

# **NATIONAL H.B.P.A.**

## **MEDICATION REFERENCE GUIDE**



**National Horsemen's  
Benevolent &  
Protective Association**

***"Horsemen Helping Horsemen"***

## DIETARY, ENVIRONMENTAL AND ENDOGENOUS SUBSTANCES IN HORSES

With the increasing sensitivity of equine drug testing, the incidence of detection is rising for substances found in race horses' diet, environment, and endogenous substances (substances manufactured by their own bodies). These substances are categorized under three headings: dietary substances, environmental substances and endogenous substances.

### DIETARY SUBSTANCES

A dietary substance is any substance that is part of the normal and ordinary feed for horses. Several dietary substances yield materials in post-race samples that may trigger administrative actions. With dietary substances there are generally clear-cut geographic, seasonal and food source influences that may trigger a chemical identification in post-race samples. The following list gives several examples:

**SALICYLATE:** Salicylic acid (salicylate), the prototype for Non-Steroidal Anti-Inflammatory Drug (NSAID), is found in the post-race urine of all horses and has long been recognized as a "normal" in horse urine. Based on a number of studies, racing regulators recently established thresholds of 6.0 mcg/ml and 750 mcg/ml of salicylate in plasma and urine respectively. These thresholds are internationally recognized. The 750 mcg/ml threshold is currently under review in some states for adoption as the urinary threshold for this agent. Salicylate is an ARCI class 4 agent.

**HORDENINE:** Hordenine is a plant alkaloid that is closely related structurally and pharmacologically to epinephrine. It gets its name from *Hordeum vulgare* (barley), which is a common source of hordenine. Other common sources include reed canary grass, brewers grains and sprouting barley. Like salicylate, hordenine can be found in a large number of post-race urine samples if they are examined using highly sensitive methods. There are regional reports of unusually high concentrations of hordenine being found in the post-race urine samples of horses racing in Minnesota and also in Queensland, Australia. It seems likely that these geographically related high concentrations of hordenine are also seasonally related. There is no formal threshold for hordenine and hordenine is not classified by ARCI.

**DIMETHYL SULFOXIDE (DMSO):** DMSO is found in all samples of horse urine and is thought to be of dietary origin. DMSO and its metabolite, dimethylsulfone (MSM) therefore occur normally in horse urine. It has the ability to increase the speed of transcutaneous absorption of other substances when they are mixed with it. For this reason, trainers often apply it to their horses topically with leg braces and medications used to reduce swelling. In horses on a diet of Lucerne hay, urinary concentrations of DMSO as high as 5 mcg/ml of urine have been reported. DMSO is a class 5 substance in the ARCI classification system. DMSO is often readily identifiable in post-race urine samples and some state labs doing post-race testing routinely report on the presences of DMSO. The international thresholds for DMSO are 1 mcg/ml in plasma and 15 mcg/ml in urine.

**MORPHINE:** In certain parts of Australia, morphine is found in significant quantities in hay. It can also be found in the poppy seeds used in baked products such as bagels and muffins. Another possible source of morphine is codeine, which is metabolized to morphine in man and, presumably in horses. The pharmacological activity of codeine in man may be due to its metabolic change to morphine.

Findings of morphine in post-race urine samples may therefore be associated with contaminated hay in certain geographic areas, inadvertent feeding of poppy seed bagels, accidental contamination from prescription codeine or morphine. Because poppies grow wild in Australia, there are likely seasonal and geographic influences at work affecting the incidence of morphine identifications in that country. No published or unpublished thresholds for morphine have been established. Morphine is an ARCI class I agent.

**SCOPOLAMINE:** Scopolamine is an alkaloid closely related to atropine. Scopolamine is available as a pharmaceutical agent and also occurs from various plant sources. The most common plant source of scopolamine in the United States is jimson weed, which grows wild across much of the southern U.S. Scopolamine identifications are rarely reported in racing horses, and unequivocally distinguishing between pharmaceutical scopolamine and scopolamine from plant sources is far from easy. However, a seasonal finding of jimson weed in the race horses' pastures or hay and an associated finding of scopolamine in post-race urine tests clearly raises the possibility of environmental contamination. Within the last several years, a number of scopolamine identifications have been made in the U.S. and elsewhere. Scopolamine is an ARCI class 3 agent. No published or unpublished thresholds for scopolamine have been reported.

**BUFOTENINE:** Bufotenine or NN-dimethylserotonin is an indole alkaloid found in the leaves and seeds of *Piptadenia* and *Amanita*. Bufotenine is hallucinogenic, and materials from frogs and toad skin are sometimes ingested for the hallucinogenic effects. There has been at least one positive identification of bufotenine in a post-race urine sample in the U.S. and a number of identifications have been made outside the U.S. Although no penalty was assessed on this U.S. case, no formal threshold for this agent in post-race urine tests exist. Bufotenine is not classified by ARCI. No seasonal or geographic associations for bufotenine identifications have so far been reported.

**ARSENIC:** Arsenic is ubiquitous in nature and is found in all horse urine samples. However, it can be used as a tonic in small amounts and as a "stopper" in large amounts. A threshold was therefore needed to distinguish between normal arsenic and unusually high concentrations of arsenic in post-race urine tests. The international threshold for arsenic is now 0.3 mcg/ml of arsenic in urine. While it is likely that there may be geographic influences on arsenic concentrations in race horses' urine, these have not been described. Arsenic is not classified by ARCI.

#### **ENVIRONMENTAL CONTAMINANTS**

Environmental contaminants are substances brought into the environment of the horse by man. They are unlikely to be found in wild horses (feral horses not closely associated with man). Race horses may be exposed to these materials pre-race, in which case metabolites of the materials will be found in their post-race samples. Identification of the parent contaminant alone in the absence of appropriate metabolites is presumptive evidence of post-collection contamination.

**CAFFEINE:** Caffeine is the most widely used psychoactive agent in the world. Humans consume considerable amounts (up to 125 mg per day). Caffeine is extensively metabolized in the horse, with only about two to three percent of a dose being excreted in the urine as unchanged caffeine. A finding of caffeine in a urine sample along with its associated metabolites generally means that the caffeine went through a horse. A finding of caffeine without associated metabolites generally means

that the caffeine did not go through a horse, with the implication that the caffeine resulted from post-collection contamination. Because of the widespread environmental presence of caffeine, the Hong Kong Jockey Club has an unpublished threshold of 0.01 mcg/ml in plasma and 0.03 mcg/ml in urine. Racing officials in Malaysia also use an in-house threshold of 0.01 mcg/ml in plasma. Caffeine is an ARCI class 2 agent.

**THEOBROMINE:** For two decades, theobromine from coca husks has been the most commonly found contaminant in horse urine in England. It proved very difficult to remove coca husks from the horse feed, so the British Jockey Club took a different approach, developing a threshold for theobromine in urine at 2 mcg/ml. Studies on theobromine were carried out at the Horse Racing Forensic Laboratory in England. Theobromine is an ARCI class 4 agent.

**NICOTINE:** Nicotine is ubiquitous in the human environment, and is occasionally identified in post-race urine samples from horses. The metabolism of nicotine in the horse has not been described; however, in man cotinine and trans-3-hydroxycotinine are its major urinary metabolites. Based on what is known about the metabolism of nicotine in humans, the likelihood of free nicotine entering horse urine by any route other than contamination is small. In the absence of cotinine or other nicotine metabolites, a nicotine identification is presumptive evidence of post-collection contamination. Nicotine is not currently classified by ARCI.

**CONTININE/trans-3-HYDROXYCOTININE:** These agents are the major urinary metabolites of nicotine in man. Significant concentrations of such agents in a post-race urine test is presumptive evidence that the horse was exposed to nicotine, perhaps in the horse's bedding if the bedding was mixed with tobacco stalks. These agents are not classified by ARCI.

**Note:** The presence of nicotine metabolites and caffeine in a urine sample should trigger investigation of whether or not the sample is a genuine equine sample.

**COCAINE:** Cocaine is not unknown in certain human environments, and cocaine and/or its metabolites have been found in tongue ties, in saliva samples from horses entering races, and in post-race urine samples from horses. Most of these identifications have been at relatively low concentrations, so their pharmacological and forensic significance is often unclear. At Illinois tracks, control of the use of cocaine on tongue ties has been implemented by the use of pre-race cocaine testing with ELISA kits. Application of this test allows for the pre-race detection of cocaine contamination. This gives the trainer the option to withdraw the horse, and most elect to do so. This approach avoids the problem of determining the source, the pharmacological effect, and the forensic significance of trace amounts of cocaine or its metabolites in post-race urine tests. Cocaine is classified as an ARCI class 1 agent.

## **ENDOGENOUS SUBSTANCES**

Endogenous substances are substances that are specifically synthesized within the horse and are independent of dietary or other sources.

**HYDROCORTISONE:** Hydrocortisone is an endogenous corticosteroid hormone produced by the adrenal gland and essential to normal life. It is also available as an injectable pharmaceutical, and its

release in the horse can be specifically stimulated by administration of ACTH. To control its use in racing horses, a urinary threshold of 1 mcg/ml has been established. Hydrocortisone is an ARCI class 4 agent.

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