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Letter to the Editor

Food and Chemical Toxicology, 2010, Association of phenylbutazone usage in horses bought for slaughter: A public health risk

Dear Dr. Hayes,

The paper "*Association of phenylbutazone usage in horses bought for slaughter: A public health risk*" by Nicolas Dodman, Nicolas Blondeau, and Ann M. Marini published by Food and Chemical Toxicology in February 2010 is a classic example of utilizing unrelated scientific information to support an unfounded conclusion. By mixing sound research conducted on humans with unrelated sound research from horses, the authors attempt to formulate an unfounded and unsubstantiated conclusion that horsemeat derived from American horses contains residues of phenylbutazone (PBZ) that are harmful to humans. This conclusion is not supported by the research cited or any other research that we have discovered.

The Research Methods described in the article indicate that 18 horses reportedly administered PBZ "were not rescued" and were presumed to have gone to slaughter. The authors document that possibly 9 horses were slaughtered within 6 months of PBZ administration. In reality, this fact represents the only real data in the entire study, although the authors make much of selected publications in their discussion to suggest otherwise. None of the 64 horses tracked in the study were tested for the presence of PBZ at any time. The repeated suggestions by the authors that some or all of the PBZ-administered and slaughtered horses contained residues is completely unsubstantiated, and is in fact refuted by studies not referenced by the authors (Tobin et al., 1982. J. Vet. Pharm. Therap. 5, 195–197; Tobin. Drugs and the Performance Horse, Charles C. Thomas, Publ, 1981; Harrison et al., 2006. J. Zoo. Wildlife Med. 37, 102–107).

The Discussion, as well as the Introduction, spends considerable time discussing data from the administration of PBZ to humans and a clear-cut relationship to aplastic anemia and leukemia. This admittedly serious side effect led to the banning of PBZ for human use by the FDA. This information is not in dispute. The authors also spend considerable space presenting information concerning utilization of PBZ in horses. Again, the data from these cited reports are not in question. What *is* unsupportable is the conclusion drawn from these unrelated studies that PBZ usage in horses presents a public health risk for humans who ingest horsemeat. There is no scientific data presented to support this conclusion.

The European Food Safety Authority has never reported an incident of horsemeat contaminated by PBZ residues. This lack of contamination is due to the rapid removal of PBZ and its metabolites from the horse. Reports by Dr. Thomas Tobin and associates of the Maxwell H. Gluck Equine Research Center have shown that the half-life of PBZ in the horse is 7.22 h. These researchers have demonstrated that 90% of a dose will be eliminated in 24 h. At 48 h post administration the level of PBZ in the blood was less than 0.4% of the initial dose and at 72 h it was 0.02%. Since, as the article states, PBZ and its metabolites are highest in the blood, it is quite supportable that the level found in muscle tissue would be totally undetectable at 72 h post administration. Given the highly sensitive detection methods available to modern science, if a drug is undetectable, it is virtually not present. Even humans that respond unpredictably ("idiosyncratically") to a drug have no stimulus to respond in the absence of the drug. In short, the presence of PBZ following slaughter, processing, and preparation of horsemeat has not been demonstrated. Thus it is scientifically impossible to link this to possible human health risks.

Finally, to support their assertion of a public health risk, the authors rely heavily on the undisputed fact that "the FDA has set no safe limits of PBZ in animal carcasses"; and "the FDA like the EU and the UK, specifically bans the use of PBZ in any horse destined for slaughter for human consumption". Even an idiosyncratic risk for a disease cannot be proved by either the presence or the absence of a regulation. If this were the case, the converse would also be true and the FDA could just as easily eliminate cancer by simply ruling it out of existence. Scientific study, put simply, is the pursuit of the truth. Regulations can have no influence on the design of the study or the interpretation of the results. This represents a second obvious and critical flaw in this work and should have prevented its publication.

We trust that future acceptance of articles by Food and Chemical Toxicology concerning the horse will be properly reviewed prior to acceptance and publication.

Thanks for your consideration.

Sincerely,

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Letter to the Editor

Food and Chemical Toxicology, 2010, author response to letter by Don Henneke, Sheryl King, William Day and Pat Evans regarding Association of phenylbutazone usage in horses bought for slaughter: A public health risk

Dear Dr. Hayes,

We are responding to the letter by Henneke, King, Day and Evans regarding our paper entitled: "Association of phenylbutazone usage in horses bought for slaughter: A public health risk."

The Food and Drug Administration (FDA) and comparable agencies in Canada, United Kingdom, and the European Union bans phenylbutazone in all food-producing animals, including horses. The FDA website describing the phenylbutazone ban is located here: http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm124078.htm. As stated by the FDA in the website: "Use in horses is limited to use in horses not intended for food. There are currently no approved uses of phenylbutazone (PBZ) in food-producing animals."

This statement by the FDA means that any horse *administered* phenylbutazone is ineligible for slaughter for human consumption. Phenylbutazone does not have a withdrawal time. Therefore, the dates the horses were given phenylbutazone in our paper are irrelevant because the drug is banned. The PBZ ban as outlined by the FDA is identical to the ban in the following countries: United States, Canada, United Kingdom, and the European Union. Thus, if a horse is administered one dose of phenylbutazone, the horse cannot enter the food chain.

The half-life of the drug in blood is irrelevant and the quoted time of elimination from muscle by the authors is unsubstantiated by scientific studies and is also irrelevant because the drug is banned.

The authors state: "None of the 64 horses tracked in the study were tested for the presence of PBZ at any time." This is an incorrect statement as one horse had documented PBZ levels as this horse won at a racetrack within the United States and a mandatory drug test is required of all horses that win a race (Dodman et al., 2010).

The purpose of our study was to determine whether horses destined for the food chain were *administered* the banned drug phenylbutazone prior to being bought for slaughter. Our central hypothesis was that horses destined for the food chain are administered PBZ prior to being slaughtered for human consumption. Veterinary records are not available to the public. However, racetracks around the country allow race day PBZ and the use of PBZ is documented and available to the public (Dodman et al., 2010). We used these racetrack drug cards to document the administration of PBZ to the 18 Thoroughbred horses bought for slaughter for human consumption. All 18 Thoroughbred horses were administered the banned drug phenylbutazone prior to being bought for slaughter for human consumption. Because PBZ is banned by the United States as well as Canada, the United Kingdom and the European Union, it was a violation that those 18 horses were slaughtered and the meat sent overseas, principally Europe, for humans to eat.

As stated by the FDA:

> Phenylbutazone is known for its ulcerogenic, nephrotoxic, and hemotoxic effects in horses, dogs, rats and humans. It is known to induce blood dyscrasias, including aplastic anemia, leucopenia, agranulocytosis, thrombocytopenia and deaths. The reported adverse reactions were associated with the human clinical use of 200 to 800 milligrams of phenylbutazone per day. Hypersensitivity reactions of the serum-sickness type have also been reported in patients with phenylbutazone. The threshold for this effect has not been defined. Therefore, it is unclear what level of exposure would be required to trigger such reactions in sensitive people. Moreover, phenylbutazone is a carcinogen, as determined by the National Toxicology Program (NTP) based on positive results in genotoxicity tests and some evidence of carcinogenicity seen in the rat and mouse in carcinogenicity bioassays NTP conducted (FDA, 2003).

In summary, horses are not raised for food in the United States and horses given banned drugs are not removed from the slaughter pipeline. PBZ is banned in horses entering the food chain by the United States, the United Kingdom, Canada and the European Union. It is the *administration* of the drug that makes a horse ineligible for slaughter for human consumption not the half-life in blood or tissue residue levels. Given the dangerous and deadly side effects, American horses given PBZ and sent to slaughter for human consumption represent a violation of orders set forth by agencies around the world tasked with keeping food safe. Moreover, children have greater sensitivity and susceptibility to aplastic anemia caused by PBZ as indicated in a short article published by the Irish Veterinary Journal (vol. 63, no. 12, pp. 766–768) where it is stated: "The difficulty with phenylbutazone is that it, or its metabolite, can cause aplastic anaemia in children. If a child were to consume an animal-based product containing even the minutest amount of bute or its metabolite then the child may develop aplastic anaemia."

The failure to remove American horses given PBZ from the slaughter pipeline prior to being slaughtered for the human food chain is a food safety violation and public health risk no matter where the horsemeat is sent for human consumption. Furthermore, unless physicians are cognizant of the fact that American horses are not raised for food and slaughtered for human consumption, it is unlikely that dietary horse meat will be considered as the source of illnesses known to be induced or caused by phenylbutazone, including cancer. The slaughter of American horses for human consumption must end immediately.

Thank you for the opportunity to respond to this letter.

Sincerely,

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