## Report regarding the finding of Dextrorphan

## in Churchill Downs equine urine sample 0086010

- 1. I have received and reviewed the information contained in the LGC litigation packet (primary lab results) relative to the testing of urine sample 0086010 collected at Churchill Downs on November 28, 2015, and the subsequent referee analysis conducted by Industrial Labs reported on February 26, 2016. An examination of these data indicate the presence of Dextrorphan, the major equine urinary metabolite of the non-narcotic antitussive dextromethorphan, a common antitussive. The concentration of this substance in urine was estimated to be approximately 15 ng/ml after enzyme hydrolysis. The specific gravity of the urine was recorded by LGC as 1.020 (page 5 of LGC packet). The pH of the sample was apparently not recorded. Both specific gravity and urine pH can greatly affect the urine level observed.
- 2. Although blood was collected and submitted to the laboratory, there is no evidence that the presence of Dextrorphan or Dextromethorphan was detected. The blood is, thus, assumed to be negative. There are no data evident for the direct analysis of the urine sample for Dextrorphan as its glucuronide (the form in which it is excreted in urine). However, a differential analysis (with enzyme hydrolysis and without) to determine whether Dextrorphan was present in its "free" form as opposed to the glucuronide form suggested that the free level was approximately 1 ng/ml and the metabolite level (Dextrorphan glucuronide) was approximately 14 ng/ml.
- 3. The absence in blood and low level of metabolite found in urine is suggestive of contamination, either of the horse or through direct contamination of the urine sample at the point of collection. The possible direct contamination of the sample or inadvertent contamination of the horse by Dextromethorphan, and thus a finding of Dextrorphan, is of concern because Dextromethorphan is one of the most common over-the-counter therapeutic medications used by humans. Dextromethorphan (DXM) is an antitussive (cough suppressant) drug of the morphinan class with mild sedative and dissociative

properties. It is one of the active ingredients in many over-the-counter cold and cough medicines, including generic labels and store brands, Benylin DM, Mucinex DM, Camydex-20 tablets, Robitussin, Nyquil, Dimetapp, Coricidin, Delsym, Theraflu, Alka Seltzer Plus, Comtrex, Pediacare, Triaminic, Tylenol Cough & Cold, Vicks Dayquil/Nyquil, Vicks Formula 44<sup>TM</sup> and more, including store brand versions of these products. These and other products are available in throat spray, tablet, lozenge, and oral syrup formats and may contain dextromethorphan at a dose of between 10-30 mg (tablets, lozenge) or 10-30 mg/dose (5-15 ml) for syrups. The primary use of Dextromethorphan is as a cough suppressant and for the temporary relief of cough caused by minor throat and bronchial irritation.

- 4. DXM has also been found to have a use in equine veterinary medicine for the treatment of cribbing (Rendon et al., 2001; Attachment 1). It has been reported that, at a dose of 1 mg/kg (approximately 500mg/horse) DXM produced effective reduction in this compulsive equine behavior for up to three hours. Its usefulness in this regard appears to be due to the fact that it acts in the brain as an agonist at what is known as NMDA (N-Methyl-d-Aspartate) receptors, apparently resulting in an attenuation of compulsive behavior.
- 5. The major metabolite of DMX in the horse is Dextrorphan, (DXO) the compound reported in this case. As a primary metabolite, it appears in the urine of horses as the glucuronide metabolite following a 300 mg oral dose at concentrations in the microgram to high nanogram (>100 ng/ml) level for up to 30 hours and remains detectable at > 50 ng/ml nanogram level for 96 hours or more (Canadian Pari-Mutual Association study; Attachment 2). This is a period of time far beyond its recognized therapeutic time range of 4-8 hours. Dextrorphan is formed primarily through liver metabolism, then undergoes secondary metabolism and is excreted in the urine as its O-glucuronide. Analysis of the urine for Dextrorphan requires enzyme treatment to remove the glucuronide.
- 6. DMX is an Association of Racing Commissioners International Category 4 drug. This category includes therapeutic medications and substances not thought or shown to have the potential for significant effects on behavior or performance.

7. In examining the data from LGC and Industrial Laboratories, I am generally in agreement with the idea that the concentration of Dextrorphan present is in the range of 15 ng/ml. It may be argued that the concentration is not relevant because this is not a permitted substance and that its mere presence is sufficient to prosecute. Nonetheless, 15 ng/ml is far different from what would be observed for the urine level from the administration of an effective dose (See CPMA study) and demonstrates that this finding is inconsistent with the administration of this substance to effect the performance of the horse (an ability for this substance that has never been demonstrated) and it is evident that this was certainly not an administration on race day.

Indeed, this level of the metabolite (15 ng/ml) of DXO is not pharmacology relevant and it can be stated to a scientific certainty that this horse was not influenced by the presence of this substance in his urine in any manner. It had no effect on his behavior or performance.

- 8. Rather, the low level of the metabolite alone strongly suggests that the source of this substance was environmental contamination, with which it is consistent. I am given to understand that one of the persons responsible for handling the horse was using the product Nyquil and may likely be a source for the contamination. Humans also excrete DXO in their urine and someone taking a cough or cold medication that comes into contact with the horse or that urinates in its stall could cause the finding reported here. Indeed, if someone dropped a 10-30 mg tablet or lozenge containing dextromethorphan near the horse and the horse consumed it, a positive would certainly result. However, even a 30 mg exposure orally to a horse would not have effected its performance. Higher doses (200-500 mg) are required before any effect of DMX or DXO would be observed or measured. Similarly, personnel collecting the sample that also used a DMX containing product could inadvertently contaminate the sample at the point of collection.
- 9. Thus, it is my opinion that the finding of DXO at 15 ng/ml in the urine of the horse in question was more likely than not caused by inadvertent environmental exposure and that this exposure, to a scientific certainty, had no effect on the performance or behavior of the horse whatsoever.
- 10. It is unfortunate that such insignificant findings result in a prosecution. The mere presence of a drug does not necessarily imply nefarious actions and the calling of positives for insignificant concentrations of an ARCI Category 4 drug serves no one. Rather than protect the integrity of the sport, such prosecutions continue to damage the image of the industry and the reputations of trainers, owners and horses. It is also unfortunate that the State of Kentucky does not rely on the

pre-review of such data by a qualified equine pharmacologist. Such a review would prevent such unnecessary prosecutions as this from going forward by reaching the conclusion that the level is pharmacologically irrelevant, that no one had an unfair advantage, no one was endangered and no one was defrauded. Kentucky is expected to be the best in the industry but its reliance on unqualified personnel, such as its Equine Medical Director, to interpret such information and make recommendations on prosecutions is far less than we would expect of the industry's leader. It is my opinion that the regulatory authorities of Kentucky are being seriously misled by those currently making decisions in this regard. Such cases should be dismissed at the time of reporting and should not be allowed to further and unnecessarily damage the image of racing.

Respectfully submitted

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Subscribed and sworn to before me on this 21 day of June, 2016 by Dr. Steven A. Barker in the Parish of East Baton Rouge, Baton Rouge, Louisiana.

Notary Public