone	Aldactone	4	B
Sulfasalazine	Azulfidine, Azaline	4	C
Terfenadine	Seldane, Triludan	4	B
Tetrahydrozoline	Tyzine	4	B
Theobromine		4	C
Thiosalicylate		4	C
Thiphenamil	Trocinate	4	B
Tocainide	Tonocard	4	B
Tranexamic acid		4	C
Triamcinolone	Vetalog, etc.	4	C

Listing by Classification

Class 4: This class includes therapeutic medications that would be expected to have less potential to affect performance than those in Class 3.

Drug	Trade Name	Drug Class	Penalty Class
Triamterene	Dyrenium	4	B
Trichlormethiazide	Naqua, Naquasone	4	C
Tolmetin	Tolectin	4	B
Tridihexethyl	Pathilon	4	B
Trimeprazine	Temaril	4	B
Triprolidine	Actidil	4	B
Tuaminoheptane	Tuamine	4	C
Vedaprofen		4	C
Verapamil	Calan, Isoptin	4	B
Xylometazoline	Otrivin	4	B
Zafirlukast	Accolate	4	C
Zeranol	Ralgro	4	C
Zileuton	Zyflo	4	C

Listing by Classification

Class 5: This class includes *the following* therapeutic medications for which concentration limits have been established.

Drug	Trade Name	DrugClass	Penalty Class
Acenocoumarol		5	C
Anisindione		5	D
Cilostazol	Pletal	5	D
Cimetidine	Tagamet	5	D
Cromolyn	Intel	5	D
Dicumarol	Dicumarol	5	D
Dimethylsulfoxide (DMSO)	Domoso	5	D
Dimethylsulphone (MSM)		5	D
Diphenadione		5	D
Esomeprazole	Nexium	5	D
Famotidine	Gaster, etc.	5	D
Lansoprazole		5	D
Mesalamine	Asacol	5	D
Misoprostel	Cytotec	5	D
Nedocromil	Tilade	5	C
Nizatidine	Axid	5	D
Omeprazole	Prilosec, Losec	5	D
Pantoprazole	Protonix	5	D
Phenindione	Hedulin	5	D
Phenprocoumon	Liquamar	5	D
Pirenzapine	Gastrozepin	5	D
Polyethylene glycol		5	C
Rabeprazole	Aciphex	5	C
Ranitidine	Zantac	5	D
Warfarin	Coumadin, Coufarin	5	D

Cobalt Situation Analysis

Rick M. Arthur, DVM Equine Medical Director

The regulatory blood threshold needs to be 25ng/ml or lower to effectively eliminate cobalt salt administration. The chart below identifies the proportion of horses that would be trigger a violation at the listed levels.

	24 hours	36 hours	48 hours	72 hours	96 hours	120 hours	168 hours
25 ppb	16/16	16/16	16/16	16/16	16/16	16/16	11/16
35 ppb	16/16	16/16	16/16	16/16	13/16	9/16	3/16
50 ppb	16/16	15/16	11/16	7/16	4/16	2/16	1/16
70 ppb	12/16	6/16	3/16	1/16	1/16	0/16	0/16

*Based on a dosage of 100mg cobalt chloride intravenously from an administration study conducted by Dr. Knych at the Maddy Lab. The manuscript describing has been accepted by the journal *Drug Testing and Analysis* and will be available on-line shortly.

There does not appear to be a documented instance of cobalt deficiency in the horse. Therefore, cobalt supplementation is unnecessary and cobalt salt administration is medically unjustified. Cobalt does stimulate erythropoiesis in humans and rats and high cobalt dosages are associated with toxicity in humans and rats. Where the horse falls and at what levels relative to blood doping and health risk is unknown. Regardless, the use of cobalt is an issue that needs to be addressed and the administration or cobalt salts, parenterally or orally at unwarranted high dosages, needs to be eliminated.

The international blood threshold proposed by Hong Kong is **2.5ng/ml** using the risk analysis of 1/10,000 false positive rate (3.72SD, the current IFHA standard). Cobalt blood analysis from Dubai, France and a number of European countries appears to support the Hong Kong proposal. The California TB & QH data (n= 125) a false positive risk at 1/10,000 results in a threshold of **13.89 ng/ml** [ng/ml and ppb (parts per billion) can be considered synonymous]. The RMTC nationally collected data supports a blood threshold of 25ng/ml with a risk analysis of 1/33,000 and a **51ng/ml** risk analysis of 1/3,487,966. The press reports of a 1/10,000 risk at 70 ng/ml from the USTA/Maylin project are mathematically incompatible with the reported sample size and reported high of 6.8ng/ml in untreated horses.

There are many cobalt containing supplements and injections. Based on administration studies in Australia, Hong Kong, and Univ of Pennsylvania, cobalt levels can reach 10ng/ml at 24 hours. The long elimination half-life of cobalt could possibly lead to cobalt accumulation. This has not been studied in horses, but in random samples, there is no evidence accumulation is a problem at normal supplement and vitamin B-12 dosages. Indiscriminate cobalt administration could possibly lead to inadvertent elevation of cobalt by negligence rather than an overt doping attempt. The data indicate cobalt greater than 25ng/ml can only be obtained by deliberate cobalt administration. Regardless, negligence warrants a lesser penalty than intentional doping. Therefore I recommend the following approach:

- Cobalt in blood at or above 25ng/ml 25ng/ml but under 50ng/ml should be a Class 4 drug violation with a Category C penalty.
- Cobalt in blood at or above 50ng/ml should be a Class 3 drug violation with a Category B penalty.

Serum cobalt concentration analysis

CHRB Samples

8-19-14

Methods

Serum cobalt concentration (ppb) was evaluated in 204 samples collected from three breeds of racehorses: Quarter Horses, Standardbreds, and Thoroughbreds, with a limit of detection of 1ppb. Samples for which serum cobalt concentration were below the limit of detection were assigned the value of 1ppb for numeric analysis. The assumption of normality was evaluated by breed using Shapiro-Wilk testing. Non-normally distributed data was Box-Cox transformed, then re-evaluated for normality using Shapiro-Wilk testing. For normally-distributed data, data were summarized using mean and standard deviation. Threshold cutoff for normally-distributed data was estimated as the mean + 3.72 standard deviations (which encompasses 99.9900389% of the population). For non-normally-distributed data, data were summarized¹ using percentiles and boxplots. Threshold cutoff for non-normally-distributed data was estimated by identifying the best-fitting² distribution for the data using Kolmogorov-Smirnov goodness of fit testing and visual evaluation, then determining the 99.9900389 percentile for that distribution.

Results

Serum cobalt concentration was not normally distributed in any of the breeds ($p < 0.0001$), and could not be normally transformed using Box-Cox transformation.

In all breeds, at least 50% of horses sampled had serum cobalt values ≤ 1 ppb (Table 1). In Quarter Horses, 43 (100%) of 43 samples contained < 15 ppb cobalt, compared to 81 (98.8%) of 82 Thoroughbred samples and 70 (88.6) of 79 Standardbred samples (Figure 1).

The best-fitting distribution for serum cobalt in 125 Quarter Horses and Thoroughbred Horses was an exponential distribution with standard deviation 1.3992 and mean 2.3992 (Figure 2). The 99.9900389 percentile for this distribution is 13.893, meaning that nearly 99.99% of serum cobalt concentrations would be expected to be less than 13.893 ppb.

Table 1. Descriptive summary of breed-specific serum cobalt concentrations (ppb) in 204 racehorses.

Breed	N	Serum cobalt concentration (ppb)				
		Min	Median	95%	99%	Max
QH	43	1	1	11.1	12	12
STB	79	1	1	290	610	610
TB	82	1	1	9.6	27	27

¹ Stata 13.1, StataCorp LP, College Station, TX

² @Risk 5.5, Palisade Corporation

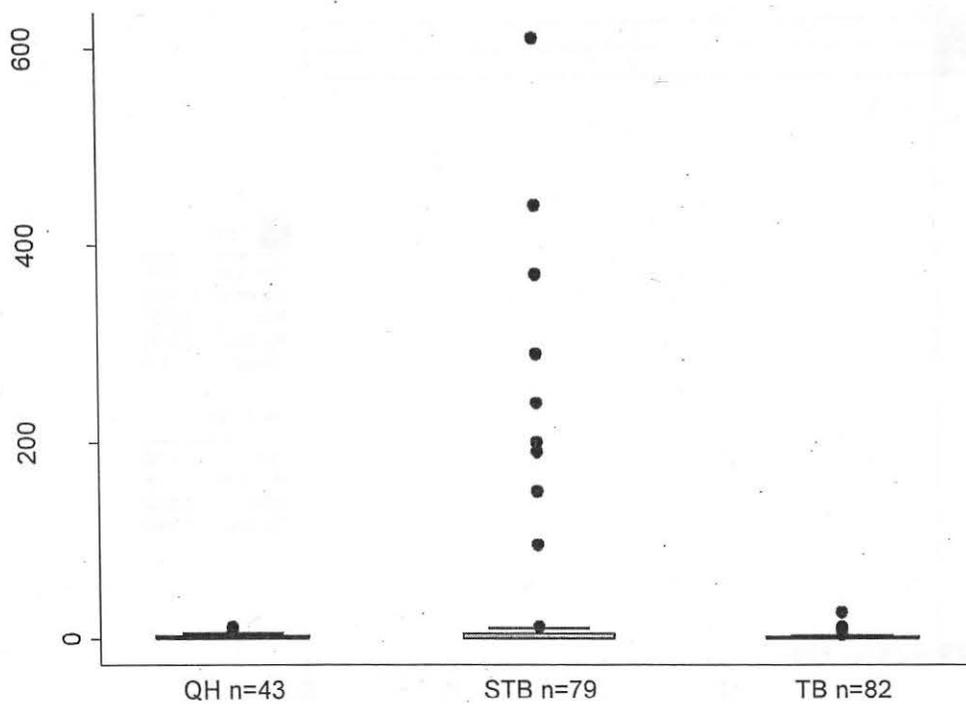


Figure 1. Breed-specific boxplots of serum cobalt concentration in 204 Quarter Horse, Standardbred, and Thoroughbred racehorses.

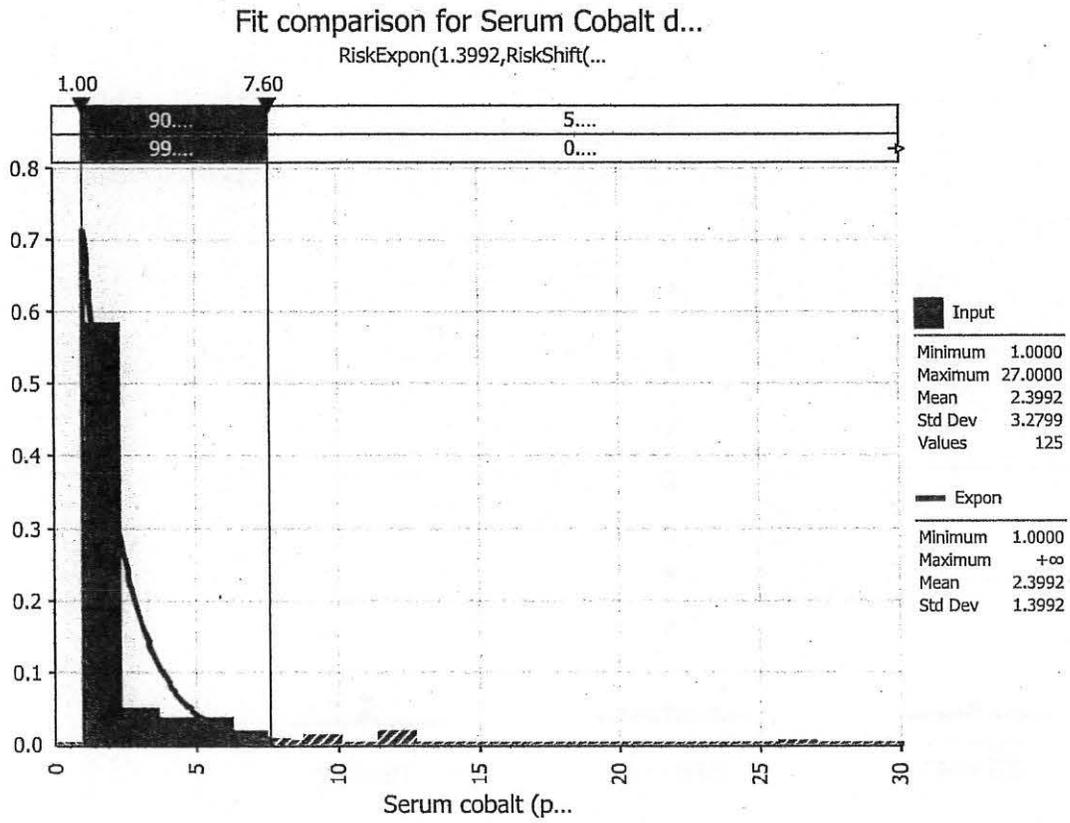
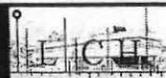


Figure 2. Best-fitting distribution for serum cobalt in 125 samples from 43 Quarter Horse and 82 Thoroughbred racehorses.

ICRAV conference, Mauritius, September 2014.



An international collaboration on cobalt for setting up a threshold value

Marie-Agnes Popot¹, Emmie N.M. Ho², Terence S.M. Wan², Rick M Arthur³, Dionne Benson⁴, Charlie Russo⁵, Pamela Hincks⁶, Clive Pearce⁶, Yves Bonnaire¹.

*Laboratoire des Courses Hippiques*¹, 15 rue de Paradis, 91370 Verrières-le-Buisson, France.

*Racing Laboratory*², The Hong Kong Jockey Club, Sha Tin Racecourse, Sha Tin, NT, Hong Kong.

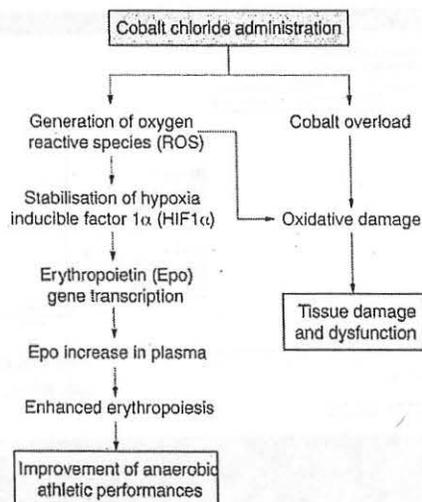
*School of veterinary medicine*³, University of California, Davis, CA 95616, USA.

*Racing Medication and Testing Consortium*⁴, Lexington, KY 40503, USA

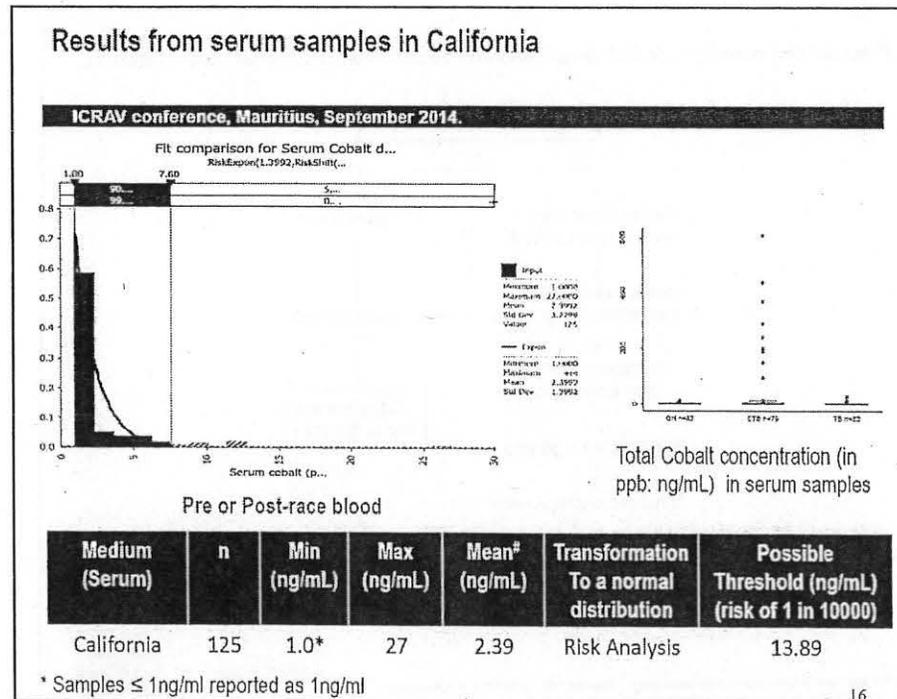
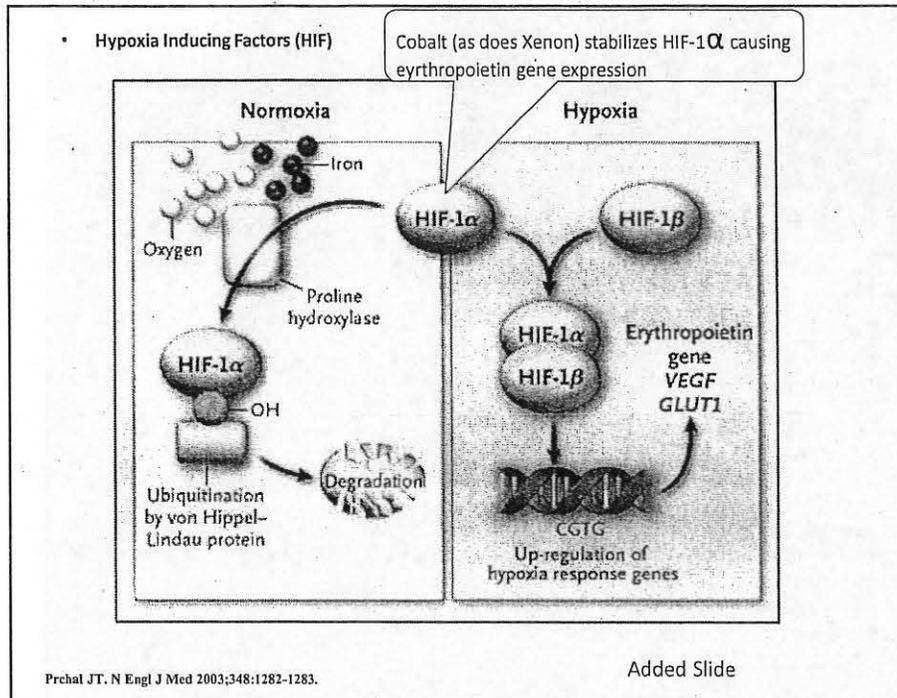
*Racing Chemistry Laboratory, ChemCentre*⁵, PO Box 1250, Bentley Delivery Centre, Western Australia, 6983, Australia.

*LGC (HFL)*⁶, UK, Newmarket Road, Fordham, Cambridgeshire, CB7 5WW, UK.

Potential ergogenic effects and complications of cobalt chloride administration in athletes.

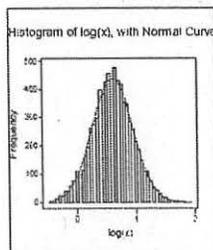


Lippi G et al. Br J Sports Med 2005;39:872-873

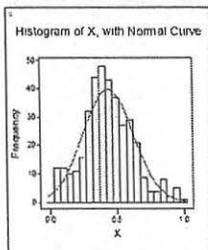


Results from raceday samples in Hong Kong and the UAE:

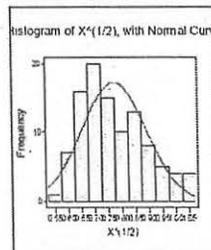
ICRAV conference, Mauritius, September 2014.



HKJC Post-race urine



HKJC Post-race blood



ERA[†] Raceday blood

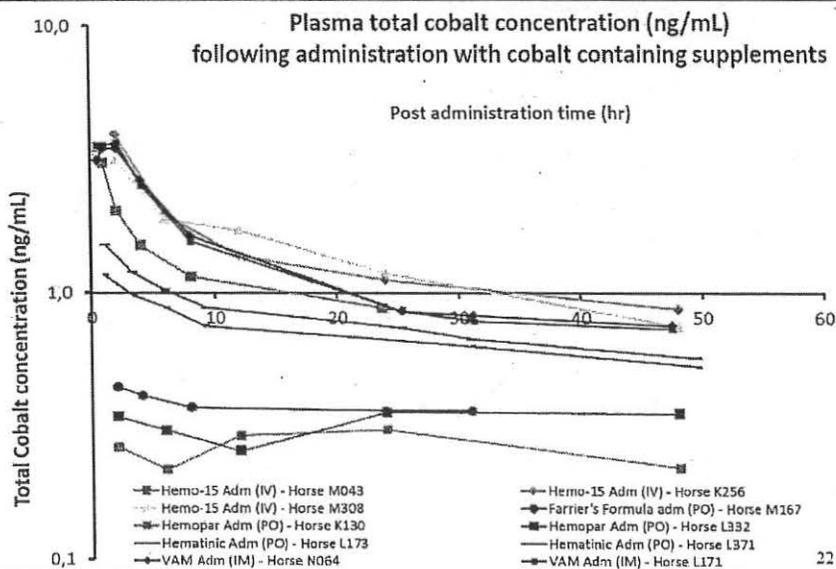
Medium	n	Min (ng/mL)	Max (ng/mL)	Mean (ng/mL)	Transformation To a normal distribution	Possible Threshold (ng/mL) (risk of 1 in 10000)
HKJC Urine	7462	0.38	60.6	5.5	Log	74.5
HKJC Plasma	375	0.03	0.98	0.44	None needed	1.14
ERA [†] Plasma	103	0.32	1.10	0.61	Square-root	1.47

[†] Emirates Racing Authority

E.N.M. Ho *et al.*, *Drug Testing Anal.*, in press (DOI 10.1002/dta1719)

Method: Administration study data in plasma (Hong Kong)

ICRAV conference, Mauritius, September 2014.



Controlling the misuse of cobalt in horses

Emmie N. M. Ho,^{a*} George H. M. Chan,^a Terence S. M. Wan,^{a*} Peter Curl,^b Christopher M. Riggs,^c Michael J. Hurley^c and David Sykes^d

Cobalt is a well-established inducer of hypoxia-like responses, which can cause gene modulation at the hypoxia inducible factor pathway to induce erythropoietin transcription. Cobalt salts are orally active, inexpensive, and easily accessible. It is an attractive blood doping agent for enhancing aerobic performance. Indeed, recent intelligence and investigations have confirmed cobalt was being abused in equine sports. In this paper, population surveys of total cobalt in raceday samples were conducted using inductively coupled plasma mass spectrometry (ICP-MS). Urinary threshold of 75 ng/mL and plasma threshold of 2 ng/mL could be proposed for the control of cobalt misuse in raceday or in-competition samples. Results from administration trials with cobalt-containing supplements showed that common supplements could elevate urinary and plasma cobalt levels above the proposed thresholds within 24 h of administration. It would therefore be necessary to ban the use of cobalt-containing supplements on raceday as well as on the day before racing in order to implement and enforce the proposed thresholds. Since the abuse with huge quantities of cobalt salts can be done during training while the use of legitimate cobalt-containing supplements are also allowed, different urinary and plasma cobalt thresholds would be required to control cobalt abuse in non-raceday or out-of-competition samples. This could be achieved by setting the thresholds above the maximum urinary and plasma cobalt concentrations observed or anticipated from the normal use of legitimate cobalt-containing supplements. Urinary threshold of 2000 ng/mL and plasma threshold of 10 ng/mL were thus proposed for the control of cobalt abuse in non-raceday or out-of-competition samples. Copyright © 2014 John Wiley & Sons, Ltd.

Keywords: cobalt; inductively coupled plasma-mass spectrometry; urine; plasma; horse; threshold

Introduction

Cobalt is a well-established chemical inducer of hypoxia-like responses and had been used to treat anaemia in pregnant women, infants, and patients with chronic anaemia.^[1] Hypoxia causes gene modulation at the hypoxia inducible factor (HIF) pathway, leading to cell and tissue adaptation to the low oxygen conditions. The main mediator hypoxia inducible factor 1 α (HIF1 α) activates genetic sequences, including those of the erythropoietin (EPO) gene, which promotes efficient adaptation to hypoxia.^[2] Apart from the haematopoietic effects, cobalt also induces the pleiotropic and non-haematopoietic effects of erythropoietin, including modification of several parameters of lipid and glucose metabolism.^[3] The seminal studies of the effects of inorganic cobalt administration in healthy men revealed that a daily intake of 150 mg of cobalt chloride would produce an increase in red blood cell (RBC) counts by about 1 million cells per microlitre of blood within 7 to 22 days. The high RBC counts would return to normal 9 to 15 days after cobalt administration.^[4] Nevertheless, cobalt salt is no longer used for anti-anaemia treatment due to its adverse effects.^[3,5] The role of cobalt in erythropoiesis is disparate. Cobalamin deficiency can result in anemia. However, supplementing with cobalamin does not benefit performance unless there is a nutritional deficit.^[6] Inorganic cobalt ion (Co²⁺) stimulates erythropoiesis through the stabilization of HIF as discussed, with increased expression of the EPO gene even in non-anemic subjects. Indeed, the activity of an International EPO Unit (IU) was originally referenced against the biological effect of 5 μ M of cobalt chloride.^[7]

Cobalt is an essential micronutrient in the form of vitamin B12 (cobalamin), but inorganic cobalt as such is not required in the human diet. Cyanocobalamin is the synthetic form of vitamin B12 and

the form commonly available in vitamin B12 supplements. The daily nutritional requirement of an adult amounts to 2 to 3 mg of cobalamin. Inorganic cobalt is also obtained from the diet. The normal daily intake is on average about 7.5 μ g.^[8] Cobalt is acutely toxic in larger doses; cobalt ions and cobalt metal (nanoparticles) are cytotoxic and induce apoptosis and at higher concentrations necrosis with inflammatory response. There is evidence suggesting that cobalt salt may cause severe gastrointestinal, endocrine, cardiovascular, haematological, reproductive, neurological, and immunological responses.^[9] Cobalt metal and salts are also genotoxic, mainly resulting from oxidative DNA damage by reactive oxygen species. Cobalt salt was further shown to inhibit thyroidal iodide uptake,^[10] and chronic cobalt chloride ingestion can cause hypothyroidism and goiter.^[11] This may be the reason why the administration of cobalt chloride for performance enhancement is suspected to be supplemented with thyroid hormone. More impor-

* Correspondence to: Emmie N. M. Ho and Terence S. M. Wan, Racing Laboratory, The Hong Kong Jockey Club, Sha Tin Racecourse, Sha Tin, N.T., Hong Kong, China. E-mail: emmie.nm.ho@hkjc.org.hk; terence.sm.wan@hkjc.org.hk

a Racing Laboratory, The Hong Kong Jockey Club, Sha Tin Racecourse, Sha Tin, N.T., Hong Kong, China

b Department of Veterinary Regulation & International Liaison, The Hong Kong Jockey Club, Sha Tin Racecourse, Sha Tin, N.T., Hong Kong, China

c Department of Veterinary Clinical Services, The Hong Kong Jockey Club, Sha Tin Racecourse, Sha Tin, N.T., Hong Kong, China

d Emirates Racing Authority, Meydan Grandstand, Al Meydan Road, Nad Al Sheba, PO Box 9452, Dubai, UAE

tantly, the cobalt-induced activation of HIF, present in almost all animal cells, with transcription of a range of hypoxia responsive HIF-target genes, probably promotes tumor development and growth.^[12,13]

Considering that cobalt salts are low cost, readily available, orally active, and effective in boosting endogenous erythropoietin production, they are attractive blood doping agents to enhance aerobic performances. Indeed, gene therapy targeting the HIF pathway has been reported as an attractive alternative to traditional techniques of blood doping since the last decade.^[14-16] The stimulated erythropoietin production and increased erythropoiesis increase the oxygen-carrying capacity of blood. Moreover, preconditioning with cobalt salts promotes tissue adaptation to hypoxia, improves hypoxic/ischemic tolerance, protects skeletal muscles from exercise-induced oxidative damage and enhances physical endurance performance.^[3,17] It has also been proposed that cobalt preconditioning could possibly avoid high altitude-induced oxidative stress and ameliorate mountain sickness. While there has been no reported study confirming the effect of cobalt on the performance of racehorses, recent intelligence from the USA and investigations of overseas out-of-competition and post-competition samples in the authors' laboratory, as well as a number of reported cases in Australia, have confirmed that cobalt is being abused in equine sports.

Due to the ability of cobalt to act as an erythropoietic agent in equine sports, a method to control cobalt misuse is needed. Inductively coupled plasma mass spectrometry (ICP-MS) is by far the best technique to quantify elements other than C, H, O, F, and the inert gases in biological samples. Besides its high sensitivity and fast turnaround time, another major advantage of using ICP-MS to quantify total cobalt in biological samples is the simple sample preparation required. Blood and urine can often be analyzed directly after dilution with acid.^[18,19] This paper describes ICP-MS methods for the quantification of total cobalt in equine plasma and urine. Equine plasma was first protein-precipitated. An aliquot of the deproteinated plasma or a portion of urine was then diluted with nitric acid and submitted directly to ICP-MS analysis. The total cobalt concentration was determined from a multi-point linear regression calibration curve using Germanium (Ge) as the internal standard.

As cobalt is naturally occurring in equine biological samples, a threshold is necessary to control its misuse in horses. With a threshold established, any equine sample is deemed to be positive for a prohibited substance if its cobalt concentration exceeds the respective threshold and if its presence in the sample can be independently confirmed using an unequivocal identification method. A few papers have reported the qualitative identification of the presence of cobalt by the formation of metal-complexes that can be analyzed by gas chromatography-mass spectrometry (GC-MS)^[20] or electrospray ionization mass spectrometry (ESI-MS).^[21,22] Based on the study reported by Minakata *et al.*,^[21] definitive liquid chromatography-mass spectrometry (LC-MS) methods for confirming the presence of cobalt in equine plasma and urine were developed by monitoring its diethyldithiocarbamate complex.

Materials and methods

Materials

Reference standard solutions of cobalt (Co) and germanium (Ge), with certified values traceable to the respective Standard Reference Material (SRM) 3113 and 3120a of the National Institute of Standards

and Technology (NIST), were obtained from High Purity Standards (Charleston, SC, USA). Triton-X (Ultra), diethyldithiocarbamate (DDC) and isoamyl alcohol (IAA) were purchased from Sigma-Aldrich (St Louis, MO, USA). Nitric acid (Suprapur grade; 65%), trichloroacetic acid (pro analysi grade), citric acid (pro-analysi grade) and sodium chloride (pro analysi grade) were obtained from Merck (Darmstadt, Germany). High purity deionised water was obtained from a Milli-Q Element A10 water purification system (Milli-Q, Molsheim, France). Blank plasma and urine samples were taken from post-race samples collected from horses after their races in Hong Kong.

Working standard solutions

The working standard solutions of Co and Ge were prepared from the respective reference standard solutions by dilution with 3.25 % (v/v) nitric acid. Only plastic containers and labware were used for all ICP-MS analyses.

Sample preparation for ICP-MS analyses

Blood

Blood samples (collected in lithium heparin tubes) were centrifuged at 3000 rpm (~1650 g) for 10 min and the plasma fraction was isolated. Germanium standard solution (40 ng) was added as an internal standard to plasma (80 μ L). The concentration of the internal standard in the plasma sample was equivalent to 500 ng/mL. The mixture was deproteinated by the addition of trichloroacetic acid (300 μ L; 10 g trichloroacetic acid and 120 mg NaCl in 100 mL deionized water) and nitric acid (3.25 %) to give a total volume of 4 mL. The mixture was vortexed briefly and left standing at room temperature for 10 min and then centrifuged at 2000 rpm (~750 g) for 10 min. The supernatant (3.6 mL) was transferred to an ICP-MS autosampler tube (a 4-mL polypropylene tube) and then infused *via* an autosampler to the ICP-MS.

Urine

Urine samples were centrifuged at 3000 rpm (~1650 g) for 10 min. Germanium standard solution (40 ng) was added as an internal standard to urine (80 μ L). The sample was then diluted with nitric acid (3.25 %) to give a total volume of 4.0 mL. The diluted sample was then infused *via* an autosampler to the ICP-MS.

Protein precipitation for plasma sample for confirmation by LC-MS

Blood samples were centrifuged at 3000 rpm (~1650 g) for 10 min and the plasma fraction was isolated. Trichloroacetic acid (50 μ L, 10 %, w/v) was added to an aliquot of plasma (300 μ L). The mixture was then vortexed for 1 min. After standing for 10 min, the mixture was centrifuged at 14 000 rpm (~13 000 g) for 1 min. Two hundred microlitres of the supernatant was then subjected to complex formation.

Sample preparation for confirmation by LC-MS

Diethyldithiocarbamate (DDC; (C₂H₅)₂NCSS⁻, 20 μ L, 1 M) was added into either deproteinated plasma (200 μ L) or urine (200 μ L). Internal standard was not used. The mixture was then vortexed for 1 min and shaken at 1400 rpm at 25 °C (in a thermo-mixer) for 10 min. Citric acid (20 μ L, 0.2 M) and isoamyl alcohol (IAA, 500 μ L) were added to the mixture. After further mixing in the thermo-mixer at 1400 rpm at 25 °C for 10 min, the mixture was centrifuged at 14

Controlling the misuse of cobalt in horses

000 rpm (~13 000 g) for 1 min. The supernatant was taken out and mixed with 100 μ L of methanol to facilitate evaporation. The mixture was blown down to dryness at 60 °C with nitrogen. The dry residue was then reconstituted with methanol (40 μ L) and subjected to LC-MS analysis.

Instrumentation

ICP-MS analyses were performed on an Agilent 7500ce inductively coupled plasma mass spectrometer equipped with a G3160A integrated autosampler and a MicroMist nebulizer (Agilent Technologies, Santa Clara, CA, USA). LC-MS analyses were performed on a Thermo Finnigan TSQ Quantum Classic mass spectrometer (Thermo Finnigan, San José, CA, USA) equipped with a Waters Acquity UPLC system (Waters Corporation, Milford, MA, USA).

ICP-MS conditions

An RF power of 1400 W was employed. The argon carrier gas flow rate was set at 1.05 L/min. The spray chamber temperature was set at 2 °C. Helium (4.0 mL/min) was used as the collision gas. The peristaltic pump speed was set at 0.2 revolutions per sec (rps) during analysis. The sample uptake rate was about 0.8 mL/min, and the sample uptake time was set at 30 s. The isotopes to be monitored for Co and Ge were m/z 59 and m/z 72, respectively. All data acquisitions were performed in Spectrum Analysis mode with triplicate measurements. Peak Area Integration mode was used, and the integration time per mass was 2 s for Co, and 1 s for Ge. The total acquisition time per sample was about 3 min. After each injection, the autosampler probe was rinsed with deionized water for 5 s in the rinse port and 5 s in the rinse vial, followed by intelligent rinse with 0.07 % Triton-X for a maximum of 100 s to minimize carry over. The autosampler probe was finally rinsed with deionized water for 20 s before the next infusion.

LC-MS conditions for confirmation of cobalt

A reversed-phase UPLC column (Waters; Acquity BEH C18; 10 cm L x 2.1 mm ID; 1.7 μ m particle size) was used for the analysis of cobalt diethyldithiocarbamate (Co-DDC) complex. The mobile phase was composed of 5 mM ammonium formate (pH 3) in deionized water as solvent A and 0.1% formic acid in acetonitrile as solvent B. A linear gradient was run at a constant flow rate of 350 μ L/min, with 100 % solvent A at the initial condition ($t=0$ min), decreasing to 0 % solvent A from $t=1$ min to $t=6$ min, and held for 0.1 min (until $t=6.1$ min). The gradient was then returned to 100 % solvent A from $t=6.1$ min and equilibrated until $t=10$ min before the next injection. The injection volume was 5 μ L.

Detection of the Co-DDC complex was performed in positive electrospray ionisation mode in a single time segment using selected reaction monitoring (SRM). Spray voltage of 3800 V and capillary temperature of 320 °C were employed. The nitrogen sheath and auxiliary gas flow rates were set at 60 and 10 arbitrary TSQ Quantum units respectively. The selected precursor ion of the Co-DDC complex was m/z 355, while the product ions monitored were m/z 116, 174, 208, and 291. The collision offset voltages were set from 25 V (for m/z 116, 174) to 35 V (for m/z 208, 291). Argon was used as the collision gas and set at 1.2 mTorr. The peak widths for the precursor and product ions in respectively Q1 and Q3 were set at 0.7 amu (FWHM). The scan width for the product ions was set at 0.01 amu and

the scan time for each transition was 50 msec. Data processing was performed using the Thermo Finnigan Xcalibur software (Version 2.0.6).

Calibrators and quality control samples for ICP-MS analyses

Calibration curves were established by analyzing a set of cobalt calibrators at concentrations of 0, 2, 4, 6, 8, and 10 ng/mL and 0, 30, 60, 90, 120, and 150 ng/mL in deionized water for equine plasma and urine, respectively. Quality control (QC) samples at 1 and 4 ng/mL (for plasma) and 60 ng/mL (for urine) were prepared in duplicate by spiking cobalt standard to blank plasma and blank urine, respectively. The calibrators, QC samples, and their corresponding blank matrices were analyzed alongside each batch of test samples using identical procedures. As a QC measure, the calibrators and QC samples were made up from Co working standard solutions that had been prepared separately. The peak area count ratios of cobalt to the internal standard (Ge) versus the spiked Co concentrations were fitted using linear regression to obtain the calibration curve. Concentrations of total cobalt in the test samples were interpolated from the calibration curve using standard ChemStation quantification software. For the QC samples, the actual recovered concentration of cobalt was derived by subtracting the concentration of the corresponding blank matrix from the total concentration determined.

Statistical analysis

Statistical analysis was performed with Minitab computer software version 13.32 (2000) (Minitab Inc., State College, PA, USA). The Kolmogorov-Smirnov normality test was used to compare the observed frequencies with the calculated distribution. Outliers in a data set were identified using the standard function from Microsoft Excel. Any number in a data set with the absolute value of Z-score exceeding 3.5 is considered an outlier.

Drug administration experiments (at manufacturers' recommended daily dosages)*Hemo-15*

Hemo-15® (10 mL each, Virbac, Milperra, NSW, Australia) was administered daily by intravenous injection to 3 thoroughbred geldings for 3 consecutive days.

VAM® Injection

VAM® Injection (11 mL each, Nature Vet, NSW, Australia) was administered twice on alternate days by intramuscular injection to 2 thoroughbred geldings.

Farrier's Formula®

Farrier's Formula® (1.5 cups, ~255 g, Life Data Labs, Inc., Cherokee, Alabama, USA) was administered daily by stomach tubing to 1 thoroughbred gelding for 3 consecutive days.

Twydil® Hemopar

Twydil® Hemopar (60 mL each, PAVESCO AG, Basel, Switzerland) was administered daily by mixing with the daily feed to 2 thoroughbred geldings for 3 consecutive days.

Twydil® Hematinic

Twydil® Hematinic (40 mL each, PAVESCO AG, Basel, Switzerland) was orally administered twice daily to 2 thoroughbred geldings for 3.5 consecutive days (totally 7 times per horse).

Blood and urine samples were collected before and after administration. Blood samples were collected in lithium heparin tubes and centrifuged upon receipt and the corresponding plasma samples were kept at below -60°C until analysis. Approval of the drug administration experiments in this study has been obtained from the Animal Ethics Committee of the Hong Kong Jockey Club (reference HKJC-ERC004).

Method validation*Quantification method by ICP-MS*

The inter-day accuracy and precision were assessed by analyzing the QC samples with cobalt spiked at various concentrations (1 and 4 ng/mL in plasma and 60 ng/mL in urine and the corresponding blank samples). The limit of detection (LoD) and limit of quantification (LoQ) of cobalt in equine urine and plasma were estimated by replicate analyses of blank sample matrices ($n = 6$ each). The impact on method recovery of the different common forms of cobalt (inorganic cobalt, cyanocobalamin and cobalt gluconate) found in some cobalt-containing supplements was evaluated by analyzing different untreated plasma samples spiked with different forms of cobalt (equivalent to 1 ng/mL cobalt) and their corresponding sample blanks. Recoveries were corrected by subtracting the cobalt concentration in the corresponding blank matrix from the total cobalt concentration determined for the spiked sample. Pairs of plasma and serum samples isolated from blood collected (with and without anticoagulant respectively) from the same horses ($n = 6$) were analyzed in quadruplicate for total cobalt to assess the method applicability to serum samples.

Confirmation method by LC-MS

The inter-day precisions of area count and retention time were assessed by analyzing cobalt spiked urine sample at 100 ng/mL and spiked plasma sample at 2 ng/mL. The detection sensitivity was evaluated by analyzing post-administration samples with their concentrations pre-determined by the ICP-MS method. Matrix suppression was studied by comparing the area counts obtained from matrix-spiked samples (corrected for contribution from their corresponding blank matrices) with those from the water spiked samples at the same cobalt concentrations. Method applicability to other forms of cobalt was studied by analyzing spiked plasma with cyanocobalamin and cobalt gluconate at cobalt equivalent concentrations of 1 and 4 ng/mL.

Results and discussion**Validation of ICP-MS quantification method for total cobalt in equine urine and plasma**

It is well known that polyatomic isobars ($^{36}\text{Ar}^{23}\text{Na}$, $^{43}\text{Ca}^{16}\text{O}$ and $^{40}\text{Ar}^{18}\text{OH}$) could interfere with ICP-MS analysis of cobalt. The contribution of various polyatomic interferences was reported to be equivalent to about 0.4 ng/mL of cobalt in human serum.^[23] Collision/reaction cell (CRC) technology has been shown to be a very effective tool to remove isobaric interferences from polyatomic species.^[24] This technique was employed in the present study using helium as the collision gas. The inter-day accuracy

and the precision of the method were determined to be within $\pm 5\%$ and $\leq 9\%$ RSD, respectively, at all QC levels in both matrices (Table 1). The LoD and LoQ were found to be 0.16 ng/mL (equivalent to $3 \times \text{SD}$) and 0.52 ng/mL (equivalent to $10 \times \text{SD}$) in equine urine, and 0.06 ng/mL and 0.21 ng/mL in equine plasma. Calibration curves were linear within the concentration range, with correlation coefficients (r) greater than 0.99 in all cases.

Method recovery based on untreated plasma samples spiked with inorganic cobalt (equivalent to 1 ng/mL cobalt) was found to be 101%, while slightly lower method recoveries of about 90% were observed for untreated plasma spiked with other forms of cobalt (cyanocobalamin and cobalt gluconate) at equivalent cobalt concentration. As the magnitude of the negative recovery (about -10%) for the non-salt forms is not significantly different from the method precision (about 9% RSD at 1 ng/mL), the impact was not considered significant for the purpose of population surveys, particularly when a high confidence limit would be used to establish the thresholds.

There was no significant difference between the total cobalt concentrations determined in plasma and serum collected from the same horse ($n = 6$), as shown in Table 2. Therefore, population data of total cobalt in either equine plasma or equine serum can be considered to be equivalent.

Total cobalt population survey in post-race equine urine

In Hong Kong, the screening of total cobalt in equine urine samples has started since 2006. Equine urine was analyzed by ICP-MS after a simple dilution with nitric acid. Germanium (Ge) was used as the internal standard because there was essentially no interference with cobalt determination. In addition, Ge is not normally present in horse urine and blood, and has a mass (72 Da) close to that of Co (59 Da), minimizing possible mass-dependent difference in detector sensitivity. The total cobalt concentration in a urine sample was interpolated directly from a multi-level linear regression calibration curve constructed using calibrators prepared from water spiked with various

Table 1. Precision and accuracy of spiked quality control (QC) samples

QC sample (ng/mL)	Number of QC samples analyzed	Precision (%RSD)	Accuracy (%)
Equine urine			
60	550	4.7	95
Equine plasma			
1	21	9.0	101
4	19	3.2	98

Table 2. Total cobalt concentrations in plasma and serum samples collected from the same horse ($n = 6$)

Horse	Total cobalt in plasma (ng/mL)	Total cobalt in serum (ng/mL)
G118	0.24	0.26
G312	0.30	0.32
L098	0.34	0.35
M113	0.35	0.34
M266	0.28	0.26
N093	0.30	0.28

concentrations of cobalt. A cobalt threshold in equine urine could be established based on a population survey of 7462 post-race urine samples collected from horses after their races in Hong Kong. The population mean \pm standard deviation (SD) was 5.5 ± 5.0 ng/mL. This set of data showed a skewed distribution and could not be used directly to establish a threshold. A normal distribution could be obtained for the whole set of data after a logarithm transformation (Figure 1a). The transformed data were then subjected to the Kolmogorov-Smirnov normality test, resulting in an acceptable significance level of 0.05. A possible threshold could then be set at a level equal to the untransformed 'mean + 3.72 SD' value of 74.5 ng/mL, representing a risk of 1 in 10 000 (assuming the degree of freedom to be infinity) for a normal sample to exceed this threshold. Based on this approach which is often used to establish internationally-accepted thresholds in the horseracing industry,^[18,19,25-27] a 'rounded-up' threshold of 75 ng/mL of total cobalt in raceday equine urine samples was proposed. The risk associated with this threshold was about 1 in 10 315 (with a degree of freedom of 7461). This proposed threshold could be used to control total cobalt concentration in a raceday urine sample.

Total cobalt population survey in post-race equine plasma

Owing to the increasing popularity of using blood samples for doping control testing, the authors have also started monitoring total cobalt in blood samples since April 2013. The sample preparation procedures for blood samples were similar to those for urine samples, except that an additional protein precipitation step was included. Total non-protein-bound cobalt in plasma was measured. A proposed cobalt threshold in equine plasma could be established based on a population of 375 post-race blood samples using the same approach described above for equine urine. The population mean \pm SD was 0.44 ± 0.19 ng/mL. This whole set of data fits a normal distribution as shown Figure 1b, resulting in an acceptable significance level of 0.068 in the Kolmogorov-Smirnov normality test. A possible threshold could then be set at the 'mean + 3.72 SD' value of 1.14 ng/mL, representing a risk of 1 in 10 000 (assuming the degree of freedom to be infinity) for a normal sample to exceed this threshold. As a relative small population was used to derive the threshold, a 'rounded-up' threshold of 2 ng/mL of total cobalt in raceday equine plasma samples was proposed. The risk associated with this threshold was about one in 1000 trillion (with a degree of freedom of 374).

The proposed total cobalt threshold in equine plasma was verified using an independent population of 109 raceday blood samples from the Emirates Racing Authority (ERA) analyzed in Hong Kong using the same quantification method. Blood samples from ERA are a good choice for cobalt population survey because, like in Hong Kong, injections are not allowed to be given on raceday, thus minimizing the risk of samples being affected by injection with cobalt-containing supplements. The mean \pm SD for the plasma total cobalt in the ERA population was determined to be 0.70 ± 0.44 ng/mL. Among these 109 samples, 6 (with plasma total Co levels at 1.5–2.8 ng/mL) were considered outliers. These 6 samples were reportedly collected from horses belonging to two trainers and the elevated cobalt levels in these 6 samples were probably remnants of earlier treatments with cobalt-containing supplements. This set of data gave, after removal of the outliers, a mean \pm SD value of 0.61 ± 0.19 ng/mL and a normal distribution after a square-root transformation with an acceptable significance level of 0.05. The untransformed 'mean + 3.72 SD' value was 1.47 ng/mL, which was below the proposed threshold of 2 ng/mL, suggesting that the proposed plasma total cobalt threshold may also be applied to raceday blood samples from other countries.

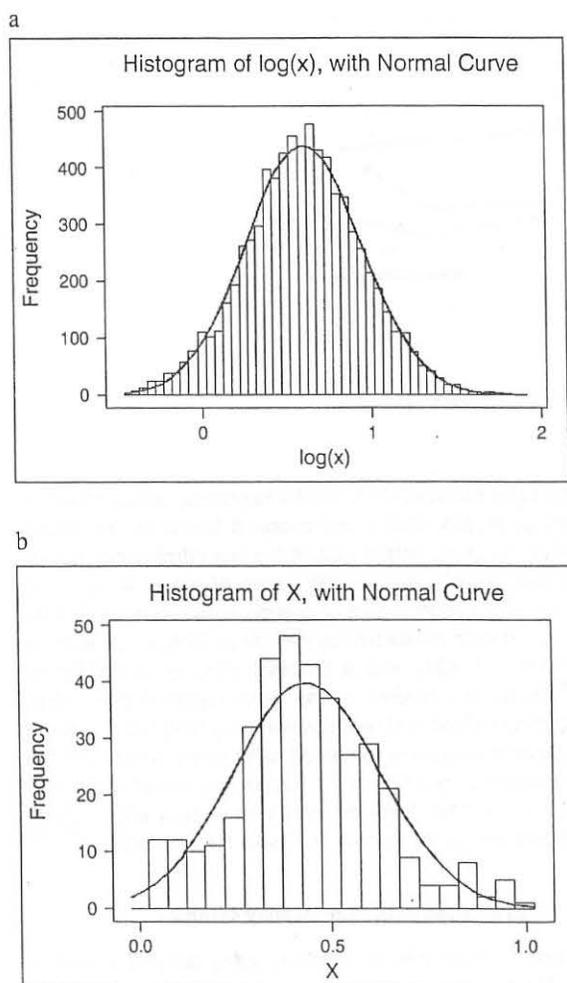


Figure 1. (a) Total cobalt concentration in equine urine samples after logarithm transformation (b) Total cobalt concentration in equine plasma samples (without transformation).

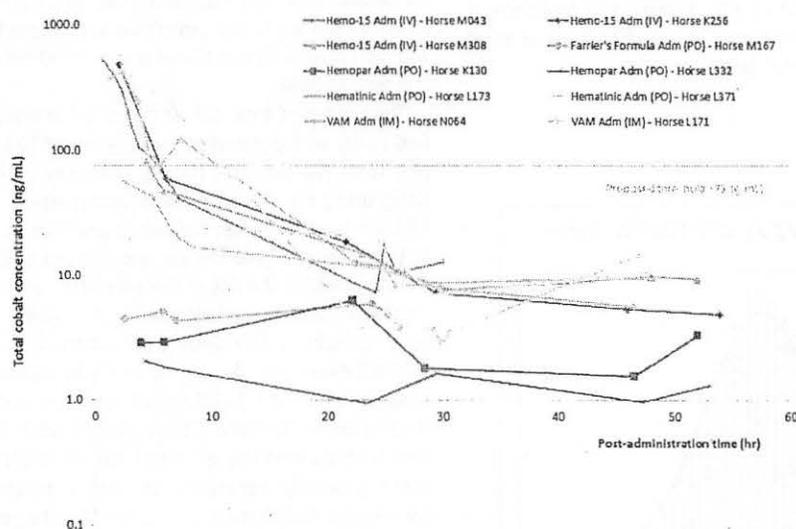
Administration trials with cobalt-containing supplements

In order to evaluate the impact of legitimate cobalt-containing supplements on the proposed thresholds, administration trials were conducted with 2 cobalt-containing injectables (Hemo-15 and VAM® Injection) and 3 cobalt-containing oral supplements (Farrier's Formula®, Hemopar, and Hematinic). The dose regimens used in the trials were based on those recommended by the manufacturers. Details of the listed cobalt ingredients and the cobalt equivalent in a daily dose for each supplement are summarized in Table 3, and the elimination profiles of total cobalt in urine and plasma are shown in Figures 2 and 3, respectively.

Elevated total cobalt levels in urine and plasma above the respective proposed thresholds were observed for the two injectables (Hemo-15 and VAM® Injection) and observed only in urine for the oral supplement with the highest daily dose of cobalt (Hematinic). Peak urinary and plasma total cobalt levels for these three products were all observed within 2 h of the last administration. Despite a

Table 3. Listed cobalt ingredients and comparison of Co equivalent per daily dose

Cobalt-containing supplement	Cobalt ingredient as listed	Recommended daily dose	Cobalt equivalent per daily dose (mg)
<i>Injections</i>			
Hemo-15	Cyanocobalamin 150 µg/mL Cobalt gluconate 0.7 mg/mL	10 mL	0.99
VAM® Injection	Cyanocobalamin 150 µg/mL Cobalt sulphate 240 µg/mL	11 mL	1.08
<i>Oral supplements</i>			
Farrier's Formula	Cobalt carbonate 1.9 mg/cup (cup = 170 gram of product)	1.5 cup (=255 gram)	1.41
Hemopar	Cyanocobalamin 800 µg/L Cobalt sulphate monohydrate 9 mg/L	60 mL	0.19
Hematinic	Cyanocobalamin 180 mg/L Cobalt carbonate 110 mg/L	80 mL (40 mL twice)	4.99 (2.5 twice)

**Figure 2.** Urinary total cobalt following administration of various forms of cobalt-containing supplements to horses.

much higher last dose of the oral supplement Hematinic than that of the two injectables, its peak total cobalt concentrations in urine and plasma was lower than those for the injectables, indicating that absorption of cobalt by the oral route is far less efficient than by way of injection. For the other two lower-dose oral supplements (Farrier's Formula® and Hemopar), no significant change in urinary and plasma total cobalt levels was observed in post-administration samples, with levels below the respective proposed thresholds at all times. Based on the proposed thresholds in urine (75 ng/mL) and plasma (2 ng/mL), VAM® Injection showed the longest detection time in urine of about 12 h, while both VAM® Injection and Hemo-15 had the longest detection time in plasma of about 6 h (Table 4). The results from these administration trials would suggest that legitimate cobalt-containing injectables should be banned not just on raceday but preferably on the day before racing in order to ensure that the proposed thresholds are not inadvertently breached in raceday samples. The use of oral supplements containing relatively high cobalt content should also be restricted to non-racedays.

The initial elimination half-life for plasma total cobalt was observed to be about 2–6.4 h, and the terminal elimination half-life

was found to be about 42–68 h. Similar to plasma, urinary total cobalt levels decreased rapidly and dropped below the proposed threshold of 75 ng/mL within 12 h of the last administration. Our findings were broadly in line with those observed in rats and human. The elimination profile of plasma cobalt appeared to be triphasic in rats with an absorption half-life of 0.9 h, an elimination phase half-life of 3.9 h, and a terminal elimination half-life of 22.9 h.^[28] In human studies, it has been reported that cobalt concentration in blood and serum was initially high but decreased rapidly due to tissue uptake combined with urinary excretion.^[8] The renal excretion reported for human was initially rapid but decreasing over the first days, followed by a second slow phase lasting several weeks, and with retention in tissues for several years.^[29,30]

Control of cobalt misuse in non-raceday samples

The control of cobalt misuse in non-raceday samples would require a different approach since numerous legitimate cobalt-containing supplements are allowed to be used during training. Indeed, cobalt levels in excess of 30 ng/mL (with one exceeding 1000 ng/mL!) have been observed by the authors' laboratory in

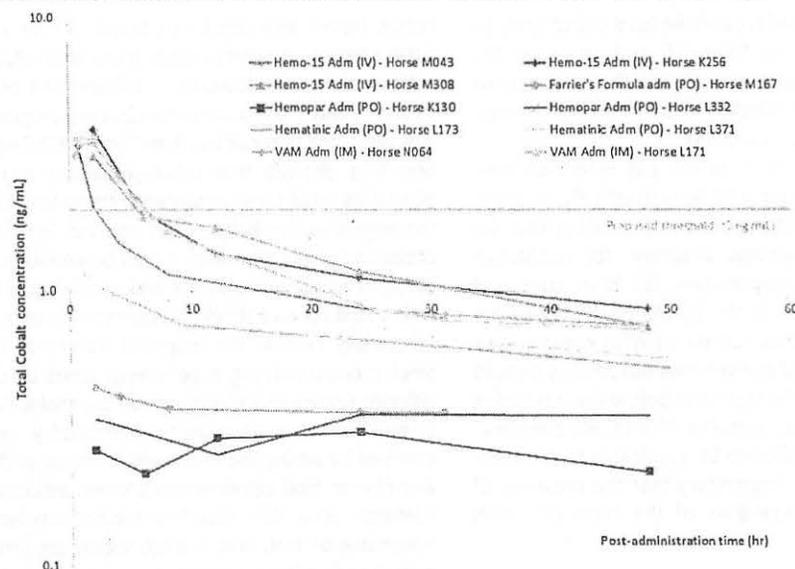


Figure 3. Plasma total cobalt following administration of various forms of cobalt-containing supplements to horses.

several non-raceday blood samples from overseas. A pragmatic approach would be to set a threshold for non-raceday samples in excess of the maximum urinary or plasma total cobalt concentrations expected to be attainable by the use of common *bona fide* cobalt-containing supplements. Based on our administration trials with various products, it would appear that administering a supplement with the largest recommended dose intravenously would provide the highest possible maximum concentration (C_{max}) in both urine and plasma to be considered as thresholds for non-raceday samples. A search on the Internet revealed that Hemo-15 was the *bona fide* cobalt-containing equine supplement with the highest recommended IV dose. Based on our trials with Hemo-15, the highest C_{max} (by extrapolation to time=0) would be from Horse K256 at respectively 6 ng/mL in plasma and 1600 ng/mL in urine. Total cobalt thresholds for non-raceday samples could thus be proposed at 10 ng/mL in plasma and 2000 ng/mL in urine. The suitability of these thresholds might warrant further verification by conducting administration trials with other legitimate cobalt-containing supplements not included in the present study.

Confirmation of cobalt in equine urine and plasma by LC-MS

When a regulatory sample is shown to have a total cobalt concentration exceeding the relevant threshold, the presence of cobalt in

the sample should ideally be established unequivocally and independently using a confirmation method. The confirmation method adopted was based on the mass-spectrometric method reported by Minakata *et al.*,^[21] with additional liquid-chromatographic separation to enhance the degree of proof. Cobalt in either urine or deproteinated plasma was complexed with diethyldithiocarbamate (DDC) and extracted with isoamyl alcohol (IAA) in the presence of citric acid. The resulting Co-DDC complex was analyzed by LC-MS in ESI mode. The precursor ion at *m/z* 355 corresponds to the Co-DCC complex [Co(DDC)₂]⁺, while the characteristic product ions monitored were *m/z* 291 [Co(C₄H₁₀NCS)₂]⁺, *m/z* 280 [Co(DDCH)]⁺, *m/z* 174 [CoC₄H₉NCS]⁺, and *m/z* 116 [C₄H₁₀NCS]⁺. Cobalt could be easily confirmed in a blood sample collected 8.1 h after the last Hemo-15 administration (Figure 4). Both the retention time and mass spectrum of Co-DDC complex obtained from the post-administration sample matched well with those from the cobalt standard. These LC-MS data met the criteria stipulated in the *AORC Guidelines for the Minimum Criteria for Identification by Chromatography and Mass Spectrometry*.^[31] The total cobalt concentration in this sample had been determined to be about 1.2 ng/mL by the ICP-MS quantification method, suggesting that this LC-MS method has adequate sensitivity to confirm the presence of cobalt in horse plasma exceeding the threshold of 2 ng/mL. Similarly, cobalt was confirmed in a post-administration urine sample collected 6.4 h

Table 4. Comparison of peak total cobalt concentrations observed and maximum detection times based on the respective proposed thresholds in urine and plasma

Administration with cobalt-containing supplement	Urine		Plasma	
	Peak total cobalt level observed (ng/mL)	Maximum detection times (hrs)	Peak total cobalt level observed (ng/mL)	Maximum detection times (hrs)
<i>Injectables</i>				
Hemo-15	81–530	6.1	3.1–3.9	5.9
VAM® Injection	374–424	11.6	3.5–3.6	6.3
<i>Oral supplements</i>				
Farrier's Formula		Elevated total cobalt level not observed		
Hemopar		Elevated total cobalt level not observed		
Hematinic	56–113	3.8	1.2–1.5	—

after the last Hemo-15 administration, and the total cobalt concentration in the sample was about 55 ng/mL and less than the proposed threshold in urine (Figure 5). Since cobalt is endogenous in the horse, small amount of cobalt was also detected in pre-administration samples (Figures 4a and 5a).

The inter-day precisions on area count and retention time were determined to be 21 % and 0.13 %, respectively, in urine, and 25 % and 0.1 %, respectively, in plasma, indicating that the confirmation method has adequate precision for qualitative identification. Significant ion-suppressions (31 % in urine and 75 % in plasma) were observed in the LC-MS analyses of both urine and plasma spiked samples compared with water spikes. Nevertheless, the method could still serve its purpose as it could reliably confirm the presence of cobalt at or below the respective proposed thresholds for raceday samples. This LC-MS confirmation method has also been verified to be applicable to cyanocobalamin and cobalt gluconate, suggesting that the presence of cobalt could be confirmed regardless of the form of cobalt present in the samples.

Conclusion

ICP-MS quantification methods for total cobalt in equine urine and plasma samples were developed and validated. Urine and deproteinated plasma samples were analyzed directly by ICP-MS after simple dilution with nitric acid. Endogenous total cobalt levels in post-race urine ($n=7462$) and plasma ($n=375$) samples were determined with the aim to establish thresholds to control the misuse of cobalt in

horses. Plasma total cobalt was found to have a normal distribution, while a logarithm transformation is required for urinary total cobalt to achieve a normal distribution. Urinary and plasma thresholds of 75 ng/mL and 2 ng/mL, respectively, were proposed for raceday samples with a risk factor of less than 1 in 10 000. Results from administration trials showed that cobalt-containing supplements, especially injectables, could cause urinary and plasma total cobalt levels to exceed the respective thresholds within the first 24 h. Therefore, the use of cobalt-containing injectables should be prohibited starting on the day before racing and the use of oral supplements containing relatively high cobalt content should be restricted to non-racedays in order to successfully institute the proposed thresholds for raceday samples. Since cobalt-containing supplements could be used during training, different urinary and plasma cobalt thresholds would be required to control the misuse of cobalt for non-raceday samples. This could be achieved by setting the thresholds in excess of the maximum urinary and plasma total cobalt concentrations anticipated from the use of common bona fide cobalt-containing supplements. Results from administration trials and Internet search suggested that Hemo-15, a high-dose supplement administered intravenously, was a good model for establishing cobalt thresholds in non-raceday samples. Based on results from the Hemo-15 administration trials, thresholds of 2000 ng/mL in urine and 10 ng/mL in plasma for total cobalt in non-raceday samples were proposed. The presence of cobalt in the test samples could be confirmed unequivocally and independently by forming a cobalt-diethylthiocarbamate complex followed by LC-MS analysis. While the diet seems to be a major factor that can influence the observed levels of cobalt in horses, there is still not much known regarding other factors, such as

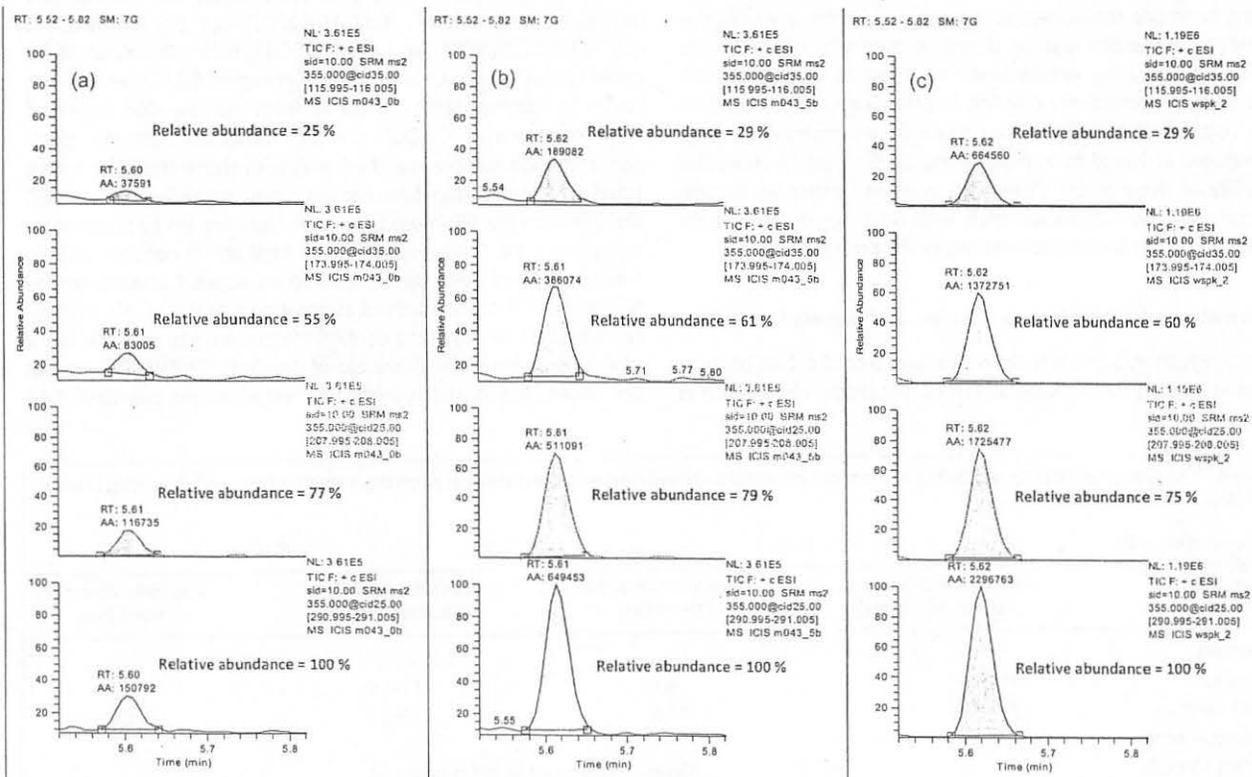


Figure 4. LC-MS product-ion chromatograms of Co-DDC obtained from (a) a pre-administration plasma sample, (b) a post-administration blood sample collected 8.1 h after IV administration of 10 mL of Hemo-15 daily for three days to a horse, and (c) a standard solution of cobalt in water.

Controlling the misuse of cobalt in horses

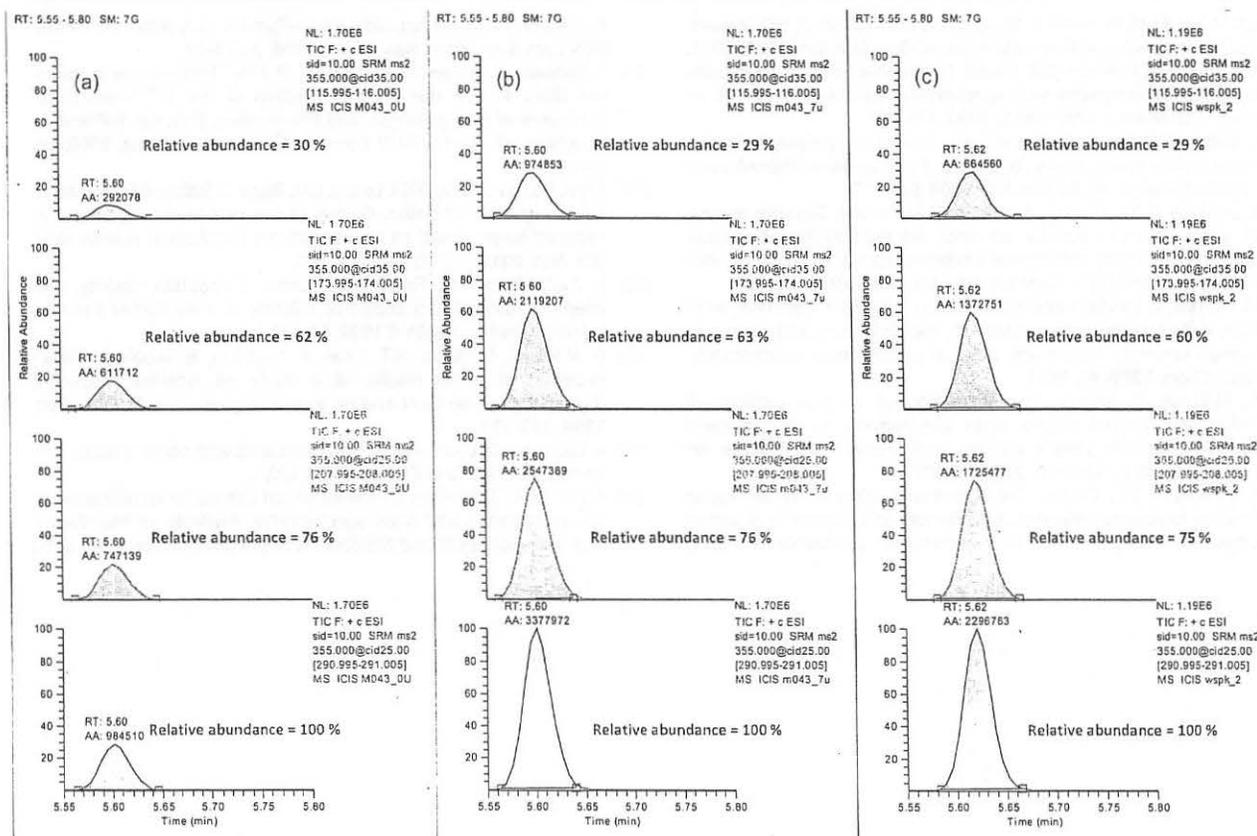


Figure 5. LC-MS product-ion chromatograms of Co-DDC obtained from (a) a pre-administration urine sample, (b) a post-administration urine sample collected 6.4 h after IV administration of 10 mL of Hemo-15 daily for three days to a horse, and (c) a standard solution of cobalt in water.

clinical or pathological conditions, that can influence the pharmacokinetics, and hence the observed levels, of cobalt in horses. In order to further improve the control of the misuse of cobalt in equine sports, a database of basal values of total cobalt in samples from a significant number of untreated horses in different regions should be established. In addition, more administration trials should be conducted with legitimate cobalt-containing equine supplements commonly used in different countries. This objective would require further international collaboration.

Acknowledgements

The authors wish to thank Chris Szeto, Shirley Tang, and Stephen Cheung of the Racing Laboratory of The Hong Kong Jockey Club for their technical assistance.

References

- R.G. Holly. Studies on iron and cobalt metabolism. *JAMA* **1955**, *158*, 1349.
- M.-A.C. Dery, M.D. Michaud, D.E. Richard. Hypoxia-inducible factor 1: regulation by hypoxic and non-hypoxic activators. *Int. J. Biochem. Cell Biol.* **2005**, *37*, 535.
- L.O. Simonsen, H. Harbak, P. Bennekou. Cobalt metabolism and toxicology—a brief update. *Sci. Total Environ.* **2012**, *432*, 210.
- J.E. Davis, J.P. Fields. Experimental production of polycythemia in humans by administration of cobalt chloride. *Exp. Biol. Med.* **1958**, *99*, 493.
- K.M. Unice, A.D. Monnot, S.H. Gaffney, B.E. Tvermoes, K.A. Thuett, D. J. Paustenbach, B.L. Finley. Inorganic cobalt supplementation: prediction of cobalt levels in whole blood and urine using a biokinetic model. *Food Chem. Toxicol.* **2012**, *50*, 2456.
- W. Jelkmann. The disparate roles of cobalt in erythropoiesis, and doping relevance. *Open J. Hematol.* **2012**, *3*.
- P.M. Cotes, D.R. Bangham. The International Reference Preparation of Erythropoietin. *B. World Health Organ.* **1966**, *35*, 751.
- T. Smith, C.J. Edmonds, C.F. Barnaby. Absorption and retention of cobalt in man by whole-body counting. *Health Phys.* **1972**, *22*, 359.
- B.L. Finley, A.D. Monnot, D.J. Paustenbach, S.H. Gaffney. Derivation of a chronic oral reference dose for cobalt. *Regul. Toxicol. Pharm.* **2012**, *64*, 491.
- K.R. Paley, E.S. Sobel, R.S. Yalow. Effect of oral and intravenous cobaltous chloride on thyroid function. *J. Clin. Endocrinol. Metab.* **1958**, *18*, 850.
- J.P. Kriss, W.H. Carnes, R.T. Gross. Hypothyroidism and thyroid hyperplasia in patients treated with cobalt. *J. Am. Med. Assoc.* **1955**, *157*, 117.
- P. Maxwell, K. Salnikow. HIF-1: an oxygen and metal responsive transcription factor. *Cancer Biol. Ther.* **2004**, *3*, 29.
- Q. Ke, M. Costa. Hypoxia-inducible factor-1 (HIF-1). *Mol. Pharmacol.* **2006**, *70*, 1469.
- G. Lippi, G.C. Guidi. Gene manipulation and improvement of athletic performances: new strategies in blood doping. *Brit. J. Sports Med.* **2004**, *38*, 641.
- G. Lippi, M. Franchini, G.C. Guidi. Cobalt chloride administration in athletes: a new perspective in blood doping. *Brit. J. Sports Med.* **2005**, *39*, 872.
- G. Lippi, M. Franchini, G.C. Guidi. Blood doping by cobalt. Should we measure cobalt in athletes? *J. Occup. Med. Toxicol.* **2006**, *1*, 18.
- S. Saxena, D. Shukla, S. Saxena, Y.A. Khan, M. Singh, A. Bansal, M. Sairam, S.K. Jain. Hypoxia preconditioning by cobalt chloride enhances endurance performance and protects skeletal muscles from exercise-induced oxidative damage in rats. *Acta Physiol.* **2010**, *200*, 249.
- E.N.M. Ho, D.K.K. Leung, T.S.M. Wan, A.S.Y. Wong. ICP-MS detection of metallic poisons in equine urine. *Proceedings of the 16th International Conference of Racing Analysts and Veterinarians.* (Eds: E. Houghton, I. Kijima-Suda, R. Wade, J.F. Wade), R&W Communications, Newmarket, **2006**, pp 469–476.

- [19] E.N.M. Ho, T.S.M. Wan, A.S.Y. Wong, K.K.H. Lam, P.J. Schiff, B.D. Stewart. Control of the misuse of bromide in horses. *Drug Test. Anal.* **2010**, *2*, 323.
- [20] S.K. Aggarwal, M. Kinter, D.A. Herold. Determination of cobalt in urine by gas chromatography-mass spectrometry employing nickel as an internal standard. *J. Chromatogr.* **1992**, *576*, 297.
- [21] K. Minakata, M. Suzuki, O. Suzuki. Application of electrospray ionization tandem mass spectrometry for the rapid and sensitive determination of cobalt in urine. *Anal. Chim. Acta* **2008**, *614*, 161.
- [22] E. Dodbiba, C. Xu, E. Wanigasekara, D.W. Armstrong. Sensitive analysis of metal cations in positive ion mode electrospray ionization mass spectrometry using commercial chelating agents and cationic ion-pairing reagents. *Rapid Commun. Mass Spectrom.* **2012**, *26*, 1005.
- [23] H. Vanhoe, C. Vandecasteele, J. Versieck, R. Dams. Determination of iron, cobalt, copper, zinc, rubidium, molybdenum, and cesium in human serum by inductively coupled plasma mass spectrometry. *Anal. Chem.* **1989**, *61*, 1851.
- [24] E. McCurdy, G. Woods. The application of collision/reaction cell inductively coupled plasma mass spectrometry to multi-element analysis in variable sample matrices, using He as a non-reactive cell gas. *J. Anal. Atom. Spectrom.* **2004**, *19*, 607.
- [25] E. Houghton, D.L. Crone. The approaches adopted by the racing industry to address endogenous substances and substances of dietary origin. *Proceedings of the 13th International Conference of Racing Analysts and Veterinarians.* (Eds: R.B. Williams, E. Houghton, J.F. Wade), R&W Communications, Newmarket, **2000**, pp 23–27.
- [26] Y. Bonnaire, L. Dehennin, M.A. Popot, P. Plou. Testosterone in mares and fillies: A new threshold. *Proceedings of the 13th International Conference of Racing Analysts and Veterinarians.* (Eds: R.B. Williams, E. Houghton, J.F. Wade), R&W Communications, Newmarket, **2000**, pp 60–63.
- [27] E.N.M. Ho, W.H. Kwok, D.K.K. Leung, C.M. Riggs, G. Sidlow, B.D. Stewart, A. S.Y. Wong and T.S.M. Wan. Control of the misuse of testosterone in castrated horses based on an international threshold in plasma. *Drug Test. Anal.* **2014**, DOI 10.1002/dta.1681
- [28] F. Ayala-Fierro, J.M. Firriolo, D.E. Carter. Disposition, toxicity, and intestinal absorption of cobaltous chloride in male Fischer 344 rats. *J. Toxicol. Environ. Health A* **1999**, *56*, 571.
- [29] G. Mosconi, M. Bacis, M.T. Vitali, P. Leghissa, E. Sabbioni. Cobalt excretion in urine: results of a study on workers producing diamond grinding tools and on a control group. *Sci. Total Environ.* **1994**, *150*, 133.
- [30] R. Lauwerys, D. Lison. Health risks associated with cobalt exposure — an overview. *Sci. Total Environ.* **1994**, *150*, 1.
- [31] AORC. AORC Guidelines for the Minimum Criteria for Identification by Chromatography and Mass Spectrometry. Available at: <http://www.aorc-online.org/AORC%20MS%20Criteria.pdf> [accessed on 5 Sep 2014]



821 CORPORATE DRIVE · LEXINGTON, KY 40503 · PHONE: 859-224-2844 · FAX: 859-296-3033 · WWW.RMTCNET.COM

RMTC Position Statement on Cobalt

Introduction

Cobalt is an endogenous substance as well as a normal dietary substance in mammals, including the horse. The cobalt dietary requirement for a horse is less than 0.05 ppm.¹ It is used in the incorporation of vitamin B₁₂ in the cecum and colon of the horse.² Strictly speaking, if B₁₂ vitamins are incorporated into the diet, any administration of cobalt is superfluous.

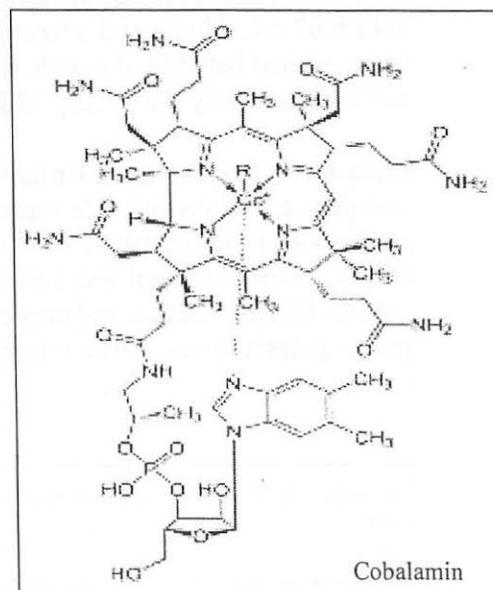
Injectable and oral preparations containing cobalt salts are being administered in various racing breeds across the United States. Although cobalt is a naturally existing and necessary dietary mineral for the horse, it is being administered in very high doses – well in excess of 0.05 ppm. High doses of cobalt containing products are used to increase erythropoiesis. This may allow a horse to oxygenate better than it would in its normal state, a form of “blood doping” similar to treating a horse with human recombinant EPO.

Because cobalt in various forms is a normal dietary component as well as an endogenous substance in the form of cobaltoproteins such as cyanocobalamin or Vitamin B₁₂ in the horse, a threshold must be set to differentiate samples collected from a horse that was normally fed and supplemented from a horse administered an extremely high dose of cobalt in enhance performance. It should be noted, however, that there are no documented cases of cobalt deficiencies in the horse in scientific literature so the use of cobalt containing supplements is unnecessary and medically unjustified.

Chemistry³

Cobalt is an element with the atomic number 27 in the periodic table. In the environment, cobalt is typically found in compounds with other elements. Pure cobalt is a hard, gray, metallic substance. The chemical symbol for cobalt is Co.

Cobalt forms the active center of cobalamins – particularly vitamin B₁₂. In the horse, vitamin B₁₂ creation occurs in the gastro-intestinal tract (specifically the cecum and the colon). Vitamin B₁₂ is used in the production of red blood cells.⁴ Cobalt is also a component of a number of other cobaltoproteins such as aminopeptidase 2, a ubiquitous enzyme involved in peptide synthesis.



¹ Kahn, C.M., *et al.*, The Merck Veterinary Manual, Merck & Co., Inc., (8th Edition) p. 1878 (1998).

² *Id.*

³ See, generally: <http://en.wikipedia.org/wiki/Cobalt>

⁴ Paustenbach, D.J., *et al.*, *A review of the health hazards posed by cobalt*, Critical Reviews in Toxicology, 2013; 43(4): 316-362.

Pharmacokinetics

Absorption

Cobalt is rapidly but incompletely absorbed following ingestion in feeds and supplements. Furthermore, bacteria in the gut utilize cobalt in the biosynthesis of cobalamin. Cobalamin from dietary sources or microbial synthesis binds with intrinsic factor in the digestive tract. The cobalamin-IF complex binds to cubilin, a membrane receptor in the terminal ileum. Upon endocytotic uptake from the ileum, cobalamin dissociates from intrinsic factor and combines with transcobalamin II in which form it enters the blood and is carried to various tissues. The serum concentration of Vitamin B12 in 16 mature, partly warm-blooded, partly Finnish race horses was 1.54 ± 0.16 nanograms per milliliter of serum.⁵

Cobalt as cobalt chloride injected intravenously rapidly binds to serum proteins. The majority of cobalt ends up stored in body tissues such as the liver, skeletal muscle, and other tissues. A portion of the injected cobalt is secreted into the gastrointestinal tract where bacteria utilize it to produce cobalamin. This appears in the systemic circulation within 2 hours after administration of intravenous cobalt indicating rapid synthesis and absorption. Thus, the serum contains cobalt ion bound to serum proteins and cobalt as a component of Vitamin B12-transcobalamin II.⁶

Distribution

Cobalt ion (from cobaltous chloride administration) is widely distributed with an apparent steady-state volume of distribution of 0.74 L/kg. Cobalt ion is slowly transported into erythrocytes via a calcium channel where it binds to cytosolic components. Analysis of total cobalt was performed as it is not certain that bound portions of the cobalt are not metabolically active nor is it clear how various sample handling would alter the amount of cobalt that is free in the sample.

Excretion

Cobalt ion (from cobaltous chloride administration) is cleared slowly with a total clearance estimated to be 0.07 mL/min/kg and a terminal phase half-life estimated to be about 156.4 hours. Due to the long terminal half-life of cobalt, there may be a substantial accumulation factor (~7-fold) if it is administered daily (*i.e.*, every 24 hours) for 3-4 half-lives.

Cobalt as a Performance Enhancer?

Cobalt as cobaltous chloride was used clinically in humans to stimulate erythropoiesis (red blood cell production) from the 1950s-1980s.⁷ This was accomplished through daily doses of cobalt chloride tablets.⁸ This treatment was successful in inducing erythropoiesis in human patients with sickle cell anemia, kidney disease, and cancer.⁹ It was also determined to be effective in inducing erythropoiesis in rats.¹⁰ The international unit for EPO was set as the equivalent of 5 mmol of cobalt.¹¹

⁵ Salminen, K. *Cobalt metabolism in horse. Serum level and biosynthesis of Vitamin B12*. Acta Vet. Scand. 16: 84-94, (1975)

⁶ *Id.*

⁷ Paustenbach, D.J., *et al.*, *A review of the health hazards posed by cobalt*, Critical Reviews in Toxicology, (2013); 43(4): 316-362.

⁸ *Id.*

⁹ Elliott, S., *Erythropoiesis-stimulating agents and other methods to enhance oxygen transport*, British Journal of Pharmacology, (2008) 154(3):529-41.

¹⁰ *Id.*

¹¹ Sytkowki, A.J., *Erythropoietin*, Germany, Wiley-VCH Verlag GmbH & Co, (2004) pp. 5, Print.

Cobalt stimulates synthesis of red blood cells by stabilizing hypoxia inducible factor (HIF).¹² In a normally oxygenated mammal, HIF degrades quickly.¹³ In hypoxia, HIF is stabilized and induces erythropoiesis by upregulating the gene for erythropoietin and related genes.¹⁴

The increased erythropoiesis that occurs as a result of this process, in turn, leads to increased oxygen carrying capacity. Increased oxygen carrying capacity leads to improved performance.

Horses, as all mammals, regulate erythropoietin production through HIFs.¹⁵ In fact, in one case, researchers induced the expression of HIF-1 α by the addition of cobalt chloride.¹⁶ The researchers found that the addition of cobalt chloride to equine tissue “consistently and rapidly induced the expression of HIF-1 α protein.”¹⁷ The increase in expression of the HIFs was 3 fold at 3 and 6 hours, double at 12 hours, and returned to normal at 24 hours.¹⁸

The World Anti-Doping Agency categorizes HIFs as banned substances on its Prohibited Substances List and prohibits enhancing oxygen transport in any manner.¹⁹

Toxicity Issues/Potential Adverse Health Effects

In addition to potential performance enhancing attributes of cobalt, there are a variety of adverse health effects of cobalt use that have been documented in humans and other mammals. Both acute and chronic toxicity issues have been reported.

Acute Toxicity

In three reported human case studies of acute cobalt toxicity following oral ingestion, symptom severity varied. Post oral ingestion, the reported symptoms included stomach mucosa necrosis, vomiting, abdominal pain, brain edema, and death.²⁰ The concentration of cobalt in one of these case studies was as high as 426,000 ppb.

Additionally, research has been done in rats and mice on the effect of a one-time exposure to oral cobalt from a variety of cobalt containing compounds. In those studies, acute oral toxicity symptoms included: diarrhea, ataxia, motor activity reduction, hypothermia, degenerative changes to the liver and heart, and increased blood flow to the kidneys and liver.²¹ Dose-dependent acute toxicity was likely related to the bioavailability of cobalt in the different substances.

¹² *Id.*

¹³ *Id.*

¹⁴ *Id.*

¹⁵ De Ceulaer, K., *et al.*, *Morphological Data Indicate a Stress Response at the Oral Border of Strangulated Small Intestine in Horses*, *Research in Veterinary Science*, (2011); 91:294-300; Deschene, K., *et al.*, *Hypoxia Regulates the Expression of Extracellular Matrix Associated Proteins in Equine Dermal Fibroblasts via HIF1*, *Journal of Dermatological Science* (2012); 65:12-18.

¹⁶ *Id.* at 14.

¹⁷ *Id.*

¹⁸ *Id.*

¹⁹ Knych, H.K., *et al.*, *Detection, Pharmacokinetics and Selected Pharmacodynamics of Cobalt Following a Single Intravenous Administration to Horses*, submitted for publication 8/22/14.

²⁰ Paustenbach, D.J., *et al.*, *A review of the health hazards posed by cobalt*, *Critical Reviews in Toxicology*, 2013; 43(4): 316-362.

²¹ Paustenbach, D.J., *et al.*, *A review of the health hazards posed by cobalt*, *Critical Reviews in Toxicology*, 2013; 43(4): 316-362.

Chronic Toxicity

Toxicity associated with chronic administration of cobalt salts to humans includes various neuropathies, thyroid dysfunction, and heart failure. Chronic exposure to cobalt added to beer to stabilize the foam results in cobalt-beer cardiomyopathy that is characterized by abrupt left ventricular failure, cardiogenic shock, and acidosis.²² The use of cobalt salts as therapeutic agents ceased in the 1980s after toxicity associated with its chronic use was reported in patients and the introduction of human recombinant erythropoietin as a safer and more effective alternative. Specifically, in human studies, a number of effects were associated with chronic cobalt administration. These effects included:

- hematological (polycythemia/increased hematocrit);
- thyroid (decreased iodine uptake causing goiter/hypothyroidism);
- neurologic effects (reversible hearing and vision impairment – particularly at high plasma concentrations);
- cardiac effects (cardiomyopathy – with very high dose); and
- dermatological effects (skin rashes, pimples, dermatitis, dermal flares).²³

In animal studies, the following effects were associated with chronic cobalt administration:

- hematological (increased red blood cells, hemoglobin, hematocrit - rats);
- thyroid (histopathological changes to thyroid – mice, changes in thyroid hormones – rats);
- neurological effects (optic toxicity and auditory system toxicity – rabbits);
- cardiac effects (general – guinea pigs, myocardial degeneration/high mortality – rats, cardiomyopathy – dogs with thiamine deficiency);
- reproductive (decreased sperm concentration in mice, testicular atrophy – rats); and
- kidney and liver (organ damage at high doses – rats and mice).²⁴

Cobalt Research

A number of research projects were performed in order to determine an appropriate regulatory threshold for cobalt in race horses.

The RMTC and the Kentucky EDRC co-sponsored an administration a study of cobalt salts at the University of California Davis under the direction of Dr. Heather Knych and the University of Kentucky's Dr. Cynthia Gaskill. In this study, Dr. Knych administered 100 mg of cobalt chloride salts intravenously into 16 research horses at UC Davis. Blood and urine samples were collected at specific time points over 10 days post administration. Dr. Gaskill analyzed the samples blood and urine samples at the University of Kentucky. The resulting scientific paper describing the pharmacokinetics and pharmacodynamics of cobalt chloride administration has been peer-reviewed and accepted for publication in *Drug Testing and Analysis* and will be available soon. An important finding of this study was a prolonged gamma (elimination) half-life (156.4 hrs) of cobalt in serum, which will be useful in regulating its use.

Additionally, laboratories from University of Kentucky (using Kentucky Equine Drug Research Council funds), Pennsylvania, UC Davis and Truesdail Laboratories (multiple jurisdictions) determined serum cobalt concentrations in samples collected from racing horses tested for cobalt as a

²² Alexander CS. *Cobalt-beer cardiomyopathy. A clinical and pathologic study of twenty-eight cases.* American Journal of Medicine, 53: 395-417, 1972).

²³ *Id.*

²⁴ *Id.*

part of research and/or screening. The inter-laboratory data agreement results showed that the method was transferrable.

The RMTC combined the cobalt serum data from these sources into one population and asked Dr. Ashley Hill to analyze the data. Dr. Hill is an epidemiologist who works with testing laboratory probability calculations for the CAHFS laboratory at University of California Davis. The objective was a threshold for cobalt equivalent of the mean plus 5 standard deviations as was done for arsenic threshold in the late 80's. Five standard deviations is the 99.99997133 percentile and approximately a probability of 1 in 3,487,966 of a false positive.

Dr. Hill performed analyses of the data using all horses (except CA STB's where veterinarians and trainers admitted administering cobalt salts) and with just TBs and QHs (all STBs excluded). Including all horses, the mean plus 5SD (99.99997133 percentile) yielded a threshold of 51 ppb. If two outliers (153 and 338 ppb) suspected of cobalt salt administration were statistically excluded and omitted, the threshold was 36.3 ppb. Similar to the CA data where trainers and veterinarians acknowledged cobalt salt administration, the STB data include some very high values that greatly influence the results. Eliminating all STBs the mean plus 5SD (99.99997133 percentile) was 35.9 ppb.

Because we suspect that a number of horses in the TB population used to develop this threshold have been treated with cobalt, Dr. Hill was tasked to determine the relative risk of a threshold of 25 ppb. A 25ppb threshold using all the QH & TB data is equivalent to 4 standard deviations and carries an estimated risk of a false positive of 1 in 33,000 horses. Note that these calculations using mean plus 4 or 5 times the SD result in higher thresholds than the mean plus 3.72 SD used in IFHA threshold calculations. Dr. Hill had previously determined a cobalt threshold from Quarter Horses in CA which was the only population in that jurisdiction with data that could be normalized and analyzed with standard statistics. Using the CA Quarter Horse sample population (n=43) and otherwise familiar statistical analysis, the equivalent mean + 5SD resulted in a cobalt threshold in serum of 24.57 ppb.

In addition to these studies, Dr. Mary Robinson of the Pennsylvania Equine Toxicology and Research Laboratory and University of Pennsylvania has completed several administrations of cobalt containing supplements. This research consisted of single-dose administration studies of cobalt containing supplements which are routinely administered to racing horses. Based upon the results from those administration studies in research horses as well as other international information, we have determined that it is extremely unlikely that typical cobalt containing substances such as these when used in a normal fashion would cause cobalt concentrations in serum or plasma to exceed a 25 ppb threshold.

The three substances that were investigated were: vitamin B₁₂ (0.07 mg IM), Red Cell (3.9 mg PO), and Vita 15 (2.4 mg IM).²⁵ At no time did the plasma concentration exceed: 1 ppb for vitamin B₁₂, 6 ppb for Red Cell, or 13 ppb for Vita 15.²⁶ Additionally, Dr. Robinson will be investigating a 10 mL dose of vitamin B₁₂ IV. Dr. Robinson's presented the results of this research at the ICRAV conference in September and will be publishing these results in the full proceedings.

²⁵ Robinson, M.A., *et al.*, *Cobalt-Containing Supplements and Sweet Feed Increase Equine Plasma and/or Urine Cobalt Concentrations*, Abstract 20th ICRAV Convention Proceedings, pp. 108.

²⁶ *Id.*

International Research and Collaborations

International cobalt thresholds in urine and blood were discussed extensively at the International Conference of Racing Analysts and Veterinarians (ICRAV) in September 2014. There were a number of presentations on efforts to determine a global threshold for cobalt as well as discussions of existing cobalt thresholds.

New South Wales in Australia is currently using a cobalt threshold of 200 ppb in urine. This threshold is based upon race day sampling where the concentrations of cobalt ranged from 1 to 3,460 ppb.²⁷ The 200 ppb urine threshold was considered as having a 1:50,160 chance of a false positive.²⁸ Australia is amenable to lowering that threshold based upon the international recommendation.²⁹

In addition to the race-day survey completed in Australia, the researchers there also performed several administrations of cobalt containing substances. Five horses were administered Hemo-15 (10 mL containing 7 mg total cobalt) and 10 mls of 150 mg/mL vitamin B-12 IV for three consecutive days.³⁰ In those horses, the blood cobalt concentration peaked at 15 minutes post administration. None of the blood samples exceeded 10 ppb in cobalt.³¹

Additionally, a presentation was made reflecting the ongoing international collaboration on cobalt.³² In this presentation, a review of various survey data was completed from several jurisdictions around the globe.³³ Below is a chart of the respective jurisdictions, number of horses, and resulting thresholds when using the international standard of a 1:10,000 chance of a false positive (*i.e.*, mean plus 3.72 times the SD).³⁴

Jurisdiction	Number of Horses	Statistical Threshold in Plasma
Hong Kong	375	1.14 ppb
United Arab Emirates	103	1.47 ppb
United States (California Data)	125	13.89 ppb

Hong Kong Jockey Club researchers have just published a peer-reviewed scientific paper that recommends a threshold of 2 ppb in serum at mean + 3.72SD (1/10,000 risk).³⁵ The Hong Kong paper includes data on plasma cobalt concentrations found in horses after administration of cobalt containing supplements (Hemo-15™, Hemopar™, Hematinic™, Farrier's Formula, VAM®).³⁶ At all times, after administration of these substances, the total plasma concentrations of cobalt were below 10 ppb.³⁷

²⁷ Wainscott, M., Hibbert, D.B.; *Study of Cobalt in Racing Standardbred Horses*, Abstract 20th ICRAV Convention Proceedings, pp. 46.

²⁸ *Id.*

²⁹ *Id.*

³⁰ *Id.*

³¹ *Id.*

³² Popot, M.A., *et al.*, *An International Collaboration on Cobalt for Setting up a Threshold Value*, Abstract 20th ICRAV Convention Proceedings, pp. 48.

³³ *Id.*

³⁴ *Id.*

³⁵ Ho, E.N.M., *et al.*, *Controlling the Misuse of Cobalt in Horses*, Drug Testing and Analysis, 2014 August 17, doi: 10.1002/dta.1719 [epub ahead of print].

³⁶ *Id.*

³⁷ *Id.*

Several thresholds are being considered across the United States and within the RMTC – based upon serum data from the pharmacokinetic study of cobalt salts in horses, the following will show the length of time that each considered threshold would likely regulate the use of cobalt salts at typical doses reported to be used in race horses. There were 16 horses in the study. The following table reflects the number of horses whose plasma concentration exceeds the suggested threshold at each time compared to the total number of horses in the study (n=16).

	24 hours	36 hours	48 hours	72 hours	96 hours	120 hours	168 hours
25 ppb	16/16	16/16	16/16	16/16	16/16	16/16	11/16
35 ppb	16/16	16/16	16/16	16/16	13/16	9/16	3/16
50 ppb	16/16	15/16	11/16	7/16	4/16	2/16	1/16
70 ppb*	12/16	6/16	3/16	1/16	1/16	0/16	0/16

* This number reflects the proposed threshold from the September 30, 2014 USTA press release.

The 25ppb threshold is the only threshold that regulates the administration of as much as 100mg of cobalt chloride at 5 days and the majority of horses at 1 week.

Pharmacokinetics and selected pharmacodynamics of cobalt following a single intravenous administration to horses

H. K. Knych,^{a,b,*} R. M. Arthur,^c M. M. Mitchell,^a I. Holser,^d R. Poppenga,^{b,d} L. L. Smith,^e M. N. Helm,^e R. A. Sams^f and C. L. Gaskill^e

Cobalt has been used by human athletes due to its purported performance-enhancing effects. It has been suggested that cobalt administration results in enhanced erythropoiesis, secondary to increased circulating erythropoietin (EPO) concentrations leading to improvements in athletic performance. Anecdotal reports of illicit administration of cobalt to horses for its suspected performance enhancing effects have led us to investigate the pharmacokinetics and pharmacodynamic effects of this compound when administered in horses, so as to better regulate its use. In the current study, 18 horses were administered a single intravenous dose of cobalt chloride or cobalt gluconate and serum and urine samples collected for up to 10 days post administration. Cobalt concentrations were measured using inductively coupled plasma mass spectrometry (ICP-MS) and pharmacokinetic parameters determined. Additional blood samples were collected for measurement of equine EPO concentrations as well as to assess any effects on red blood cell parameters. Horses were observed for adverse effects and heart rate monitored for the first 4 h post administration. Cobalt was characterized by a large volume of distribution (0.939 L/kg) and a prolonged gamma half-life (156.4 h). Cobalt serum concentrations were still above baseline values at 10 days post administration. A single administration of cobalt had no effect on EPO concentrations, red blood cell parameters or heart rate in any of the horses studied and no adverse effects were noted. Based on the prolonged gamma half-life and prolonged residence time, regulators should be able to detect administration of a single dose of cobalt to horses. Copyright © 2014 John Wiley & Sons, Ltd.

Keywords: cobalt; horses; detection; pharmacokinetics

Introduction

The use of cobalt as a performance-enhancing agent has been reported in human and equine athletes and stems from reports of beneficial therapeutic effects in the treatment of anaemia in patients suffering from a number of ailments, including chronic renal failure,^[1-4] rheumatoid arthritis,^[5] chronic suppurative infection,^[6] and sickle-cell disease.^[7] Cobalt acts by stabilizing a factor known as hypoxia inducible factor 1 α (HIF1 α). HIF1 α regulates cellular and systemic oxygen homeostasis by binding to DNA coding for genes such as erythropoietin (EPO). Under normoxic conditions, HIF1 α is rapidly degraded. Under hypoxic conditions, or following cobalt administration, degradation of HIF1 α is inhibited, leading to activation of the EPO gene, increasing the number of reticulocytes, red blood cells and hemoglobin.^[8]

While effective in the treatment of anaemia, chronic administration of cobalt, presumably due to deposition of cobalt in tissues and organs, has been associated with a number of toxic effects, which has limited its use as a therapeutic agent. Adverse effects including gastrointestinal sickness, thyroidal dysfunction, and myocardial toxicity^[9] have been reported and as a result much safer agents have replaced the use of cobalt. However, even with the reported adverse effects, the use of cobalt intended as a blood doping agent persists.

It has been postulated that the enhanced erythropoiesis, secondary to increased circulating EPO concentrations, has the potential to improve anaerobic athletic performance in human

athletes.^[10] While cobalt is not specifically prohibited in human sports, the World Anti-Doping Agency (WADA), includes hypoxia-inducible factor stabilizers as banned substances on the 2013 Prohibited Substances List. Even so, the regulation of its use as a substance of abuse is challenging, as cobalt is a

* Correspondence to: H. K. Knych, K.L. Maddy Equine Analytical Chemistry Laboratory, School of Veterinary Medicine, University of California, 620 Health Science Drive, Davis, CA 95616, USA.
E-mail: hkknych@ucdavis.edu

a K.L. Maddy Equine Analytical Chemistry Laboratory, School of Veterinary Medicine, University of California, 620 West Health Science Drive, Davis, CA, 95616, USA

b Department of Veterinary Molecular Biosciences, School of Veterinary Medicine, University of California, One Shields Avenue, Davis, CA, 95616, USA

c School of Veterinary Medicine, University of California, One Shields Avenue, Davis, CA, 95616, USA

d California Animal Health and Food Safety Laboratory, School of Veterinary Medicine, University of California, 620 West Health Science Drive, Davis, CA, 95616, USA

e University of Kentucky Veterinary Diagnostic Laboratory, Department of Veterinary Science, University of Kentucky, 1490 Bull Lea Road, Lexington, KY, 40511, USA

f LGC Science, Inc., 1745 Alysheba Way #160, Lexington, KY, 40509, USA

naturally occurring substance in the body and it is virtually impossible to differentiate between exogenous and endogenous sources. Although distinguishing exogenous cobalt from endogenous may not be possible, the large volume of distribution and the prolonged elimination half-life in humans^[11-13] may prove valuable in regulating the abuse of cobalt in athletes by establishing a threshold level. To the authors' knowledge, the pharmacokinetics of cobalt in the horse have not been described and the administration of cobalt to horses as a potential performance enhancing agent, necessitates further study of this substance so as to better regulate its use. The purpose of the current study was to describe the pharmacokinetics of cobalt following intravenous administration to horses. Secondly, because of the erythropoietic effects associated with use of cobalt in humans and anecdotal reports of adverse reactions in horses during intravenous cobalt administration we sought to describe select physiologic effects of cobalt administration to horses.

Experimental

Animals

Prior to the full pharmacokinetic study, a pilot study was conducted to evaluate potential adverse effects following intravenous cobalt administration, to determine the optimal sample collection tube type for cobalt analysis, and to select the cobalt formulation to use for the full PK study. For the pilot study, two university owned research horses, including one Thoroughbred and one Quarter Horse mare (ages: 17 and 22 years of age; weight: 552 and 634 kg) were studied. For the full PK study, 16 university-owned and exercised adult Thoroughbred horses including 8 geldings and 8 mares (age: 4-7 years; weight: 494-626 kg) were studied. Prior to and throughout the course of the study, horses were exercised five days a week. The general exercise protocol was meant to simulate the strenuous exercise of race training. The exercise regimen for these horses consists of three days per week on an Equineciser (Centaur Horse Walkers Inc., Mira Loma, CA, USA) (5 min walk; 30 min trot; 5 min walk) and two days per week on a high speed treadmill (Mustang 2200, Graber AG, Switzerland; Day 1: 5 min @ 1.6 m/s; 5 min @ 4 m/s; 5 min @ 7 m/s; 5 min @ 1.6 m/s all at 6% incline. Day 2: 3 min @ 1.6 m/s; 4 min @ 4.0 m/s; 2 min @ 7.0 m/s; 2 min @ 11.0 m/s and 5 min @ 1.6 m/s all at 3% incline). All horses were subject to regular fitness testing, including weekly heart rate measurements and calculation of V_{200} (running velocity that elicited a heart rate 200 bpm) and monthly measurements of end run plasma lactate concentrations, as a means by which to ensure that the fitness level of the horses used in this study were as comparable as possible to the average racehorse.

Before beginning the study, horses were determined healthy and free of disease by physical examination, complete blood count, and a serum biochemistry panel that included aspartate aminotransferase, creatinine phosphokinase, alkaline phosphatase, total bilirubin, sorbitol dehydrogenase, blood urea nitrogen, and creatinine. Blood analyses were performed by the Clinical Pathology Laboratory of the William R. Pritchard Veterinary Medical Teaching Hospital of the University of California, Davis, using their standard protocols. Horses did not receive any medication for at least two weeks prior to commencement of this study or any vitamin or mineral supplements for a minimum of twelve months prior to cobalt administration. Food and water were available *ad libitum* throughout the duration of the study. This study was approved by the Institutional Animal Care and Use Committee of the University of California, Davis.

Instrumentation and cobalt administration

A14-gauge catheter was aseptically placed in each external jugular vein. The right jugular vein catheter was used for cobalt administration while the contralateral catheter was used for sample collection. The right jugular vein catheter was removed following dosing. For the pilot study, one horse received 169 mg of cobalt gluconate (equivalent to 22 mg of cobalt) and one horse received 109 mg of cobalt chloride (equivalent to 49 mg of cobalt). The dosing formulation was randomly assigned to each horse using a computerized random number generator. For the full PK study, all horses received cobalt chloride. As there is currently no commercially available FDA approved injectable cobalt formulation, the products used in the current study were purchased from a compounding pharmacy. The concentration of each formulation was measured as described in the Sample Analysis section below. For administration, the doses of either cobalt chloride or cobalt gluconate were diluted in 1 L of Lactated Ringers Solution and administered over 10 min via the intravenous catheter. Upon completion of administration, the catheter was flushed with heparinized saline (10 IU/mL).

Sample collection

Blood samples were collected at time 0 (prior to the start of the cobalt infusion) and at 5 and 10 min following commencement of the infusion. Additional samples were then collected at 5, 10, 15, 30, and 45 min, and 1, 2, 3, 4, 5, 6, 8, 12, 18, 24, 36, 48, 72, 96, 120, 168, and 240 h following completion of the 10 min infusion. Prior to drawing each sample of blood for analysis of cobalt concentrations, 10 mL of blood was aspirated and discarded from the catheter and T-Port extension set (combined internal volume <2 mL). The catheter was flushed with 10 mL of a dilute heparinized saline solution (10 IU/mL) following each sampling time. The jugular vein catheter, used for sample collection, was removed following the 18-h sample collection and the remaining samples collected via direct venipuncture. Blood samples were collected into serum separator tubes and placed at room temperature prior to centrifugation at 3000 rpm for 10 min at 4°C. Serum was then immediately transferred into storage cryovials (Phenix Research Products, Chandler, NC, USA) and stored at -20°C until analysis. For the horse receiving the cobalt chloride formulation in the pilot study, two additional sets of blood samples were collected, one set in trace metal free serum tubes (Becton Dickinson, Franklin Lakes, NJ, USA) and a second set in trace metal free tubes containing K2EDTA (Becton Dickinson, Franklin Lakes, NJ, USA), for comparison of cobalt concentrations between different tube types. Samples were collected at 0 (immediately prior to cobalt administration) and 30 min, 4, 12, and 48 h and 5 and 7 days post cobalt chloride administration. Samples were stored as described above for the first set of samples.

Urine samples were collected at time 0 (immediately prior to cobalt administration) and at 4, 24, 48, 72, 96, 120, 168, and 240 h post cobalt administrations for the pilot and full PK study. Urine samples were collected either by free catch or urinary catheterization (mares) when necessary. Urine samples were stored at -20°C until analysis.

Determination of cobalt concentrations

Analyses of the dosing solutions as well as cobalt concentrations for the pilot study were conducted at the California Animal Health and Food Safety Laboratory at the University of California, Davis (UCD) and analyses of samples generated from the full PK study were performed at the University of Kentucky Veterinary Diagnostic

Laboratory (UK). Quantitative methods for determining total cobalt in serum and urine by ICP-MS as described for the full PK study were based on previously published methods.^[14] Complete method validation was performed prior to this study and relevant analytical figures of merit were determined. The instrument response was linear with respect to cobalt concentration over a range of 0.038 to 38.5 ng/mL. The upper limit of the linear dynamic range remains unknown; however quantitative results for all samples in the PK study were within the established range. Average recoveries and inter-assay variation coefficients were determined to be 89.2% and 1.99% for newborn calf serum overspiked at 1.000 ng/mL and 88.5% and 2.84% when overspiked at 10.00 ng/mL. Likewise, the average recovery for overspiked urine positive controls, analyzed concurrently with the study samples, was 99.8% and 4.56%. Further, the method limit of quantitation was determined to be 1.0 ng/mL. Method validation at UCD was done with reference materials NIST 1640 water with a certified value of 20.28 ng/mL and QMEQAS09B-05 blood from INSPQ (Institut national de santé publique) with a value of 4.64 ng/mL. Average recoveries and inter-assay variation coefficients were determined to be 96.9% and 9.85% for NIST 1640 and 92.7% and 8.9% for QMEQAS09B-05. Similar analytical instrumentation and operating conditions were used in both laboratories. Unless otherwise specified, all analytical instrumentation and acquisition parameters were equivalent between UCD and UK.

Ethylenediaminetetraacetic acid (EDTA in acid form; Trace Metal Grade (99.9% pure) and Triton X-100 were obtained from Sigma Aldrich (St. Louis, MO, USA). Ammonium hydroxide (Trace analysis grade), nitric acid (TraceMetal grade) and butanol (99.5%) were obtained from Thermo Fisher Scientific (Pittsburgh, PA, USA). Calibration standard solutions for analysis of the pilot samples (UCD) were prepared by diluting from single element standards of 1000 µg/mL (Inorganic Ventures; Christiansburg, VA, USA) and those for the full PK study (UK) from a custom-mixed multi-element standard solution (Inorganic Ventures) that contained 10 µg/mL cobalt. The internal standard solution was prepared from a commercially available multi-element standard solution that contained 100 µg/mL germanium (Inorganic Ventures, Christiansburg, VA, USA). Distilled, deionized water was prepared in-house using a Barnstead Mega-Pure distillation system (Model MP-6A) and a Barnstead EASYpure II RF water conditioner (Model D7031; Thermo Scientific, Dubuque, IA, USA).

Urine and serum samples were stored at -20 °C until analysis. On the day of analysis, samples were allowed to completely thaw at room temperature (20 °C to 21 °C), mixed by vortex-pulsing, and as needed, centrifuged at 3000 rpm for 10 min to pellet any undissolved particulate material in the bottom of the tube. A 200-µL aliquot of each sample (or supernatant fluid) was transferred to a labelled, 15-mL disposable centrifuge tube and diluted by the addition of 5-mL ICP-MS diluent. The ICP-MS diluent used for the pilot study analysis (UCD) consisted of 0.5% (v/v) nitric acid, 0.05% (w/v) Triton X-100, 2% (v/v) isopropanol and 5 ng/mL bismuth (²⁰⁹Bi). The ICP-MS diluent used for analysis of samples generated from the full PK study (UK) was an aqueous mixture of 0.05% (w/v) EDTA, 1.0% (w/v) ammonium hydroxide, 0.05% (w/v) Triton X-100 and 2.0% (w/v) butanol (2.0% (w/v)) that contained a final concentration of 15 ng/mL germanium. Aliquots (200-µL) of calibrant solutions were also diluted with 5-mL ICP-MS diluent.

The pilot study (UCD) used NIST 1640 water, QMEQAS09B-05 blood as reference materials and equine serum from Sigma (Lot H1270) as a control. The Sigma equine serum was run in duplicate with a sample fortified at 10 ng/mL cobalt. Baseline urine from the

cobalt gluconate dosed horse was used as a control and was run in duplicate with a spiked sample at 10 ng/mL cobalt. For the full PK study (UK), control samples were analyzed immediately following calibration and after every 10 to 12 samples throughout the daily sample batch. Positive controls were matrix matched or matched to the expected cobalt concentrations for the samples. Positive controls included Newborn Calf Serum (Cell Culture Grade; Sigma Aldrich, St Louis, MO, USA) fortified with 1 ng / mL cobalt and urine collected from a control horse fortified with 10 ng/mL cobalt. Negative controls were either 10% (w/w) nitric acid in distilled deionized water or control equine urine that was not fortified with cobalt. Aliquots (200 µL) from each of these control solutions were diluted with 5-mL ICP-MS diluent.

An Agilent 7500ce octapole reaction system inductively coupled plasma mass spectrometer (ORS)-ICP-MS; Agilent Technologies, Tokyo, Japan) operating in helium mode was used for cobalt analyses at both UCD and UK. It was equipped with a Micromist concentric glass nebulizer, a double-pass Scott-type spray chamber cooled to 2 °C, and a peristaltic pump set at 0.10 rps for sample aerosolization and introduction to the torch. The configuration of the (ORS)-ICP-MS is such that ions pass through an octapole reaction cell immediately before mass analysis in the quadrupole mass analyzer of the ICP-MS. This cell was pressurized with helium gas to minimize polyatomic interferences arising from either sample matrix components or environmental conditions that impede analysis. Operation instrumental conditions and measurement parameters are provided in Table 1. The quadrupole mass analyzer was set to perform sequential single-ion monitoring to detect the signals for *m/z* 59 and 72, corresponding to singly-charged radical cations of isotopes ⁵⁹Co and ⁷²Ge. In the preliminary study *m/z* 209, corresponding to ²⁰⁹Bi was run in place of *m/z* 72.

The ratio of the detected signals for ⁵⁹Co and ⁷²Ge was plotted against the concentration of cobalt in the calibrant solutions to create calibration curves on a daily basis. Cobalt concentrations were interpolated from the linear trendline of the corresponding calibration curve and reported. Because the calibrant solutions, controls and samples were all diluted in the same manner, the dilution factor for the analyses was 1. Serum and urine cobalt results were reported in ng/mL. The minimum level of quantitation (MLQ) for the method was 1.0 ng/mL.

Table 1. (ORS)-ICP-MS operating conditions and measurement parameters

Parameter	Setting
RF Power	1500 W
Sample uptake rate	0.10 rps
Carrier gas flow rate	0.90 L/min
Makeup gas flow rate (Argon)	0.22 L/min
Nebulizer gas flow rate (Argon)	0.22 L/min
Signal Measurements Parameters	
Isotopes	⁵⁹ Co and ⁷² Ge (as an internal standard)
Samples per peak	3
Sample time per point	1.5 for ⁵⁹ Co / 0.1 for ⁷² Ge
Number of replicates	3
Reaction Cell Parameters	
Helium gas flow rate	3.4 – 4.0 mL/min (optimized daily)
Octapole bias	-18 V
Quadrupole bias	-15 V

Pharmacokinetic calculations

Compartmental analysis was used for determination of pharmacokinetic parameters for cobalt using commercially available software (Phoenix WinNonlin Version 6.0, Pharsight, Cary, NC, USA). The area under the curve and area under the moment curve were calculated using the log up-linear down trapezoidal method and extrapolated to infinity using the last measured serum concentration divided by the terminal slope λ_2 .

Determination of RBC parameters

Red blood cell (RBC) parameters, including total RBC count, hemoglobin, haematocrit, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and red cell distribution width (RDW) were assessed prior to cobalt administration and on days 4, 7, and 10. Blood samples were collected as described for determination of cobalt concentrations into blood tubes containing EDTA. Red blood cell analyses were performed using a Siemens ADVIA® 120 Hematology System (Siemens Medical Solutions USA, Inc., Malvern, PA, USA) by the Clinical Pathology Laboratory of the William R. Pritchard Veterinary Medical Teaching Hospital of the University of California, Davis, using their standard protocols.

Determination of EPO concentrations

Samples for determination of EPO concentrations were collected in serum separator tubes as described above and stored at 4 °C. Serum EPO concentrations were measured within 24 h of collection of the final sample (10 days post cobalt administration) at the K.L. Maddy Equine Analytical Chemistry Laboratory using a commercially available equine ELISA kit (CUSABIO kit, Life Sciences Advanced Technologies, Inc., St Petersburg, FL, USA) according to the manufacturer's protocol. One hundred μ L of undiluted serum from each sample was tested. Samples were run in duplicate at each time point for each horse and the average value reported. The ELISA plates were read at 450 nm with wavelength correction set to 540 nm on a Tecan Sunrise™ instrument using their Magellan™ Data Analysis Software (Tecan Trading AG, Mannedorf, Switzerland). Data were analyzed using CurveExpert Professional 1.3 (Daniel G. Hyams, Hixon, TN, USA) by generating a standard curve using a four parameter logistic (4-PL) curve fit.

Monitoring of behavioural and physiologic parameters

Horses were unrestrained for the duration of the study and were only restrained, if necessary, for sample collection. Horses were continuously monitored for any adverse or behavioral effects for 8 h post cobalt administration. Subsequent observations were made prior to blood sample collection at each time point. All assessments were made from outside the stall. Horses were equipped with a Holter monitor (Forrest Medical, East Syracuse, NY, USA) to assess any potential effect on heart rate and rhythm. Heart rate and rhythm were recorded continuously for a minimum of 30 min pre and 4 h post cobalt administration. Heart rate was determined at pre-determined time points via manual counting of P-QRS-T complexes over a 1-min time period. The percentage of atrial signals blocked by the atrio-ventricular node before and after cobalt administration was calculated using the formula, (atrial rate – ventricular rate)/atrial rate. The atrial and ventricular rates were determined by manually counting P waves and P-QRS-T complexes, respectively, over a 1-min period at pre-determined time points.

Statistical analysis

Statistical analyses, using commercially available software (SAS, Cary, NC, USA), were performed to assess significant differences in EPO concentrations, RBC parameters, heart rate and %AV block both pre and post cobalt administration for individual horses. Raw data for all variables were checked for normality using the Wilk-Shapiro test and then log transformed as necessary to bring the residual distribution in close agreement with a normal distribution. Data for all variables were subsequently analyzed using a mixed model ANOVA with repeated measures. Significance was set at $p < 0.05$.

Results

The compounded cobalt dosing solutions were tested for potency by measuring their cobalt concentrations. The calculated cobalt chloride concentration was 109 mg/mL (labelled as 200 mg/mL), based upon a measured cobalt concentration of 49 mg/mL and the calculated cobalt gluconate concentration was 1.69 mg/mL (labelled as 2 mg/mL) based upon a measured cobalt concentration of 0.22 mg/mL.

Cobalt serum concentrations were comparable between the serum and the trace metal free tubes (Table 2). Cobalt concentrations

Table 2. Cobalt concentrations in whole blood and serum following intravenous administration of 109 mg of cobalt chloride to one horse in the pilot study. The limit of quantitation of the analytical method was 1.0 ng/mL

Time	Whole Blood Concentration (ng/mL)	Serum Concentration (ng/mL)	Serum Concentration (trace element free tubes) (ng/mL)
Baseline	< 1.0	< 1.0	< 1.0
30 minutes	305	429	431
4 hours	164	236	237
12 hours	106	146	148
48 hours	46	78	80
5 days	25	53	61
7 days	23	68	NS

NS, no sample collected.

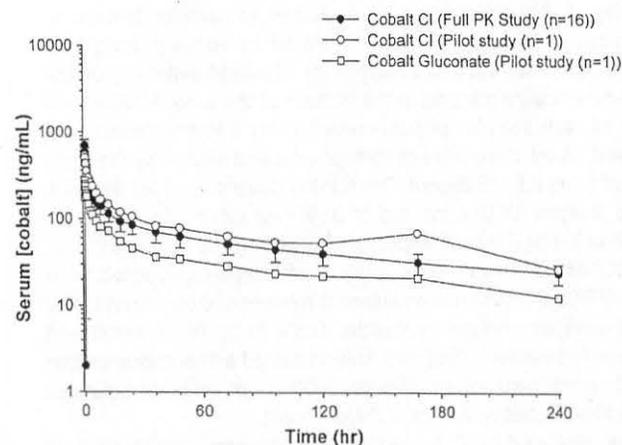


Figure 1. Serum cobalt concentration versus time curve following intravenous administration of 109 mg of cobalt chloride (49 mg of cobalt) or 169 mg of cobalt gluconate (22 mg of cobalt) to horses.

were 1.4–3.0 times higher in serum as compared to whole blood at the time points selected for measurement (Table 2). Cobalt serum concentration versus time curves for the pilot and full PK studies are depicted in Figure 1. Cobalt was detected in all pre-administration samples but the average concentration was below

the LOQ of 1 ng/mL in serum. Cobalt concentrations remained above baseline values at 10 days post administration (the last time point sampled). Based on coefficient of variation, Akaike Information Criterion^[15] and visual inspection of the residual plots, a three-compartment model infusion model ($C_p = Ae^{-\alpha t} - e^{-\alpha t^*} + Be^{-\beta t}$)

Table 3. Pharmacokinetic parameters of cobalt following a single intravenous administration of 49 mg of cobalt (109 mg cobalt chloride) or 22 mg cobalt (169 mg cobalt gluconate) to 2 sedentary research horses. All values in this table were generated using compartmental analysis

	AUC _{0-inf} (h*µg/mL)	AUMC (h*h*µg/mL)	MRT (h)	Vd _{ss} (L/kg)	V ₁ (L/kg)	V ₂ (L/kg)	V ₃ (L/kg)	Alpha HL (h)	Beta HL (h)	Gamma HL (h)	Cl (mL/min/kg)
Co chloride	21.9	3984	182	0.737	0.099	0.124	0.514	0.143	4.45	137	0.068
Co gluconate	9.79	1841	188	0.667	0.118	0.086	0.426	0.536	6.43	147	0.059

Table 4. Pharmacokinetic parameters of cobalt following a single intravenous administration of 49 mg of cobalt as cobalt chloride to 16 exercised Thoroughbred horses. All values in this table were generated using compartmental analysis.

	AUC _{0-inf} (h*µg/mL)	AUMC (h*h*µg/mL)	MRT (h)	Vd _{ss} (L/kg)	V ₁ (L/kg)	V ₂ (L/kg)	V ₃ (L/kg)	Alpha HL (h)	Beta HL (h)	Gamma HL (h)	Cl (mL/min/kg)
Horse 1	14.0	2567	184	1.22	0.176	0.232	0.809	0.630	6.45	141	0.111
Horse 2	21.0	3350	159	0.679	0.130	0.074	0.475	0.640	4.02	120	0.071
Horse 3	21.0	5240	249	1.12	0.162	0.246	0.709	1.16	13.9	200	0.075
Horse 4	16.5	3023	184	1.00	0.125	0.130	0.741	0.788	6.12	145	0.091
Horse 5	15.7	2516	160	0.80	0.128	0.143	0.524	0.951	8.11	128	0.083
Horse 6	21.6	4598	213	0.922	0.169	0.161	0.592	0.679	6.87	161	0.072
Horse 7	17.6	3917	223	1.10	0.155	0.165	0.784	1.14	8.56	176	0.083
Horse 8	44.7	14341	321	0.713	0.148	0.193	0.372	1.66	23.3	253	0.037
Horse 9	31.5	12016	382	1.13	0.168	0.305	0.653	1.68	25.8	306	0.049
Horse 10	17.6	2733	156	0.806	0.157	0.151	0.500	0.981	8.49	123	0.086
Horse 11	19.1	2731	143	0.731	0.053	0.015	0.528	0.021	2.49	106	0.085
Horse 12	17.5	2666	152	0.839	0.044	0.114	0.682	0.022	3.00	117	0.092
Horse 13	13.9	2031	146	0.938	0.133	0.198	0.607	0.418	6.17	114	0.106
Horse 14	14.3	2107	148	0.926	0.084	0.143	0.699	0.082	2.68	111	0.104
Horse 15	23.3	4548	195	0.833	0.125	0.139	0.568	0.393	5.50	148	0.071
Horse 16	13.3	2465	185	1.28	0.116	0.188	0.978	0.347	5.72	148	0.116
Mean	20.2	4428	200	0.939	0.129	0.162	0.639	0.72 [†]	8.63 [†]	156 [†]	0.083
Median	17.6	2878	184	0.924	0.131	0.156	0.630	0.66	6.52	146	0.084

AUC_{0-inf}, area under the plasma concentration time curve from 0 to infinity; AUMC, area under the moment curve; MRT, mean residence time; Vd_{ss}, volume of distribution at steady state; Cl, clearance. [†] harmonic mean

Table 5. Urine cobalt concentrations following intravenous administration of 49 mg of cobalt as cobalt chloride or 22 mg cobalt as cobalt gluconate to horses

Time (hr)	Pilot Study		Full Study	
	Co Chloride (n = 1) (ng/mL)	Co Gluconate (n = 1) (ng/mL)	Co Chloride (n = 16) Mean (±SD) (ng/mL)	Median (ng/mL)
Baseline	< 1	< 1	2.3 ± 1.2	2
4	7687	3281	3855 ± 1378	3511
24	730	498	240 ± 69	222
48	295	108	91 ± 37	87
72	221	67	48 ± 21	53
96	125	41	34 ± 10	29
120	90.0	30	29 ± 8	29
168	50	47	18 ± 5	20
240	NS	NS	14 ± 5	13

NS, no sample collected.

Table 6. Red blood cell parameters following intravenous administration of 49 mg of cobalt (109 mg cobalt chloride) to 16 horses

	RBC (M/ μ L)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)
Baseline	8.6 \pm 0.5	14.2 \pm 0.9	40.1 \pm 2.3	46.8 \pm 1.3	16.6 \pm 0.4	35.4 \pm 0.6	16.7 \pm 0.5
Day 4	8.4 \pm 0.5	13.9 \pm 0.8	40.5 \pm 2.2	48.5 \pm 1.4	16.6 \pm 0.5	34.2 \pm 0.7	19.0 \pm 1.0
Day 7	8.2 \pm 0.5	13.6 \pm 0.8	38.5 \pm 2.1	46.9 \pm 1.4	16.6 \pm 0.6	35.4 \pm 0.8	16.6 \pm 0.3
Day 10	8.1 \pm 0.5	13.5 \pm 0.9	38.6 \pm 2.4	47.8 \pm 1.8	16.7 \pm 0.5	34.9 \pm 1.0	18.1 \pm 1.4

RBC, red blood cell count; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin, MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width.

$t - e^{-Bt^*} + C^{\gamma t} - e^{-\gamma t^*}$) with a weighting factor of 1/ gave the best fit to cobalt concentration data points from individual animals. Pharmacokinetic modeling was based on the measured cobalt concentrations. Selected pharmacokinetic parameters are listed in Tables 3 and 4 for the pilot and full studies, respectively. The volume of distribution was large and cobalt demonstrated a prolonged gamma half-life. Cobalt urine concentrations are reported in Table 5 for both studies. Urine cobalt in pre-administration samples averaged 2.3 ± 1.2 ng/mL in the 16 exercised horses.

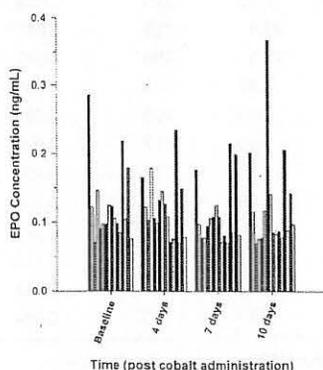
No adverse reactions or behavioral effects were noted at any time post cobalt administration. There were no significant differences noted in red blood cell parameters (Table 6) or EPO concentrations (Figure 2) at any of the time points assessed following cobalt administration. Changes in heart rate ranged from -6.7% (decrease from baseline) to +6.8% (increase from baseline). The %AV

block, relative to baseline, ranged from 1.6 to 7.8%. Changes in heart rate and % AV block, were not significantly different from baseline at any time post cobalt administration.

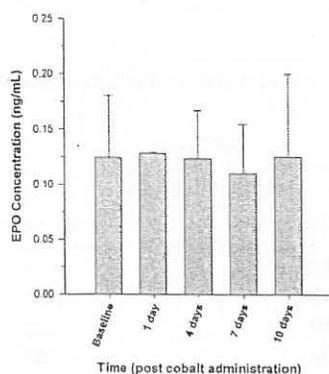
Discussion

Anecdotal reports of illicit administration of cobalt salts at doses in excess of 200 mg to performance horses, for its suspected performance enhancing effects has led us to investigate the pharmacokinetics and pharmacodynamic effects of cobalt chloride and cobalt gluconate when administered to this species. A pilot study was conducted initially due to anecdotal reports of toxicity following intravenous cobalt administration. For the pilot study, two commonly used formulations of cobalt (cobalt gluconate and cobalt chloride) were administered, and although only one horse was studied per formulation, the pharmacokinetic parameters were comparable between the two. Cobalt chloride was chosen for the full study because it was readily available. It is important to note that as there is no Food and Drug Administration approved injectable product, cobalt formulations were purchased from a compounding pharmacy for use in the current study. As such, the actual concentration of the product was measured to ensure that it was the same as described on the label. In this case, both cobalt gluconate and cobalt chloride concentrations in the purchased products were much less than the labelled concentration. However, while concentrations were lower in the current study this may not always be the case. The potential for higher than labelled concentrations, raises concerns with respect to potential dose dependent adverse effects, associated with the higher concentrations.

Following injection of radiolabelled cobalt chloride to laboratory animals, cobalt reportedly concentrates in the liver, kidneys, skeleton and skeletal muscle. Hollins and McCullough^[16] reported that at 1072 h post intraperitoneal administration of radiolabelled cobalt chloride, the liver, skeleton and muscle contained 20–25% of total body activity with 7–8% accumulating in the kidney. In the same study, at 386 days post administration, 65% of the total body activity was localized in the skeleton and 7% in the liver. In mice, cobalt disappearance from blood was nearly complete 24 h after injection of cobalt chloride.^[17] Interestingly, at 24 h onwards, large concentrations of cobalt were found in cartilage of the trachea and larynx and bones of the skull, the periosteum of the vertebrae and the pelvic bone.^[17] While it was not possible to determine the distribution pattern of cobalt in the current study, based on the large volume of distribution ($V_{d_{ss}}$: 0.93 L/kg), cobalt also appears to be widely distributed in horses. This is similar to previous reports in humans, whereby the $V_{d_{ss}}$ was reported to be 0.6 L/kg following intravenous administration of radiolabelled cobalt chloride.^[13] In that same study, the investigators hypothesized, based on a whole body scan, that the large $V_{d_{ss}}$ was due to accumulation of cobalt (50% of the dose) in the liver.^[13]



A. Erythropoietin (EPO) concentrations in individual horses following a single intravenous administration of 109 mg/mL (49 mg of cobalt) to 16 exercised Thoroughbred horses



B. Average erythropoietin (EPO) concentrations following a single intravenous administration of 109 mg/mL (49 mg of cobalt) to 16 exercised Thoroughbred horses.

Figure 2. (A) Erythropoietin (EPO) concentrations in individual horses following a single intravenous administration of 109 mg/mL (49 mg of cobalt) to 16 exercised Thoroughbred horses. (B) Average erythropoietin (EPO) concentrations following a single intravenous administration of 109 mg/mL (49 mg of cobalt) to 16 exercised Thoroughbred horses.

In addition to concentrating in a number of organs, cobalt is capable of partitioning into red blood cells (RBC). Partitioning of cobalt into RBCs has been attributed to calcium pumps and uptake appears to be irreversible due to binding of cobalt to cytosolic components.^[18] While cobalt can reach high concentrations in RBCs relative to serum, in rats this occurs only after long-term exposure.^[19] Following short-term exposure, the majority of administered cobalt is found in serum, with concentrations 1.2-fold higher than that in RBCs.^[12,20] This is in close agreement with the results of serum and whole blood analysis in the current study, whereby concentrations of cobalt in whole blood were lower than that of serum at the time points selected for testing (Table 2; baseline to 7 days post administration) following a single administration (short-term exposure). However, it is important to note that this profile may change following chronic administration of cobalt to horses.

Of particular importance when regulating the use of cobalt in performance horses is that cobalt administration appears to be associated with long-term retention, which may aid in detecting illicit administration. In the presently reported study, the gamma half-life was prolonged following intravenous administration (4.4 to 10.5 days); however, it is important to note that serum concentrations were above the pre-dose concentration were still easily quantifiable in the last sample collected. The elimination half-life of inorganic cobalt in humans varies greatly from study to study and appears to be dependent upon the duration of sample collection.^[21] Reports of very prolonged biological half-lives for cobalt in humans are common.^[11,12,22,23] In one study, following a single intravenous dose to humans, 40% of the administered cobalt was excreted during the first 24 h post administration and 70% within one week.^[12] In that same study, 10% of the administered dose was still present one-year post cobalt administration.^[12]

The effectiveness of cobalt in increasing RBC production has been demonstrated in humans.^[1-7] In the current study, there was no significant change in EPO concentrations following cobalt administration over the 10-day study period. It should be noted, however, that only a single cobalt administration was studied and the results may be different with multiple or chronic administration. Even if cobalt is ultimately proven to increase RBC production in horses, extrapolation from one species, especially human to horse, should be done with extreme caution. Unlike humans, horses, because of their contractile spleen, are capable of haemoconcentration. With respect to fit racehorses, haematocrit can easily reach up to 65% when running at VO₂ max. If cobalt does in fact increase RBCs in horses, administration to a racehorse that is already reaching a haematocrit of 65% can increase the potential for adverse cardiovascular complications.

In summary, this study described plasma and urine cobalt concentrations following intravenous administration of cobalt chloride and cobalt gluconate. The rapid rise in cobalt concentrations over baseline levels, the prolonged retention time and subsequent long gamma half-life suggest that detection of cobalt administration may be possible for several days and possibly weeks following administration of a single dose. Although EPO concentrations did not change in the current study and no adverse effects were noted, further study may be necessary to determine if this occurs with long-term exposure.

Acknowledgements

Financial support for the cobalt administration portion of this project was provided by the Racing Medication and Testing

Consortium. Analysis of serum and urine concentrations for the full study was conducted at the University of Kentucky, Veterinary Diagnostic Laboratory with funding provided by the Kentucky Equine Drug Research Council. The authors would like to acknowledge Dr Eugene Steffey for editorial assistance, Dr Neil Willits for assistance with statistical analysis and Stacy Steinmetz, Haley Casbeer, Alex White, Sabine Hargrave, Nadia Chapman and Madison Herick for technical support.

References

- [1] E.A. Bowie, P.J. Hurley. Cobalt chloride in the treatment of refractory anaemia in patients undergoing long-term haemodialysis. *Aust. NZ J. Med.* **1975**, *5*, 306.
- [2] J.R. Curtis, G.C. Goode, J. Herrington, L.E. Urdaneta. Possible cobalt toxicity in maintenance hemodialysis patients after treatment with cobaltous chloride: A study of blood and tissue cobalt concentrations in normal subjects and patients with terminal and renal failure. *Clin. Nephrol.* **1976**, *5*, 61.
- [3] J.M. Duckham, H.A. Lee. The treatment of refractory anaemia of chronic renal failure with cobalt chloride. *Q. J. Med.* **1976**, *45*, 277.
- [4] F.H. Gardner. The use of cobaltous chloride in the anemia associated with chronic renal disease. *J. Lab. Clin. Med.* **1953**, *41*, 56.
- [5] P.P. Weinsaft, L.H. Bernstein. Cobaltous chloride in the treatment of certain refractory anemias. *Am. J. Med. Sci.* **1955**, *230*, 264.
- [6] J.C. Robinson, G.W. Jame, R.M. Kark. The effect of oral therapy with cobaltous chloride on the blood of patients suffering with chronic suppurative infection. *New Engl. J. Med.* **1949**, *240*, 749.
- [7] J. Wolf, I.J. Levy. Treatment of sickle cell anemia with cobalt chloride. *AMA Arch. Intern. Med.* **1954**, *93*, 387.
- [8] L. Weißbecker. Die kobalttherapie. *Dtsch. Med. Wochenschr.* **1950**, *75*, 116.
- [9] B. Ebert, W. Jelkmann. Intolerability of cobalt salt as an erythropoietic agent. *Drug Test. Anal.* **2014**, *6*, 185.
- [10] G. Lippi, M. Franchini, G.C. Guidi. Blood doping by cobalt: Should we measure cobalt in athletes? *J. Occup. Med. Toxicol.* **2006**, *18*, 1.
- [11] E.G. Letourneau, G.C. Jack, R.S. McCullough, J.G. Hollins. The metabolism of cobalt by the normal human male: Whole body retention and radiation dosimetry. *Health Phys.* **1972**, *22*, 451.
- [12] T. Smith, C.J. Edmonds, C.F. Barnaby. Absorption and retention of cobalt in man by whole-body counting. *Health Phys.* **1972**, *22*, 359.
- [13] H.M.L. Jansen, S. Knollema, L.V. van der Duin, A.T.M. Willemsen, A. Wiersma, E.J.F. Franssen, F.G.M. Russel, J. Korf, A.M.J. Paans. Pharmacokinetics and dosimetry of cobalt-55 and cobalt-57. *J. Nucl. Med.* **1996**, *37*, 2082.
- [14] R. Wahlen, L. Evans, J. Turner, R. Hearn. The use of collision/reaction cell ICP-MS for the determination of elements in blood and serum samples. *Spectroscopy* **2005**, *20*, 84.
- [15] K. Yamaoke, T. Nakagawa, T. Uno. Application of Akaike's information criterion (AIC) in the evaluation of linear pharmacokinetic equations. *J. Pharmacokinet. Biopharm.* **1978**, *6*, 165.
- [16] J.G. Hollins. Radiation dosimetry of internal contamination by inorganic compounds of cobalt: An analysis of cobalt metabolism in rats. *Health Phys.* **1971**, *21*, 233.
- [17] H. Flodh. Autoradiographic studies on distribution of radiocobalt chloride in pregnant mice. *Acta Radiol.* **1968**, *7*, 121.
- [18] L.O. Simonsen, H. Harbak, P. Bennekou. Cobalt metabolism and toxicology-a brief update. *Sci. Total Environ.* **2012**, *432*, 210.
- [19] S.E. Bryan, M.L. Good, K.S. Morgan, F. Morton. Cobalt deposition in rat erythrocytes and cardiac tissue as evidence for the biosynthesis of cobalt porphyrins. *FEBS Lett.* **1970**, *6*, 270.
- [20] J. Edel, G. Pozzi, E. Sabbioni, R. Pietra, S. Devos. Metabolic and toxicological studies on cobalt. *Sci. Total Environ.* **1994**, *150*, 233.
- [21] R.W. Leggett. The biokinetics of inorganic cobalt in the human body. *Sci. Total Environ.* **2008**, *389*, 259.
- [22] E. Beleznyay, M. Osvay. Long term clearance of accidentally inhaled ⁶⁰Co aerosols in humans. *Health Phys.* **1994**, *66*, 392.
- [23] D. Newton, J. Rundo. The long-term retention of inhaled cobalt-60. *Health Phys.* **1971**, *21*, 377.

Intolerability of cobalt salt as erythropoietic agent

Bastian Ebert and Wolfgang Jelkmann*

Unfair athletes seek ways to stimulate erythropoiesis, because the mass of haemoglobin is a critical factor in aerobic sports. Here, the potential misuse of cobalt deserves special attention. Cobalt ions (Co^{2+}) stabilize the hypoxia-inducible transcription factors (HIFs) that increase the expression of the erythropoietin (Epo) gene. Co^{2+} is orally active, easy to obtain, and inexpensive. However, its intake can bear risks to health. To elaborate this issue, a review of the pertinent literature was retrieved by a search with the keywords 'anaemia', 'cobalt', 'cobalt chloride', 'erythropoiesis', 'erythropoietin', 'Epo', 'side-effects' and 'treatment', amongst others. In earlier years, cobalt chloride was administered at daily doses of 25 to 300 mg for use as an anti-anaemic agent. Co^{2+} therapy proved effective in stimulating erythropoiesis in both non-renal and renal anaemia, yet there were also serious medical adverse effects. The intake of inorganic cobalt can cause severe organ damage, concerning primarily the gastrointestinal tract, the thyroid, the heart and the sensory systems. These insights should keep athletes off taking Co^{2+} to stimulate erythropoiesis. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: anaemia therapy; cobalt; doping; erythropoiesis; erythropoietin

Introduction

Cheating athletes seek ways to stimulate erythropoiesis, because the aerobic capacity correlates with the total mass of haemoglobin (Hb). Erythropoiesis requires the glycoprotein hormone erythropoietin (Epo), which is produced in the kidneys and – to a minor degree – in a few other organs such as the liver. Recombinant human Epo (rhEpo) and its analogues have been misused for doping purposes,^[1,2] but their intake may be proven by drug testing^[3,4] and they are expensive. An alternative doping threat are the numerous small molecule chemicals that increase the expression of the Epo gene (*EPO*).^[5] With respect to doping practices, of particular interest are cobalt (II) ions (Co^{2+}). The mechanism of the action of Co^{2+} is completely separate from that of the organic cobalt-containing vitamin, cobalamin.^[6] Co^{2+} activates the hypoxia-inducible transcription factors (HIFs) that increase *EPO* expression.^[7] By this way, Co^{2+} stimulates Epo production, as first observed in experimental animals in the late 1950s.^[8] Co^{2+} is the reference substance for the *in vivo* calibration of rhEpo drug substance; 5 μmol Co^{2+} elicits the same erythropoiesis-stimulating activity as one International Unit (IU) of rhEpo.^[9] Weißbecker^[10] first noted that the oral administration of CoCl_2 increases reticulocytes, red blood cells (RBCs) and [Hb] in healthy men. In another investigation of healthy humans, Davies and Fields^[11] showed that the daily intake of 150 mg CoCl_2 increases RBC numbers by about 1 Mio. per μl within 7 to 22 days, with the values returning to normal within 9 to 15 days after cessation of Co^{2+} administration.^[11] From the late 1940s to the late 1970s cobalt chloride (CoCl_2) was applied to treat anaemic patients.^[10,12] The medicine was usually given as tablets, in divided doses at meal times.

Herein, a comprehensive literature search was performed to identify potential risks to health on the intake of Co^{2+} , since suspicion has been raised that cobalt salts could be misused by athletes as an alternative to rhEpo.^[6,13] First, the physiology of

the uptake and excretion of Co^{2+} is summarized. Second, clinical reports are evaluated of the use of Co^{2+} as an anti-anaemia treatment. The focus is on the adverse events in association with this therapy. The article will improve the knowledge of the health danger associated with the abuse of Co^{2+} as a doping means.

Methods

Pertinent literature was searched using the following databases: MEDLINE (National Library of Medicine (NLM), Bethesda, MD, USA), Springer-Verlag database (Springer-Verlag GmbH & Co KG, Heidelberg, Germany), Thieme Verlag database (Georg Thieme Verlag, Stuttgart, Germany), Wiley online library (Hoboken, NJ, USA), XToxline (NLM, Bethesda, MD, USA) with the keywords 'doping', 'blood doping', 'cobalt chloride', 'cobalt', 'erythropoiesis', 'Epo', 'erythropoietin', 'anaemia', 'side effects', 'improvement in performance', 'HIF' and 'treatment'. Published literature up to November 2012 was taken into account.

Uptake and excretion of inorganic cobalt

Cobalt is obtained from the diet; the normal daily intake is on average about 7.5 μg . According to studies in healthy humans, the gastrointestinal uptake amounts to 5–20% on oral intake of 1 μg to 1.2 mg CoCl_2 .^[14] The absorption of soluble cobalt is higher for females than for males.^[15] Rat studies with radioactive $^{57}\text{Co}^{2+}$, added to the drinking water, indicate that Co^{2+} is stored mainly in liver, lung and kidneys.^[16] The cobalt concentration in human specimen can be measured by graphite furnace atomic

* Correspondence to: Wolfgang Jelkmann, Institute of Physiology, University of Luebeck, Ratzeburger Allee 160, D-23562 Luebeck, Germany. E-mail: jelkmann@physio.uni-luebeck.de

Institute of Physiology, University of Luebeck, D-23562 Luebeck, Germany

absorption spectrometry, it amounts to 0.1 - 0.5 μL in blood plasma.^[17] Jefferson *et al.*^[18] have demonstrated elevated cobalt concentrations in about 50% of high-altitude dwellers with excessive erythrocytosis. The percentage of free Co^{2+} is only 5–12% of the total in the blood plasma, with the remainder being bound to albumin.^[19,20] Cobalt is eliminated predominantly in urine with a small amount excreted in bile.^[21] The normal cobalt concentration in urine is $<2 \mu\text{L}$ in non-occupationally exposed persons.^[17] On CoCl_2 intake, the urinary cobalt concentration is higher in women (median: 109.7 nmol/mmol creatinine) than in men (38.4 nmol/mmol creatinine).^[15] Following a single intravenous (IV) administration of inorganic cobalt in adult males, 40% of the cobalt was excreted during the first 24 h, 70% in one week and 80 % in one month, while 10 % was still present after one year.^[14]

Clinical trials

Clinical trials on the use of Co^{2+} as an anti-anaemic agent were performed from the late 1940s to the late 1970s.^[10,21] Co^{2+} salt (mostly CoCl_2) was usually administered as tablets and at daily doses of 25–300 mg (molar mass of CoCl_2 hexahydrate: 238 Da). The medicine was used for the treatment of anaemias of different etiologies, including septic infection,^[12] myeloid hypoplasia,^[22–25] sickle-cell disease,^[26,27] rheumatoid arthritis,^[28] and chronic kidney disease (CKD).^[28–37] Some of the most important clinical observations are summarized in the following.

In 1949, Robinson *et al.*^[12] described the primal treatment of nine septic patients who received daily oral doses of 20–60 mg of CoCl_2 for two to six weeks. The therapy increased RBC counts, [Hb] and haematocrit (Hct). Allegedly, there were no adverse effects, apart from an appetite loss in two patients.^[12] At the same time, Weißbecker^[10] described his three years' experiences, resuming that 100 mg of CoCl_2 taken spread over the day was effective in stimulating erythropoiesis. The treatment was recommended primarily for patients with hypochromic or infectious anaemia, but it was also proposed in the treatment of pernicious anaemia and thalassaemia minor. 'Serious' complications were not noted in any of the approximately 100 patients under study.^[10] Since the intramuscular (IM) injection of CoCl_2 proved to be painful Weißbecker^[38] suggested to use inorganic cobalt (5 mg once or twice a day) with an amino acid complex for the IM route, as this combination would ensure a slow dissociation at the site of injection. However, there were no details reported with respect to the tolerance of such formulations.

Seaman and Koler^[22] treated a 40-year-old female patient suffering from anaemia due to bone marrow hypoplasia with daily oral doses of 100 mg CoCl_2 . The number of reticulocytes and RBCs, as well as [Hb] were increased after one month, but later there was relapse of bone marrow hypoplasia.^[22] In another hypoplastic patient CoCl_2 therapy caused an increase in the fraction of reticulocytes in the bone marrow, though not in RBC numbers or [Hb].^[22] Voyce^[23] reported on a patient with pure red cell aplasia (PRCA), whose [Hb] rose from $<70 \text{ g/L}$ to $>120 \text{ g/L}$ on treatment with 100 mg CoCl_2 twice a day (b.i.d.). In another case of PRCA haematological recovery was achieved on two months oral treatment with 50 mg CoCl_2 b.i.d.^[24] Anaemia improvement was observed in four patients with sickle-cell anaemia treated with 300 mg CoCl_2 for six weeks.^[26] Weinsaft and Bernstein^[28] administered daily 80 mg CoCl_2 to eight patients with therapy-resistant anaemias of differing etiologies. RBC numbers, [Hb] and Hct increased on 2–8 months Co^{2+}

treatment. However, two patients died: one 66 days after the start of Co^{2+} application due to a haemorrhage, the other after 135 days because of renal and cardiac failure. The authors did not comment on the possible relationship between death and Co^{2+} therapy.^[28]

Geill^[32] treated a total of 107 anaemic CKD patients with a combination of 55 mg iron and 20 mg CoCl_2 , b.i.d. or three times a day (t.i.d.) for three months. This therapy resulted in a rise in RBC numbers and [Hb]. An 82-year-old female patient developed erythrocytosis and thrombosis of the superior mesenteric artery during the treatment period.^[32] When Gardner^[29] treated 17 CKD patients with daily oral doses of 50–150 mg CoCl_2 , erythropoiesis was stimulated in most patients within one month. In six out of twelve nephrectomized patients on dialysis who received daily 25–50 mg CoCl_2 , [Hb] increased,^[36] indicating that Co^{2+} can stimulate Epo production at extra-renal sites, most likely in the liver. Kasanen *et al.*^[31] treated anaemic CKD patients orally with cobalt chloride equivalent to either 5 or 15 mg cobalt per day. [Hb] increased on average at the lower dose from 79 g/L to 92 g/L and at the higher dose from 92 g/L to 107 g/L within a month. The maximum reticulocyte count (2.1–3.8% of RBCs) was measured one week after initiation of therapy.^[31] Bowie and Hurley^[34] treated 14 anaemic CKD patients on dialysis with 25 mg CoCl_2 orally for four weeks, and with 50 mg of CoCl_2 for another four weeks. On average, Hct increased by 23% and RBC mass by 20%. Similar effects were seen by Schleisner^[30] who applied daily doses of 60 mg CoCl_2 . Curtis *et al.*^[33,35] administered 50 mg of CoCl_2 daily for three months to 23 CKD patients on haemodialysis. This treatment resulted in an increase in [Hb] by 10 g/L in approximately 50% of the patients. One patient died three months after completing a course of Co^{2+} therapy. Histological examination of his myocardial tissue revealed that he had developed cardiomyopathy. At post-mortem the myocardial cobalt concentration was 1.65 $\mu\text{g/g}$, some 25–80 times higher than in control samples. Curtis *et al.*^[35] performed a prospective study of the cobalt concentrations in the blood of healthy controls and of haemodialysis patients after two weeks of administration of CoCl_2 . In both groups, there were long-term increases in blood concentrations of cobalt, which returned to normal six weeks after Co^{2+} discontinuation.^[35]

Unwanted effects of Co^{2+} ingestion

Several aspects of the biochemical properties of inorganic cobalt (metallic and stable salts) with respect to bio-accessibility and potential hazards have been summarized previously.^[39–41] A monograph describing toxic effects of CoCl_2 has been compiled by the staff of the Birmingham Centre of the National Poisons Information Service of the UK.^[42] The uptake of cobalt and its compounds in the human body can occur in different ways (orally, dermally, inhalative, intravenously, subcutaneously). Depending on the route of administration the toxicity of cobalt differs with respect to the site and severity of damage. In addition, the exposure time and the quantitative amount of cobalt intake are critical. On high dosing ($>25 \text{ mg/day}$) there is danger of intolerability and organ injury.^[42,43]

Acute CoCl_2 poisoning

Mucklow *et al.*^[44] have reported on a 6-year-old boy who developed abdominal pain and vomited after taking a drink containing 2.5 g CoCl_2 . The cobalt concentration in his blood plasma was 7.23 $\mu\text{mol/L}$ (normal value $<0.02 \mu\text{mol/L}$) seven hours post

Drug effects of cobalt

ingestion and 0.09 $\mu\text{mol/L}$ one month later.^[44] Jacobziner and Raybin^[45] have described a worse case: A 19-month-old boy died about seven hours after he had swallowed a mouthful (~30 ml) of CoCl_2 solution. The autopsy revealed a necrotic gastric mucosa; liver, kidney and spleen were overloaded with cobalt.^[45]

Gastrointestinal sickness

Weißbecker^[10] first noted that the oral administration of 500 mg of CoCl_2 can cause gastrointestinal sickness. Schirmacher^[46] has described the impressive case of a 35-year-old woman who developed nausea, vomiting and weight loss in addition to neurological symptoms, when she was treated with 25 mg CoCl_2 four times a day (q.i.d.). Several authors have confirmed gastrointestinal complaints in association with the oral intake of CoCl_2 .^[26,28-31,33-36,38,46,47]

Thyroidal dysfunction

Co^{2+} inhibits thyroidal iodide uptake.^[48] Thus, myxoedema and thyroid hyperplasia were relatively common side effects of Co^{2+} treatment.^[49] Kriss *et al.*^[27] observed thyroid gland abnormalities during Co^{2+} therapy in five patients. Among them were four children with sickle cell disease, who were treated with 30 to 100 mg of CoCl_2 daily for 14–30 weeks. A few weeks after cessation of therapy the goiter and the dysfunction of the thyroid gland resumed. Since the unwanted effects were clearly attributed to the Co^{2+} treatment, the authors criticized the prevalently careless use of Co^{2+} as a therapeutic means.^[27]

Myocardial effects

Cardiomyopathies were observed in hard metal workers who inhaled cobalt in concentrations exceeding 100 micrograms Co/m^3 air with different cobalt exposure duration.^[50] Heart failure may also result from the pharmacologic administration of Co^{2+} . Reportedly, a 17-year-old woman with CKD died from rapidly progressive dilated cardiomyopathy after nine months CoCl_2 therapy (25 mg b.i.d.). At necropsy the myocardial cobalt content was 8.9 $\mu\text{g/g}$ (dried tissue), compared to a normal of 0.2 $\mu\text{g/g}$.^[37]

The cobalt-associated 'beer drinker's cardiomyopathy' was a special syndrome.^[51,52] Cobalt chloride/sulfate (1–1.5 mg per litre) was earlier added to beer to act as a foam stabilizer. The syndrome characteristics were cardiomegaly, galloping rhythm, cyanosis, low cardiac ejection, pericardial effusion and hypotension.^[53] The disease occurred in people who daily consumed several litres of the Co^{2+} -added beer,^[51,52] still the cobalt amounts (up to 10 mg/day) were less than the doses used in anaemia treatment.

Weißbecker^[10] earlier noted an increase in systolic blood pressure in all of the patients who had undergone Co^{2+} therapy. This is in harmony with present knowledge that the treatment with rhEpo can be associated with an increase in blood pressure, although the mechanisms of this increase are not fully understood.^[54,55]

Nerval and sensory effects

Schirmacher^[46] has described the instructive case of a 35-year-old woman who was treated with 100 mg of CoCl_2 every day because of renal anaemia. Due to neurological disease, CoCl_2 administration was discontinued after six months. On examination, the patient presented with a bilateral neural hearing loss, a loss of vibration sense in both legs and a lack of posterior tibial reflex, in addition to a diffuse thyroid enlargement.^[46] There are other reports indicating

hearing impairment on Co^{2+} therapy.^[29,30,36,46] When Gardner^[29] treated 17 CKD patients with daily oral doses of 50–150 mg CoCl_2 , four patients complained about the onset of tinnitus after four to 16 weeks. One patient also presented with a reduction hearing after 12 weeks of therapy. The audiogram showed a hearing loss at frequencies >1000 Hz, which was reversible when the Co^{2+} therapy was discontinued.^[29] Other investigators confirmed a hearing loss on CoCl_2 therapy, and its reversibility on treatment cessation.^[34]

Licht *et al.*^[25] have described an optic nerve atrophy of a 32-year-old patient who was treated on the basis of a pancytopenia with up to 200 mg of CoCl_2 daily in four treatment intervals, each lasting three to four months, for a total of three years. Apart from nausea and vomiting, the patient developed a reduced choroideal perfusion and atrophy of the optic nerve with a visual acuity.^[25]

Discussion

This paper focuses on unwanted effects associated with the therapeutic administration of Co^{2+} for stimulation of erythropoiesis. Evidence suggests that Co^{2+} may cause severe gastrointestinal, endocrine, cardiovascular, haematological, reproductive, neurological, and immunological responses.^[43] The treatment with Co^{2+} was abandoned in the late 1970s. Instead, androgens were increasingly used for treatment of anemic patients,^[56] until rhEpo became available approximately 10 years thereafter.

Co^{2+} activates the hypoxia-inducible transcription factors (HIFs) that enhance *EPO* expression. The HIFs are heterodimeric proteins composed of α - and β -subunits. The C-termini of the HIF- α subunits comprise O_2 -dependent degradation domains, in which proline residues are hydroxylated by means of specific HIF- α prolyl hydroxylases in the presence of O_2 ('normoxia'). Prolyl hydroxylated HIF- α binds the von Hippel-Lindau tumor suppressor protein (pVHL) in complex with an ubiquitin-protein E_3 -ligase and undergoes immediate proteasomal degradation. Co^{2+} is thought to bind to HIF- α thereby preventing the interaction with pVHL and the proteasomal degradation, even under normoxic conditions.^[57-59] HIF- α then translocates into the nucleus, where it couples with HIF-1 β and binds to hypoxia-response elements (HREs) in the *EPO* enhancer.

Suspicion has been raised that Co^{2+} salts could be misused by athletes as an alternative to conventional blood doping by RBC transfusion or rhEpo injection.^[13] Indeed, CoCl_2 is readily available, inexpensive, easy to dose, and very efficient. However, the intake of inorganic cobalt bears serious risks to health. Taken together, therapeutic doses of CoCl_2 have ranged from 25 to 300 mg per day, usually taken as tablets or in drinks. There were only a few trials of the IV or IM administration of Co^{2+} .^[38] The parenteral route of application prevents gastrointestinal unwanted effects. However, the specific toxicity of the IV administration of Co^{2+} has not been investigated, and the IM administration may be painful. The risk of the occurrence of unwanted events increases with the dose and length of treatment interval. The duration of the therapeutic administration of Co^{2+} averaged approximately 10 weeks. Finley *et al.*^[43] have recently determined a chronic oral reference dose (RfD) for inorganic cobalt, employing the standard US EPA risk assessment methodology for establishing a chronic RfD, a potential point of departure dose (POD) of 0.9 mg cobalt per kg body weight (b.w.) and day, and an aggregate uncertainty factor of 30 to the POD. This approach has yielded a chronic oral RfD of

0.03 mg cobalt per kg b.w. and day, a value considered to be protective of non-cancer health effects in the general population for a lifetime of daily exposure to cobalt.^[43] Thus, the oral RfD is much lower than the Co^{2+} doses used to increase RBC production in humans.

Co^{2+} , by means of stabilising HIF, can activate several hundred other genes apart from *EPO*.^[60] These include genes encoding proteins that are involved in tumor growth (e.g. vascular endothelial growth factor and multidrug resistance transporter P-glycoprotein). Indeed, the administration of cobalt salt was found to promote the development of carcinomas in experimental animals.^[61] Furthermore, inorganic cobalt proved to induce DNA strand breaks, DNA-protein cross-linkage, sister chromatid exchanges and formation of micronuclei in mammalian cell cultures.^[62]

Some of the HIF-activated genes encode proteins which may increase physical performance independent of erythropoiesis (e.g. glycolytic enzymes, glucose transporters, angiogenic peptides). Research has been initiated to investigate effects of Co^{2+} in this regard. The administration of cobalt salt did not affect the formation of capillaries in skeletal muscle of experimental animals.^[63] However, preconditioning with high-dosed CoCl_2 (12.5 mg/kg b.w.) protected hypoxic rats against high altitude pulmonary edema.^[64] In another rat study preconditioning by CoCl_2 supplementation increased mitochondrial biogenesis, glucose uptake and metabolism by aerobic respiration in skeletal muscle, which increased physical performance.^[65]

First attempts have been made to develop strategies for detection of cobalt salt doping in athletes. It has been proposed to use the cobalt content of RBCs as a parameter, as the CoCl_2 uptake by the RBCs is practically irreversible and reflects the plasma cobalt concentration.^[66] Unice *et al.*^[67] used a biokinetic model to estimate whole blood and urine cobalt levels resulting from oral exposure or ingestion of cobalt in amounts exceeding typical dietary intake rates. Following 10 days of cobalt supplementation at a daily rate of 0.4 to 1.0 mg, the predicted cobalt concentrations ranged from 1.7 to 10 $\mu\text{g/L}$ in blood, and 20 to 120 $\mu\text{g/L}$ in urine. Chronic supplementation (> 1 year) at a rate of 1.0 mg cobalt per day was predicted to result in blood levels of 5.7 to 13 $\mu\text{g/L}$, and in urine from 65 to 150 $\mu\text{g/L}$.

More detailed information on the health hazards of cobalt salt is demandable to discourage athletes from a potentially deleterious doping practice. In addition, knowledge on the pharmacokinetics of cobalt will be advantageous for anti-doping laboratories planning to establish methods for detection of cobalt in biological samples. Co^{2+} stimulates *EPO* expression by stabilising HIF- α . The '2013 Prohibited List' of the World Anti-Doping Agency (WADA) cites (S2), among others, hypoxia-inducible factor (HIF) stabilizers. Whether this would suffice to sanction athletes misusing Co^{2+} to improve performance could become a matter of legal debate.

References

- W. Jelkmann. Erythropoiesis stimulating agents and techniques: A challenge for doping analysts. *Curr. Med. Chem.* **2009**, *16*, 1236.
- W. Jelkmann, C. Lundby. Blood doping and its detection. *Blood* **2011**, *118*, 2395.
- C. Reichel, G. Gmeiner. Erythropoietin and analogs. *Handb. Exp. Pharmacol.* **2010**, *195*, 251.
- M. Okano, M. Sato, E. Kaneko, S. Kageyama. Doping control of biosimilar epoetin kappa and other recombinant erythropoietins after intravenous application. *Drug Test. Anal.* **2011**, *3*, 798.
- S. Beuck, W. Schanzer, M. Thevis. Hypoxia-inducible factor stabilizers and other small-molecule erythropoiesis-stimulating agents in current and preventive doping analysis. *Drug Test. Anal.* **2012**, *4*, 830.
- W. Jelkmann. The disparate roles of cobalt in erythropoiesis, and doping relevance. *Open J. Hematol.* **2012**, *3*, 1.
- F. J. Rodriguez-Jimenez, V. Moreno-Manzano. Modulation of hypoxia-inducible factors (HIF) from an integrative pharmacological perspective. *Cell. Mol. Life Sci.* **2012**, *69*, 519.
- E. Goldwasser, L. O. Jacobson, W. Fried, L. F. Plzak. Studies on erythropoiesis V. The effect of cobalt on the production of erythropoietin. *Blood* **1958**, *13*, 55.
- W. Jelkmann. Efficacy of recombinant erythropoietins: Is there unity of international units? *Nephrol. Dial. Transpl.* **2009**, *24*, 1366.
- L. Weißbecker. Die Kobalttherapie. *Dtsch. Med. Wochenschr.* **1950**, *75*, 116.
- J. E. Davis, J. P. Fields. Experimental production of polycythemia in humans by administration of cobalt chloride. *Proc. Soc. Exp. Biol. Med.* **1958**, *99*, 493.
- J. C. Robinson, G. W. James III, R. M. Kark. The effect of oral therapy with cobaltous chloride on the blood of patients suffering with chronic suppurative infection. *New Engl. J. Med.* **1949**, *240*, 749.
- G. Lippi, M. Franchini, G. C. Guidi. Blood doping by cobalt. Should we measure cobalt in athletes? *J. Occup. Med. Toxicol.* **2006**, *1*, 18.
- T. Smith, C. J. Edmonds, C. F. Barnaby. Absorption and retention of cobalt in man by whole-body counting. *Health Phys.* **1972**, *22*, 359.
- J. M. Christensen, O. M. Poulsen, M. Thomsen. A short-term crossover study on oral administration of soluble and insoluble cobalt compounds: Sex differences in biological levels. *Int. Arch. Occup. Environ. Health* **1993**, *65*, 233.
- J. Edel, G. Pozzi, E. Sabbioni, R. Pietra, S. Devos. Metabolic and toxicological studies on cobalt. *Sci. Total Environ.* **1994**, *150*, 233.
- WHO International Agency for Research on Cancer Working Group. Cobalt in hard metals and cobalt sulfate, gallium arsenide, indium phosphide and vanadium pentoxide. *IARC Monogr. Eval. Carcinog. Risks Hum.* **2006**, *86*, 1. Available at: <http://monographs.iarc.fr/ENG/Monographs/vol86/mono86.pdf> Access date: [16 August 2013].
- J. A. Jefferson, E. Escudero, M. E. Hurtado, J. Pando, R. Tapia, E. R. Swenson, J. Prchal, G. F. Schreiner, R. B. Schoene, A. Hurtado, R. J. Johnson. Excessive erythrocytosis, chronic mountain sickness, and serum cobalt levels. *Lancet* **2002**, *359*, 407.
- A. K. Nandedkar, M. S. Hong, F. Friedberg. Co^{2+} binding by plasma albumin. *Biochem. Med.* **1974**, *9*, 177.
- H. M. Jansen, S. Knollema, L. V. van der Duin, A. T. Willemsen, A. Wiersma, E. J. Franssen, F. G. Russel, J. Korf, A. M. Paans. Pharmacokinetics and dosimetry of cobalt-55 and cobalt-57. *J. Nucl. Med.* **1996**, *37*, 2082.
- A. Taylor, V. Marks. Cobalt: A review. *J. Hum. Nutr.* **1978**, *32*, 165.
- A. J. Seaman, R. D. Koler. Acquired erythrocytic hypoplasia: A recovery during cobalt therapy; report of two cases with review of the literature. *Acta Haematol.* **1953**, *9*, 153.
- M. A. Joyce. A case of pure red-cell aplasia successfully treated with cobalt. *Brit. J. Haematol.* **1963**, *9*, 412.
- J. R. Fountain, M. Dales. Pure redcell aplasia successfully treated with cobalt. *Lancet* **1955**, *268*, 541.
- A. Licht, M. Oliver, E. A. Rachmilewitz. Optic atrophy following treatment with cobalt chloride in a patient with pancytopenia and hypercellular marrow. *Isr. J. Med. Sci.* **1972**, *8*, 61.
- J. Wolf, I. J. Levy. Treatment of sickle cell anemia with cobalt chloride. *AMA Arch. Intern. Med.* **1954**, *93*, 387.
- J. P. Kriss, W. H. Carnes, R. T. Gross. Hypothyroidism and thyroid hyperplasia in patients treated with cobalt. *J. Am. Med. Assoc.* **1955**, *157*, 117.
- P. P. Weinsaft, L. H. Bernstein. Cobaltous chloride in the treatment of certain refractory anemias. *Am. J. Med. Sci.* **1955**, *230*, 264.
- F. H. Gardner. The use of cobaltous chloride in the anemia associated with chronic renal disease. *J. Lab. Clin. Med.* **1953**, *41*, 56.
- P. Schleisner. Cobalt in anaemia. *Acta Med. Scand.* **1956**, *154*, 177.
- A. Kasanen, M. Kulonen, J. Forsstrom. Oral cobalt therapy in renal anemia. *Ann. Med. Intern. Fenn.* **1963**, *52*, 43.
- T. Geill. On the treatment of the nephrogenic anaemias with a combined cobalt-iron preparation. *Gerontol. Clin.* **1969**, *11*, 48.
- M. S. Edwards, J. R. Curtis. Use of cobaltous chloride in anaemia of maintenance hemodialysis patients. *Lancet* **1971**, *2*, 582.
- E. A. Bowie, P. J. Hurley. Cobalt chloride in the treatment of refractory anaemia in patients undergoing long-term haemodialysis. *Aust. N.Z. J. Med.* **1975**, *5*, 306.

- [35] J. R. Curtis, G. C. Goode, J. Herrington, L. E. Urdaneta. Possible cobalt toxicity in maintenance hemodialysis patients after treatment with cobaltous chloride: A study of blood and tissue cobalt concentrations in normal subjects and patients with terminal and renal failure. *Clin. Nephrol.* **1976**, *5*, 61.
- [36] J. M. Duckham, H. A. Lee. The treatment of refractory anaemia of chronic renal failure with cobalt chloride. *Q. J. Med.* **1976**, *45*, 277.
- [37] I. H. Manifold, M. M. Platts, A. Kennedy. Cobalt cardiomyopathy in a patient on maintenance haemodialysis. *Brit. Med. J.* **1978**, *2*, 1609.
- [38] L. Weissbecker. Neue Möglichkeiten der Kobalttherapie. *Klin. Wochenschr.* **1951**, *29*, 80.
- [39] D. G. Barceloux. Cobalt. *J. Toxicol. Clin. Toxicol.* **1999**, *37*, 201.
- [40] A. Oller, H. Bates. Metals in perspective: Introduction. *J. Environ. Monitor.* **2004**, *6*, 145.
- [41] L. O. Simonsen, H. Harbak, P. Bennekou. Cobalt metabolism and toxicology-A brief update. *Sci. Total Environ.* **2012**, *432*, 210.
- [42] S. Bradberry, M. Sabatta, J. Vale. Cobalt Chloride. Available at: www.inchem.org/documents/ukpids/ukpids/ukpid50.htm Access date: [16 August 2013].
- [43] B. L. Finley, A.D. Monnot, D.J. Paustenbach, S.H. Gaffney. Derivation of a chronic oral reference dose for cobalt. *Regul. Toxicol. Pharm.* **2012**, *64*, 491.
- [44] E. S. Mucklow, S. J. Griffin, H. T. Delves, B. Suchak. Cobalt poisoning in a 6-year-old. *Lancet* **1990**, *335*, 981.
- [45] H. Jacobziner, H. W. Raybin. Poison control...accidental cobalt poisoning. *Arch. Pediatr.* **1961**, *78*, 200.
- [46] U. O. Schirmacher. Case of cobalt poisoning. *Brit. Med. J.* **1967**, *1*, 544.
- [47] L. Berk, J. H. Burchenal, T. Wood, W.B. Castle. Oxygen saturation of sternal marrow blood with special reference to pathogenesis of polycythemia vera. *Proc. Soc. Exp. Biol. Med.* **1948**, *69*, 316.
- [48] K. R. Paley, E. S. Sobel, R. S. Yalow. Effect of oral and intravenous cobaltous chloride on thyroid function. *J. Clin. Endocr. Metab.* **1958**, *18*, 850.
- [49] J. C. Weaver, V. M. Kostainsek, D. N. Richards Jr. Cobalt tumor of the thyroid gland. *Calif. Med.* **1956**, *85*, 110.
- [50] P. Seghizzi, F. D'Adda, D. Borleri, F. Barbic, G. Mosconi. Cobalt myocardiopathy. A critical review of literature. *Sci. Total Environ.* **1994**, *150*, 105.
- [51] Y. Morin, A. Tetu, G. Mercier. Cobalt cardiomyopathy: Clinical aspects. *Brit. Heart J.* **1971**, *33*(8), 175.
- [52] C. S. Alexander. Cobalt-beer cardiomyopathy. A clinical and pathologic study of twenty-eight cases. *Am. J. Med.* **1972**, *53*, 395.
- [53] D. Lison. Human toxicity of cobalt-containing dust and experimental studies on the mechanism of interstitial lung disease (hard metal disease). *Crit. Rev. Toxicol.* **1996**, *26*, 585.
- [54] R. Krapf, H. N. Hulter. Arterial hypertension induced by erythropoietin and erythropoiesis-stimulating agents (ESA). *Clin. J. Am. Soc. Nephrol.* **2009**, *4*, 470.
- [55] W. Jelkmann, S. Elliott. Erythropoietin and the vascular wall: The controversy continues. *Nutr. Metab. Cardiovasc. Dis.* **2012** [Epub ahead of print]. PMID: 22682530.
- [56] N. T. Shahidi. Androgens and erythropoiesis. *New Engl. J. Med.* **1973**, *289*, 72.
- [57] K. Kanaya, T. Kamitani. pVHL-independent ubiquitination of HIF1alpha and its stabilization by cobalt ion. *Biochem. Biophys. Res. Commun.* **2003**, *306*, 750.
- [58] Y. Yuan, D. Beitner-Johnson, D. E. Millhorn. Hypoxia-inducible factor 2alpha binds to cobalt in vitro. *Biochem. Biophys. Res. Commun.* **2001**, *288*, 849.
- [59] Y. Yuan, G. Hilliard, T. Ferguson, D. E. Millhorn. Cobalt inhibits the interaction between hypoxia-inducible factor-alpha and von Hippel-Lindau protein by direct binding to hypoxia-inducible factor-alpha. *J. Biol. Chem.* **2003**, *278*, 15911.
- [60] S. Nagel, N. P. Talbot, J. Mecinovic, T. G. Smith, A. M. Buchan, C. J. Schofield. Therapeutic manipulation of the HIF hydroxylases. *Antioxid. Redox Signal.* **2010**, *12*, 481.
- [61] M. De Boeck, M. Kirsch-Volders, D. Lison. Cobalt and antimony: Genotoxicity and carcinogenicity. *Mutat. Res.* **2003**, *533*, 135.
- [62] D. Beyersmann, A. Hartwig. The genetic toxicology of cobalt. *Toxicol. Appl. Pharmacol.* **1992**, *115*, 137.
- [63] J. Suzuki. Time-course changes in VEGF expression and capillarity in the early stage of exercise training with Co treatment in rat skeletal muscles. *Acta Physiol. Scand.* **2004**, *181*, 225.
- [64] D. Shukla, S. Saxena, J. Purushothaman, K. Shrivastava, M. Singh, S. Shukla, V. K. Malhotra, S. Mustoori, A. Bansal. Hypoxic preconditioning with cobalt ameliorates hypobaric hypoxia induced pulmonary edema in rat. *Eur. J. Pharmacol.* **2011**, *656*, 101.
- [65] S. Saxena, D. Shukla, A. Bansal. Augmentation of aerobic respiration and mitochondrial biogenesis in skeletal muscle by hypoxia preconditioning with cobalt chloride. *Toxicol. Appl. Pharmacol.* **2012**, *264*, 324.
- [66] L. O. Simonsen, A. M. Brown, H. Harbak, B. I. Kristensen, P. Bennekou. Cobalt uptake and binding in human red blood cells. *Blood Cell Mol. Dis.* **2011**, *46*, 266.
- [67] K. M. Unice, A. D. Monnot, S. H. Gaffney, B. E. Tvermoes, K. A. Thuet, D. J. Paustenbach, B. L. Finley. Inorganic cobalt supplementation: Prediction of cobalt levels in whole blood and urine using a biokinetic model. *Food Chem. Toxicol.* **2012**, *50*, 2456.

CALIFORNIA HORSE RACING BOARD

MARCH 19, 2015
REGULAR BOARD MEETING

There is no board package material for Item 6

STAFF ANALYSIS
ADOPTION OF CRITERIA TO EVALUATE THE REHABILITATION OF A PERSON
WHEN CONSIDERING DENIAL OF A LICENSE PURSUANT TO BUSINESS AND
PROFESSIONS CODE SECTION 480 AND CONSIDERING SUSPENSION OR
REVOCAION OF A LICENSE PURSUANT TO BUSINESS AND PROFESSIONS CODE
SECTION 490

Regular Board Meeting
March 19, 2015

ISSUE

Business and Professions Code section 482 states that every board that falls under the provisions of the Business and Professions Code shall adopt criteria to evaluate the rehabilitation of a person who has committed an act, offense, or crime when considering the denial of a license under section 480, or the suspension or revocation of a license under section 490. Presently, the Board does not have such criteria in place. Adoption of the proposed rehabilitation criteria will bring the Board in line with the requirements of section 482, and help provide consistent evaluation of applicants and licensees who have committed acts, offenses, or crimes that permit the denial, suspension, or revocation of a license.

ANALYSIS

Business and Professions Code section 19440 provides that the Board shall have all powers necessary and proper to enable it to carry out fully and effectually the purpose of this chapter. Responsibilities of the Board shall include, but are not limited to, licensing of each racing association and all persons, other than the public at large, who participate in a horse racing meeting with parimutuel wagering. Business and Professions Code section 19461 states that every license granted under this chapter is subject to suspension or revocation by the board in any case where the board has reason to believe that any condition regarding it has not been complied with, or that any law, rule, or regulation of the board affecting it has been broken or violated. Rule 1489, Grounds for Denial or Refusal of License, explains that, in addition to any other valid reason, the Board may refuse to issue a license or deny a license to any person who has been convicted of a crime punishable by imprisonment in a California state prison or a federal prison, or who has been convicted of a crime involving moral turpitude; who has been convicted of a crime in another jurisdiction which if committed in this state would be a felony; who has made any material misrepresentations or false statements to the Board or its agents in his or her application for a license or otherwise, or who fails to answer any material question on an application for a license; who is unqualified to engage in the activities for which a license is required; who fails to disclose the true ownership or interest in any or all horses as required by an application; who is subject to exclusion or ejection from the racing inclosure or is within the classes of persons prohibited from participating in pari-mutuel wagering; who has committed an act involving moral turpitude, or intemperate acts which have exposed others to danger, or acts in connection with horse racing and/or a legalized gaming business which were fraudulent or in violation of a trust or duty; who has unlawfully engaged in or who has been convicted of possession, use or sale of any narcotic, dangerous drug, or marijuana; who is not permitted by

any law to engage in the occupation for which the license is sought; or who has violated, or who aids, abets or conspires with any person to violate any provision of the rules or the Horse Racing Law. Finally, Rule 1900, Grounds for Suspension or Revocation, provides that any rule which is a ground for denial of a license is also ground for suspension or revocation of a license.

In instances where a license is denied, suspended, or revoked, however, nothing prohibits a person from reapplying for a license after such a determination has been made. Business and Professions Code section 486 provides that upon denial of a license, an applicant may reapply for that license after one year unless the Board prescribes an earlier date. Likewise, Business and Professions Code section 491 conveys, by reference to Government Code section 11522, that a licensee who has had their license suspended or revoked may appeal that decision after one year. Both provisions additionally express that the rehabilitation criteria adopted by the Board shall be provided to the applicant or licensee when their license is denied, suspended, or revoked. In Horse Racing Law, the only provision that expressly allows for permanent revocation of a license is Business and Professions Code section 19582(b)(1), which permits the permanent revocation of a person's license if they are guilty of three class I or class II medication violations under section 19581.

According to Business and Professions Code section 482, the Board shall adopt criteria to evaluate the rehabilitation of a person who has committed an act, offense, or crime when considering the denial of a license pursuant to section 480, or the suspension or revocation of a license pursuant to section 490.

The proposed criteria were developed by CHRB counsel to bring the Board into conformity with Business and Professions Code section 482, as well as to assist investigators and licensing staff in conducting consistent evaluations of applicants and licensees who have committed acts, offenses, or crimes that permit the denial, suspension, or revocation of their license.

Pursuant to the proposed criteria, when evaluating the rehabilitation of a licensee or applicant whose license has been denied, suspended, or revoked, the Board may consider the following:

- (a) The nature and severity of the act(s) or offense(s), including its relation to horse racing or pari-mutuel wagering and the protection of the public.
- (b) The total criminal record, including evidence of any act(s) or offense(s) committed subsequent to the act(s) or offense(s) under consideration as grounds for denial, suspension or revocation which also could be considered grounds for denial, suspension, or revocation under Business and Professions Code sections 480 or 490.
- (c) The time that has elapsed since commission of the act(s) or offense(s).
- (d) The extent to which the person seeking licensure or the licensee has complied with any terms of parole, probation, restitution or any other sanctions lawfully imposed against the person or licensee.
- (e) The credibility of the person seeking licensure or the licensee, and his or her acceptance of responsibility and remorse for the conduct.
- (f) Evidence, if any, of rehabilitation submitted by the person seeking licensure or the licensee. If the evidence of rehabilitation consists of written statements by third parties in support of

the person seeking licensure or the licensee, the written statements should include a description of their relationship to the person or licensee, a description of the length of time their relationship has existed, a description of the rehabilitative efforts of the person seeking licensure or the licensee and should contain the following sentence at the end: "I declare under penalty of perjury, under the laws of the State of California, that the foregoing is true and correct." The written statement should be signed by the third party making the statement and dated.

BACKGROUND

Business and Professions Code section 482 provides as follows:

Each board under the provisions of this code shall develop criteria to evaluate the rehabilitation of a person when: (a) Considering the denial of a license by the board under Section 480; or (b) Considering suspension or revocation of a license under Section 490. Each board shall take into account all competent evidence of rehabilitation furnished by the applicant or licensee.

To date, the Board has been without rehabilitative criteria for evaluating applicants and licensees who have committed certain acts, offenses, or crimes. Adoption of the proposed criteria would address this issue, and bring the Board in conformity with section 482.

RECOMMENDATION

This item is presented to the Board for discussion and action.

CALIFORNIA HORSE RACING BOARD
1010 HURLEY WAY, SUITE 300



CALIFORNIA HORSE RACING BOARD REHABILITATION CRITERIA FOR LICENSE DENIALS, SUSPENSIONS, OR REVOCATIONS

When considering the denial of a license issued by the California Horse Racing Board pursuant to Business and Professions Code section 480, or suspension or revocation of licensure pursuant to Business and Professions Code section 490, on the grounds that the person seeking licensure or holding a California Horse Racing Board license has been convicted of a crime, the Board, in evaluating the rehabilitation of such person and his or her eligibility for licensure may consider the following criteria:

- (a) The nature and severity of the act(s) or offense(s), including its relation to horse racing or pari-mutuel wagering and the protection of the public.
- (b) The total criminal record, including evidence of any act(s) or offense(s) committed subsequent to the act(s) or offense(s) under consideration as grounds for denial, suspension or revocation which also could be considered grounds for denial, suspension, or revocation under Business and Professions Code sections 480 or 490.
- (c) The time that has elapsed since commission of the act(s) or offense(s).
- (d) The extent to which the person seeking licensure or the licensee has complied with any terms of parole, probation, restitution or any other sanctions lawfully imposed against the person or licensee.
- (e) The credibility of the person seeking licensure or the licensee, and his or her acceptance of responsibility and remorse for the conduct.
- (f) Evidence, if any, of rehabilitation submitted by the person seeking licensure or the licensee. If the evidence of rehabilitation consists of written statements by third parties in support of the person seeking licensure or the licensee, the written statements should include a description of their relationship to the person or licensee, a description of the length of time their relationship has existed, a description of the rehabilitative efforts of the person seeking licensure or the licensee and should contain the following sentence at the end: "I declare under penalty of perjury, under the laws of the State of California, that the foregoing is true and correct." The written statement should be signed by the third party making the statement and dated.

BUSINESS AND PROFESSIONS CODE – BPC

DIVISION 1.5. DENIAL, SUSPENSION AND REVOCATION OF LICENSES [475 - 499]

(Division 1.5 added by Stats. 1972, Ch. 903.)

CHAPTER 2. Denial of Licenses [480 - 489]

(Chapter 2 added by Stats. 1972, Ch. 903.)

480.

(a) A board may deny a license regulated by this code on the grounds that the applicant has one of the following:

(1) Been convicted of a crime. A conviction within the meaning of this section means a plea or verdict of guilty or a conviction following a plea of nolo contendere. Any action that a board is permitted to take following the establishment of a conviction may be taken when the time for appeal has elapsed, or the judgment of conviction has been affirmed on appeal, or when an order granting probation is made suspending the imposition of sentence, irrespective of a subsequent order under the provisions of Section 1203.4, 1203.4a, or 1203.41 of the Penal Code.

(2) Done any act involving dishonesty, fraud, or deceit with the intent to substantially benefit himself or herself or another, or substantially injure another.

(3) (A) Done any act that if done by a licentiate of the business or profession in question, would be grounds for suspension or revocation of license.

(B) The board may deny a license pursuant to this subdivision only if the crime or act is substantially related to the qualifications, functions, or duties of the business or profession for which application is made.

(b) Notwithstanding any other provision of this code, a person shall not be denied a license solely on the basis that he or she has been convicted of a felony if he or she has obtained a certificate of rehabilitation under Chapter 3.5 (commencing with Section 4852.01) of Title 6 of Part 3 of the Penal Code or that he or she has been convicted of a misdemeanor if he or she has met all applicable requirements of the criteria of rehabilitation developed by the board to evaluate the rehabilitation of a person when considering the denial of a license under subdivision (a) of Section 482.

(c) Notwithstanding any other provisions of this code, a person shall not be denied a license solely on the basis of a conviction that has been dismissed pursuant to Section 1203.4, 1203.4a, or 1203.41 of the Penal Code. An applicant who has a conviction that has been dismissed pursuant to Section 1203.4, 1203.4a, or 1203.41 of the Penal Code shall provide proof of the dismissal.

(d) A board may deny a license regulated by this code on the ground that the applicant knowingly made a false statement of fact that is required to be revealed in the application for the license.

(Amended by Stats. 2014, Ch. 737, Sec. 1. Effective January 1, 2015.)

BUSINESS AND PROFESSIONS CODE – BPC**DIVISION 1.5. DENIAL, SUSPENSION AND REVOCATION OF LICENSES [475 - 499]**

(Division 1.5 added by Stats. 1972, Ch. 903.)

CHAPTER 2. Denial of Licenses [480 - 489]

(Chapter 2 added by Stats. 1972, Ch. 903.)

482.

Each board under the provisions of this code shall develop criteria to evaluate the rehabilitation of a person when:

- (a) Considering the denial of a license by the board under Section 480; or
- (b) Considering suspension or revocation of a license under Section 490.

Each board shall take into account all competent evidence of rehabilitation furnished by the applicant or licensee.

(Amended by Stats. 1974, Ch. 1321.)

BUSINESS AND PROFESSIONS CODE - BPC**DIVISION 1.5. DENIAL, SUSPENSION AND REVOCATION OF LICENSES [475 - 499]**

(Division 1.5 added by Stats. 1972, Ch. 903.)

CHAPTER 3. Suspension and Revocation of Licenses [490 - 494.6]

(Chapter 3 added by Stats. 1972, Ch. 903.)

490.

(a) In addition to any other action that a board is permitted to take against a licensee, a board may suspend or revoke a license on the ground that the licensee has been convicted of a crime, if the crime is substantially related to the qualifications, functions, or duties of the business or profession for which the license was issued.

(b) Notwithstanding any other provision of law, a board may exercise any authority to discipline a licensee for conviction of a crime that is independent of the authority granted under subdivision (a) only if the crime is substantially related to the qualifications, functions, or duties of the business or profession for which the licensee's license was issued.

(c) A conviction within the meaning of this section means a plea or verdict of guilty or a conviction following a plea of nolo contendere. An action that a board is permitted to take following the establishment of a conviction may be taken when the time for appeal has elapsed, or the judgment of conviction has been affirmed on appeal, or when an order granting probation is made suspending the imposition of sentence, irrespective of a subsequent order under Section 1203.4 of the Penal Code.

(d) The Legislature hereby finds and declares that the application of this section has been made unclear by the holding in *Petropoulos v. Department of Real Estate* (2006) 142 Cal.App.4th 554, and that the holding in that case has placed a significant number of statutes and regulations in question, resulting in potential harm to the consumers of California from licensees who have been convicted of crimes. Therefore, the Legislature finds and declares that this section establishes an independent basis for a board to impose discipline upon a licensee, and that the amendments to this section made by Chapter 33 of the Statutes of 2008 do not constitute a change to, but rather are declaratory of, existing law.

(Amended by Stats. 2010, Ch. 328, Sec. 2. Effective January 1, 2011.)

STAFF ANALYSIS
DISCUSSION AND ACTION BY THE BOARD REGARDING THE PROPOSED
ADJUSTMENT OF THE 2015 SOUTHERN CALIFORNIA RACING CALENDAR, TO
ALLOCATE SEPTEMBER 26TH AND SEPTEMBER 27TH FROM SANTA ANITA TO
FAIRPLEX, AT LOS ALAMITOS

Regular Board Meeting
March 19, 2015

ISSUE

Los Angeles County Fair Association (Fairplex) at Los Alamitos has asked the Board to reconsider and revise the race dates allocated to Fairplex for 2015. The Board approved a start date of Thursday, September 10, 2015 for Fairplex and a closing day of Friday, September 25, 2015. The Board allocated Los Angeles Turf Club (LATC) the weekend of September 26 and 27 in anticipation that the 2015 Breeders' Cup would be held at LATC. The transcript from the September 2013 meeting clearly shows that the Board "built in some flexibility in the Fairplex dates" ... "subject to when the Breeders' Cup happens." Given that the 2015 Breeders' Cup will not be run at LATC, Fairplex at Los Alamitos is seeking a restoration of its traditional race dates, i.e., opening Thursday, September 10, 2015 and concluding Sunday, September 27, 2015. The adjustment would also necessitate a change to the LATC Autumn calendar as well, with a revised start date of Wednesday, September 30 or Thursday, October 1, as requested at licensure. The closing date of October 25 would remain unchanged.

BACKGROUND

Business and Professions Code section 19530 provides the Board the authority to allocate racing weeks to an applicant pursuant to the provisions of the horse racing law and to specify such racing days, dates, and hours for horse racing meetings as will be in the public interest, and will subserve the purposes of the law. Business and Professions Code section 19531 states the Board shall make allocations for racing weeks, including simultaneous racing between zones as it deems appropriate. The maximum number of racing weeks that may be allocated for horse racing other than at fairs, shall be as follows: (a) For thoroughbred racing: 44 weeks per year in the northern zone; 42 weeks per year in the central zone; and seven weeks per year in the southern zone. (b) For harness racing: 25 weeks per year in the northern zone. (c) For quarter horse racing: 25 weeks per year in the northern zone. (d) For harness racing and quarter horse racing: a total of 77 weeks per year in the combined central and southern zones. Business and Professions Code section 19532(a) specifies any association licensed to conduct thoroughbred racing in the northern zone may receive no more than 35 weeks of that racing. (b) Any association licensed to conduct thoroughbred racing in the central zone may receive no more than 17 weeks of that racing, except that any association which conducts a split meeting may receive up to 20 weeks of that racing. No more than one such split meeting may be licensed in any one year. Business and Professions Code section 19549 provides the maximum number of racing weeks that may be allocated to a fair shall be four weeks each, except under specified conditions.

Board Rule 1430, Allocation of Racing Weeks and Dates, states the Board shall allocate racing weeks and dates for the conduct of horse racing in this State for such time periods and at such racing facilities as the Board determines will best subserve the purposes of the Horse Racing Law and which will be in the best interests of the people of California in accord with the intent of the Horse Racing Law.

RECOMMENDATION

This item is presented to the Board for discussion and action.

ALLOCATED - 2015 SOUTHERN CALIFORNIA THOROUGHBRED RACE DATES

December						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
	22	23	24	25	26	27
28	29	30	31			
January						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

LATC @ Santa Anita (12/26/14 - 7/1/15)	LATC @ Santa Anita (9/26/15 - 10/25/15)
Los Alamitos TB @ Los Alamitos (7/2/15 - 7/12/15)	DMTC @ Del Mar (10/28/15 - 12/2/15) Fall
DMTC @ Del Mar (7/15/15 - 9/7/15) Summer	Los Alamitos TB @ Los Alamitos (12/3/15 - 12/20/15)
LATC @ Los Alamitos (9/10/15 - 9/25/15)	

February						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28

March						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

April						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

May						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						
September						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30			

June						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30				
October						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

July						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	
November						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30					

August						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30	31					
December						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

PROPOSED MODIFICATIONS TO THE ALLOCATED - 2015 SOUTHERN CALIFORNIA THOROUGHBRED RACE DATES

December						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
	22	23	24	25	26	27
28	29	30	31			

LATC @ Santa Anita (12/26/14 - 7/1/15)	
Los Alamitos TB @ Los Alamitos (7/2/15 - 7/12/15)	
DMTC @ Del Mar (7/15/15 - 9/7/15) Summer	
LACF @ Los Alamitos (9/10/15 - 9/27/15)	

LATC @ Santa Anita (9/28/15 - 10/25/15)	
DMTC @ Del Mar (10/28/15 - 12/2/15) Fall	
Los Alamitos TB @ Los Alamitos (12/3/15 - 12/20/15)	

January						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

February						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28

March						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

April						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

May						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

June						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30				

July						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

August						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30	31					

September						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30			

October						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

November						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30					

December						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

Proposal: To allocate September 26 & 27 From Santa Anita to LA County Fair at Los Alamitos.

MEETING
STATE OF CALIFORNIA
HORSE RACING BOARD

In the Matter of)
)
Regular Meeting)

SHERATON FAIRPLEX CONFERENCE CENTER
SONOMA BALLROOM
601 WEST MCKINLEY AVENUE
POMONA, CALIFORNIA

THURSDAY, SEPTEMBER 19, 2013

9:30 A.M.

Reported by:
Martha L. Nelson

1 2014 will be Santa Anita Park, 12/26/13 through 7/1 -- or
2 7/5/14; is that right?

3 VICE CHAIR WINNER: No.

4 CHAIR ISRAEL: To 7/2? All right. Well, so,
5 okay. Okay. All right, 7/2, you're right. Okay.

6 Then -- then Del Mar will be as it exists.

7 VICE CHAIR WINNER: As it exists in our document?

8 CHAIR ISRAEL: In our -- in our document.

9 Fairplex will be 9/14 to 9/23. Santa Anita will be 9/25
10 through 11/2. Okay.

11 Now, so now you have to add between Santa Anita
12 and Del Mar at the beginning Los Alamitos, 7/20 -- 7/3
13 through 7/13. Okay. Now, you need to adjust Del Mar's fall
14 meet so that it ends on December 3rd; is that correct?

15 MS. WAGNER: Uh-huh.

16 CHAIR ISRAEL: Is that right, December 3rd, Josh?
17 Joe? Somebody -- okay. Okay. So Del Mar will run 11/5
18 through 12/3. And from 12/4 through 12/21 will be Los
19 Alamitos in 2014. Okay.

20 Now, in 2015 Santa Anita's meet will end on July
21 1, the first meet. Del Mar will run 7/15 through 9/7.
22 Fairplex will run 9/10 through 9/25. And is 2015 the
23 year -- or it 2014, 2015 --

24 MR. SEDER: Yes. Mike Seder.

25 CHAIR ISRAEL: 2015 is the year we're -- where

1 we've built in some flexibility on the Fairplex dates.

2 MR. SEDER: Subject to when Breeders' Cup happens.

3 CHAIR ISRAEL: Subject to when Breeders' Cup --
4 okay. And Santa Anita will run 9/26 through 10/15. Los
5 Alamitos then -- so between Del Mar and Santa Anita the
6 first time Los Alamitos will run 7/2 through 7/12. Then Del
7 Mar will end on 12/2/15. And Los Alamitos will run 12/3 to
8 12/20/15.

9 MR. HAINES: Excuse me, Commissioner.

10 CHAIR ISRAEL: Yes. Did I get something wrong?

11 MR. HAINES: We're looking -- we heard you to say
12 that Santa Anita would run 9/26 through 10/15.

13 CHAIR ISRAEL: That's what's written here. That's
14 wrong. That's completely wrong. It's through -- it's
15 through 10/27.

16 There's two weeks -- you've got two weeks where
17 nobody is running, Jackie.

18 COMMISSIONER CHOPER: Yeah.

19 CHAIR ISRAEL: That's -- that's completely wrong.
20 And Del Mar runs 10/28 --

21 MS. WAGNER: That must be a typo.

22 CHAIR ISRAEL: -- through 12/2

23 MR. HAINES: I believe it's 10/25.

24 MS. WAGNER: Hold on.

25 CHAIR ISRAEL: Okay. Yes, it must be 25.

1 VICE CHAIR WINNER: It's a typo.

2 CHAIR ISRAEL: It's 25.

3 MS. WAGNER: Uh-huh. Yeah.

4 CHAIR ISRAEL: Okay. It's wrong in the packet.

5 VICE CHAIR WINNER: Is this to or through?

6 CHAIR ISRAEL: They say too.

7 VICE CHAIR WINNER: Yeah. It should say through,
8 just as you said it, because it includes those dates.

9 (Colloquy Between Commissioners and Ms. Wagner.)

10 CHAIR ISRAEL: Well, again, two tracks aren't
11 running at the same time. We're just going to say that.

12 MS. WAGNER: Yes.

13 CHAIR ISRAEL: Okay. So, now I'll review what we
14 just did in the form of -- since I don't think we need any
15 more discussion because we already discussed all the
16 permutations here --

17 MR. SEDER: Mr. Chair --

18 CHAIR ISRAEL: Yes, Mike?

19 MR. SEDER: May I interrupt for a second?

20 CHAIR ISRAEL: Sure.

21 MR. SEDER: This is Mike Seder, Barretts Sales and
22 Racing. I want to just clarify on the 2015 dates --

23 CHAIR ISRAEL: Right.

24 MR. SEDER: Fairplex's traditional -- I said
25 Fairplex. Barretts Sales and Racing's traditional dates --

1 CHAIR ISRAEL: It should go back to Fairplex by
2 then.

3 MR. SEDER: Thank you.

4 CHAIR ISRAEL: The handle would improve.

5 MR. SEDER: It would take us through September the
6 29th.

7 CHAIR ISRAEL: Right.

8 MR. SEDER: And in the -- in the event that
9 Breeders' Cup happens at the end of October we're looking at
10 these dates through the 25th. But there would be an
11 economic consideration to make us whole for giving up those
12 days.

13 CHAIR ISRAEL: Yes.

14 MR. SEDER: And in the event the Breeders' Cup is
15 run the first week of November, then we would --

16 CHAIR ISRAEL: You would revert to your old
17 tradition.

18 MR. SEDER: -- revert back to the 29th of
19 September.

20 VICE CHAIR WINNER: That's a part -- that's part
21 of the understanding.

22 CHAIR ISRAEL: That was part of -- that's a part
23 of the understanding we reached back in May initially. And
24 it obviously is something to be dealt with, you know, two
25 years from now when licensing -- or a little bit less than

STAFF ANALYSIS
DISCUSSION AND ACTION BY THE BOARD REGARDING THE PROPOSED
ADJUSTMENT OF THE 2015 NORTHERN CALIFORNIA RACING CALENDAR
TO MODIFY THE ALLOCATED FRESNO OCTOBER 1, 2015
STARTING DATE TO OCTOBER 8, 2015

Regular Board Meeting
March 19, 2015

ISSUE

California Authority of Racing Fairs (CARF) is requesting an adjustment to the 2015 race dates allocated to the Fresno Fair (Fresno). The Board allocated Fresno race dates of October 1, 2015 through October 12, 2015. CARF is requesting the Board modify the starting date for the Fresno race meeting from October 1, 2015 to October 7, 2015. CARF has shared that Fresno's live horse racing would begin October 8, 2015.

ANALYSIS

CARF has provided that in order for horse racing to run concurrently with the Fresno Fair, the race dates would need to be modified. CARF has additionally provided . . . *"the dates presently shown in the calendar for Fresno Fair would require it to conduct racing without Fair activities, a scenario which would hurt the Fair and its racing meeting.*

A change to the October calendar would involve a change in Golden Gate Fields schedule. Consequently, we've met several times with principals at GGF and Santa Anita and with representatives of the Thoroughbred Owners of California (TOC) to discuss this matter. We want the Board to know that CARF and the Fresno Fair are working with other affected parties and making every effort to find a mutually agreeable solution to this matter.

If the Fresno start date is not revised to October 7, the initial purse and stakes schedule we have proposed for Fresno Fair may need to be revised. If this were to occur, it could also affect purses and stakes at other Fairs."

BACKGROUND

Business and Professions Code section 19530 provides the Board the authority to allocate racing weeks to an applicant pursuant to the provisions of the horse racing law and to specify such racing days, dates, and hours for horse racing meetings as will be in the public interest, and will subserve the purposes of the law. Business and Professions Code section 19531 states the Board shall make allocations for racing weeks, including simultaneous racing between zones as it deems appropriate. The maximum number of racing weeks that may be allocated for horse racing other than at fairs, shall be as follows: (a) For thoroughbred racing: 44 weeks per year in the northern zone; 42 weeks per year in the central zone; and seven weeks per year in the southern zone. (b) For harness racing: 25 weeks per year in the northern zone. (c) For quarter horse racing: 25 weeks per year in the northern zone. (d) For harness racing and quarter horse racing: a

total of 77 weeks per year in the combined central and southern zones. Business and Professions Code section 19532(a) specifies any association licensed to conduct thoroughbred racing in the northern zone may receive no more than 35 weeks of that racing. (b) Any association licensed to conduct thoroughbred racing in the central zone may receive no more than 17 weeks of that racing, except that any association which conducts a split meeting may receive up to 20 weeks of that racing. No more than one such split meeting may be licensed in any one year. Business and Professions Code section 19549 provides the maximum number of racing weeks that may be allocated to a fair shall be four weeks each, except under specified conditions.

Board Rule 1430, Allocation of Racing Weeks and Dates, states the Board shall allocate racing weeks and dates for the conduct of horse racing in this State for such time periods and at such racing facilities as the Board determines will best subserve the purposes of the Horse Racing Law and which will be in the best interests of the people of California in accord with the intent of the Horse Racing Law.

RECOMMENDATION

This item is presented to the Board for discussion and action.



a California joint powers agency

1776 Tribute Road, Suite 205
 Sacramento, CA 95815
 Office: 916.927.7223 Fax: 916.263.3341
 www.calairs.com

March 6, 2015

Mr. Rick Baedeker, Executive Director
 California Horse Racing Board
 1010 Hurley Way
 Sacramento, CA 95825

Dear Rick,

We respectfully request that a matter be placed on the Board agenda for the meeting of March 19. We respectfully request that the Board approve certain adjustments to the October dates shown in 2015 racing calendar for Northern California.

The present calendar shows a starting date of October 1, 2015, for this year's Fresno Fair meeting. This year the Fresno Fair actually opens on **October 7, 2015**. In order for horse racing to run concurrently with the two weeks of the Fair in Fresno, racing would need to begin on Oct 7.

CARF and the Fresno Fair respectfully request that the Board approve a revised start date of October 7, 2015 for this year's Fresno Fair meeting.

The dates presently shown in the calendar for Fresno Fair would require it to conduct racing without Fair activities, a scenario which would hurt the Fair and its racing meeting.

A change to the October calendar would involve a change in Golden Gate Fields schedule. Consequently, we've met several times with principals at GGF and Santa Anita and with representatives of the Thoroughbred Owners of California (TOC) to discuss this matter. We want the Board to know that CARF and the Fresno Fair are working with other affected parties and making every effort to find a mutually agreeable solution to this matter.

If the Fresno start date is not revised to October 7, the initial purse and stakes schedule we have proposed for Fresno Fair may need to be revised. If this were to occur, it could also affect purses and stakes at other Fairs.

We respectfully suggest that time is of the essence in this matter. The parties which would be affected are planning right now for their respective meetings in the Fall. For this reason, we have requested that the matter be put on the March 19 agenda to seek the Board's approval for a prompt resolution.

We very much appreciate the Board's consideration of this matter.

Respectfully submitted,

/s/

Christopher Korby
Executive Director

ALLOCATED - 2015 NORTHERN CALIFORNIA RACE DATES

PRA Golden Gate Fields (12/26/14 - 6/15/15)	PRA Golden Gate Fields (8/21/15 - 9/13/15)
Alameda County Fair (6/17/15 - 7/6/15)	San Joaquin County Fair (9/18/15 - 9/27/15)
State Fair @ Cal Expo (7/9/15 - 7/26/15)	Fresno County Fair (10/1/15 -10/12/15)
Sonoma County Fair (7/30/15 - 8/16/15)	PRA Golden Gate Fields (10/15/15 - 12/20/15)
Humboldt County Fair (8/19/15 - (8/30/15)	

December						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
			24	25	26	27
28	29	30	31			

January						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

February						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28

March						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

April						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

May						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

June						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30				

July						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

August						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30	31					

September						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30			

October						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

November						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30					

December						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

PROPOSED MODIFICATIONS TO THE ALLOCATED - 2015 NORTHERN CALIFORNIA RACE DATES

	PRA Golden Gate Fields (12/26/14 - 6/15/15)	PRA Golden Gate Fields (8/21/15 - 9/13/15)	
	Alameda County Fair (6/17/15 - 7/6/15)	San Joaquin County Fair (9/18/15 - 9/27/15)	
	State Fair @ Cal Expo (7/9/15 - 7/26/15)	Fresno County Fair (10/8/15 -10/12/15)	
	Sonoma County Fair (7/30/15 - 8/16/15)	PRA Golden Gate Fields (10/15/15 - 12/20/15)	
	Humboldt County Fair (8/19/15 - 8/30/15)		

December	February	March	April
Sun Mon Tue Wed Thu Fri Sat			
24 25 26 27	5 6 7	5 6 7	1 2 3 4
28 29 30 31	8 9 10 11 12 13 14	8 9 10 11 12 13 14	5 6 7 8 9 10 11
4 5 6 7 8 9 10	15 16 17 18 19 20 21	15 16 17 18 19 20 21	12 13 14 15 16 17 18
11 12 13 14 15 16 17	22 23 24 25 26 27 28	22 23 24 25 26 27 28	19 20 21 22 23 24 25
18 19 20 21 22 23 24		29 30 31	26 27 28 29 30
25 26 27 28 29 30 31			

May	June	July	August
Sun Mon Tue Wed Thu Fri Sat			
1 2	4 5 6	1 2 3 4	1
3 4 5 6 7 8 9	7 8 9 10 11 12 13	5 6 7 8 9 10 11	2 3 4 5 6 7 8
10 11 12 13 14 15 16	14 15 16 17 18 19 20	12 13 14 15 16 17 18	9 10 11 12 13 14 15
17 18 19 20 21 22 23	21 22 23 24 25 26 27	19 20 21 22 23 24 25	16 17 18 19 20 21 22
24 25 26 27 28 29 30	28 29 30	26 27 28 29 30 31	23 24 25 26 27 28 29
31			30 31

September	October	November	December
Sun Mon Tue Wed Thu Fri Sat			
1 2 3 4 5	1 2 3	1 2 3 4 5 6 7	1 2 3 4 5
6 7 8 9 10 11 12	4 5 6 7 8 9 10	8 9 10 11 12 13 14	6 7 8 9 10 11 12
13 14 15 16 17 18 19	11 12 13 14 15 16 17	15 16 17 18 19 20 21	13 14 15 16 17 18 19
20 21 22 23 24 25 26	18 19 20 21 22 23 24	22 23 24 25 26 27 28	20 21 22 23 24 25 26
27 28 29 30	25 26 27 28 29 30 31	29 30	27 28 29 30 31

Proposal: The request is to move Fresno's starting Race Date from October 1, 2015, to October 8, 2015.

Regular Board Meeting
March 19, 2015