Melamine/Cyanuric Acid Fact Sheet

**History – 2007 Outbreak**
In early 2007, large numbers (estimated to be in the thousands) of dogs and cats in North America developed acute renal failure associated with ingestion of certain brands of pet food. Shortly thereafter, a pet food company observed acute renal failure in cats engaged in a routine palatability study, prompting the March 2007 voluntary recall of food produced by Canadian-based Menu Foods at plants in the United States (US). Clinical and pathologic features of this apparently unique toxicosis were rapidly disseminated throughout the US veterinary community, primarily through the Internet.

By the end of March, melamine was identified in wheat gluten, a thickening agent primarily used in wet pet foods, supplied by Chinese manufacturers to Menu Foods. It was also discovered in tissues and urine from an affected cat. Melamine was subsequently found in rice protein from a different source in China and, following an outbreak of renal failure in South Africa, in corn gluten in that country. Following the discovery of melamine in pet food, veterinary scientists were not convinced, given published toxicology studies, that melamine alone was responsible for the observed nephrotoxicity. Continued investigation revealed the presence of a critical second contaminant, cyanuric acid, in contaminated pet foods and in renal tissues of fatally poisoned animals.

**History – 2004 Outbreak**
A clinically similar outbreak of pet food-associated renal failure occurred in Asia in 2004. It affected an estimated 6,000 dogs and involved commercially prepared pet food. Reexamination of renal tissue from these Asian dogs following the 2007 outbreak confirmed that they were also victims of melamine/cyanuric acid toxicosis.

**Cause**
Melamine is synthesized from urea and made into industrial products such as melamine resin, a very durable plastic, and melamine foam, a cleaning agent. Nitrogen content has long been used as an indirect means for assessing the protein content of foods, and melamine is 66% nitrogen. It is now generally accepted that melamine was intentionally added by suppliers in China to falsely elevate the measured protein content and the monetary value of vegetable proteins. It was also apparent this was a longstanding practice. While melamine alone is relatively nontoxic in dogs and rodents, melamine and cyanuric acid together are highly toxic. The cyanuric acid may have also been added intentionally or it may have been a by-product of melamine synthesis. Melamine and cyanuric acid are excreted unchanged into the urine, and, when given together, form insoluble crystals that obstruct and damage renal tubules and cause kidney failure.

**Clinical and Pathologic Findings**
Poisoned animals had clinical and laboratory evidence of uremia, including anorexia, vomiting, lethargy, polyuria, azotemia and hyperphosphatemia. Most animals died or were euthanized because of severe uremia. Histologically, characteristic lesions included mild distal renal tubular necrosis with unique intratubular crystals, variable inflammation and, in more chronic cases, fibrosis.
Melamine and Human Health
In 2008, an estimated 294,000 infants and children in China ingested milk-based formula tainted by melamine. Almost 53,000 children required hospitalization due to urolithiasis; acute renal failure was reported in 2.5%. As was the case with the contaminated wheat, rice and corn glutens, melamine was believed to have been added to infant formula to artificially elevate measured protein content.

Conclusion
The veterinary and medical communities, along with regulatory agencies, should develop cooperative programs to identify potential origins of contamination prior to outbreaks of toxicoses. These programs would not only more effectively identify risk but also rapidly recognize and manage outbreaks.

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