June 15, 2011

**Target Animal Safety Review Memorandum**

**Background**

Ralph Obenauf, Patricia Atkins, Lazlo Ernyei, and William Driscoll, employees of SPEX CertiPrep

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, Incorporated, 203 Norcross Avenue, Metuchen, New Jersey 08840, presented an abstract and poster at the annual meeting of the Federation of Analytical Chemistry and Spectroscopy Societies (FACSS), October 17-21, 2010 in Raleigh, North Carolina, entitled “Trace Metal Analysis of Commercial Pet Food for Toxic Metals by ICP and ICP-MS.” The authors stated the purpose of the study “was to examine pet foods from various sources to determine if they contained potentially toxic elements and if higher quality ingredients equated to less toxic elements present in the food.” The poster listed analytical results for 17 elements (arsenic, beryllium, cadmium, cobalt, chromium, cesium, mercury, molybdenum, nickel, lead, antimony, selenium, tin, thorium, thallium, uranium, and vanadium) measured in 58 pet foods, consisting of 31 dry foods (18 for dogs, 13 for cats) and 27 wet foods (13 for dogs, 14 for cats). Information in the poster indicated that similar measurements were made on canned tuna, sardines, and chicken marketed for human consumption.

The authors calculated daily exposures expressed as quantity of element consumed per kilogram (kg) body weight (BW) per day by assuming a 10 pound (lb.) cat consumed 1 cup (100 grams (g)) of dry food or 1 small can (175 g) of wet food per day; or a 50 lb. dog consumed 5 cups (500 g) of dry food or 1 large can (375 g) of wet food per day. The calculated exposures for the respective metals were compared to reference dose (RfD) values set by the Environmental Protection Agency (EPA) and the permissible tolerable daily intake (PTDI) values set by the World Health Organization (WHO) for people. The authors indicated that dogs and cats eating the foods with the greatest concentrations of various elements would be consuming between 2 to 120 times the respective RfD’s set by the EPA for people for arsenic, cadmium, mercury, thallium, uranium, and vanadium. The poster also stated that, “Significantly high concentrations of toxic metals were found in many of the food samples” listing the number of pet food samples and the analytical results that the authors deemed to be “significant.”

The release of the poster caused Susan Thixton to request a statement from the Association of American Feed Control Officials, Inc. (AAFCO) on the results, and AAFCO in turn requested the Center for Veterinary Medicine (CVM) provide an evaluation of the information presented in the poster.

When the poster was released, it appeared the authors intended to publish the results in a peer- reviewed journal. CVM indicated that it would prefer to see the journal publication before commenting. A manuscript, entitled “Analysis of Toxic Trace Metals in Pet Foods Using Cryogenic Grinding and Quantitation by ICP-MS, Part I” authored by P. Atkins, L. Ernyei, W. Driscoll, R. Obenauf and R. Thomas, appeared in the January 2011 issue of Spectroscopy® published by Advanstar Communications, Incorporated.1 A manuscript entitled “Analysis of Toxic Trace Metals in Pet Foods Using Cryogenic Grinding and Quantitation by ICP-MS, Part

Page 2 of 25 – 11024 Target Animal Safety Review

II by the same authors appeared in the February 2011 issue of Spectroscopy®.2 A comment on the results of the studies and their implications along with a recommendation for owners of pets from the editor of Spectroscopy®, Laura Bush, also appeared in the February edition of Spectroscopy

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(page 12, From the Editor – Do You Get What You Pay For?). A webinar on the same subject matter was given by the firm on February 10, 2011 and information from the webinar and journal articles was posted to YouTube in early March 2011.

In the manuscripts, the authors did not change the approach used in the poster for calculation of exposures or the reference standards to which the calculated exposures were compared. However, the manuscripts only contained information on 15 of the 17 elements for which results were included in the poster. No information was provided in the manuscripts for selenium or tin, although the poster contained limited information implying that the content of these two elements in pet foods was problematic, particularly in regard to tin being characterized as one of the “highest results for trace toxic metals.” The first of the two publications renewed requests from Susan Thixton and AAFCO for statements and evaluations of the information presented in the manuscript. Subsequently, Ms. Thixton contacted the CVM Communications staff directly. The CVM was also contacted by Mollie Morrisette concerning the results of the publications.

**Veterinary Medical Officer’s Review\***

Although the execution of the inductively coupled plasma-mass spectrometry (ICP-MS) to obtain the concentrations of elements reported in the manuscripts may have been done to current scientific methodological standards, the manipulations, comparisons, characterizations, and interpretations of those concentrations beyond a strict mathematical treatment are seriously flawed in multiple respects. There are three critical mistakes in the approach taken by the authors to interpret the analytical results that are fatal to the scientific conclusions drawn by the authors, and multiple minor mistakes and mischaracterizations detract from the scientific integrity of the publications. Because of the multiple flaws, or mistakes, described below, the overall implied conclusion that some or all of the pet food samples contained one or more elements in toxic amounts for dogs or cats is unjustified.

***Critical Mistakes***

The first mistake, and the one most critical, is the selection of the EPA RfD and WHO PTDI values for comparison and judging whether the calculated exposures are excessive and problematic for dogs or cats. The authors state in the conclusion section of their second manuscript (p. 59) that they, “do not know if the EPA RfD and WHO [P]TDI values apply the same to animal physiology.” However, in multiple other statements throughout the manuscript the authors use the EPA and WHO values to indicate that the metal content of pet foods is excessive with the quantities being at least problematic, if not toxic, repeatedly characterizing the metals as “toxic trace metals” and “contaminants” (Part II, pp. 46, 54-59). The authors justify the use of the EPA RfD and WHO PTDI values because, “[t]here are no guidelines set down by the FDA for trace-element contaminants in pet food” (Part II, p. 46).

\* This review uses the terms “metal,” “mineral” and “element” interchangeably, although each term may be more

accurate with respect to certain chemical elements and in certain specific contexts.

Page 3 of 25 – 11024 Target Animal Safety Review

It is true that FDA has not promulgated guidance, action levels, or tolerances for maximum content in feeds for the 15 elements measured and discussed in the manuscripts. The specific 15 elements measured in the Atkins et al. studies, as well as other elements in the periodic table, may be naturally occurring constituents of feeds and feed ingredients. The Federal Food, Drug, and Cosmetic Act (the Act) requires that the amount of a poisonous or deleterious substance that is itself not directly added to food, but rather is a constitutive component of food, needs to be present in an amount that ordinarily renders the product injurious to health before the food can be considered adulterated and actionable under the prohibitions of the Act. To meet this adulteration standard for elements present in animal feeds, including pet foods, the FDA considers the information and recommendations of the National Research Council of the National Academies (NRC) Committee on Minerals and Toxic Substances in Diets and Water for Animals (MTSA Committee) as published in Mineral Tolerance of Animals Second Revised Edition, 2005.

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The MTSA Committee is an independent group of scientists with recognized scientific expertise in the effects of elements on metabolism and health of animals. In the 2005 publication, this committee provided maximum tolerable levels (MTL) for 37 individual elements, for rare earth minerals, for sodium chloride, and for nitrates and nitrites in the feed of rodents, poultry, swine, horses, cattle, sheep and/or fish based on indexes of animal health after reviewing pertinent information in the scientific literature. Because the values recommended by the MTSA Committee are based on results from studies in a wide variety of animals, including dogs and cats, these MTL are the appropriate comparators for animal diets and physiology rather than the EPA RfD and WHO PTDI values for people.

The second critical mistake made by Atkins et al. is the lack of any scientific basis for the amount of food consumed by the reference-size 50 lb. dog or 10 lb. cat. There is much scientific information in the public domain on typical daily energy requirements of pet dogs and cats as well as typical caloric densities of dry and wet dog and cat foods. Also, each of the products that were tested should have contained recommended amounts to feed for a specific weight of dog or cat in a “feeding directions” section of the label, and this information should have been available to the authors. Setting expected daily amounts for consumption based on either daily energy requirements and actual or assumed energy density of the products, or from suggested amounts in feeding directions would have been more justifiable and credible than the approach taken by the authors in which they arbitrarily assumed that a 50 lb. dog would consume 5 cups, with one cup weighing 100 g, or one can with net contents of 375 g wet food per day; or that a 10 lb. cat would consume 1 cup of dry food, or one can with net contents of 175 g of wet food per day.

The equation for energy requirements of pet dogs in table 15-4, page 359, in the NRC 2006 edition of Nutrient Requirements of Dogs and Cats4 indicates an average adult pet dog will typically require approximately 989 kilocalories (kcal) of metabolizable energy (ME) per day to maintain a body weight of 50 lb. [95\*((50/2.2)0.75)=989]. As-fed, dry dog foods that are not calorie-restricted products will typically contain somewhere between 315 and 425 kcal ME per cup. Energy requirements for an average 50 lb. pet dog will be met by slightly more than 3 cups, but less than 31⁄4 cups of even the least calorie-dense maintenance formulas (i.e., the

Page 4 of 25 – 11024 Target Animal Safety Review

formulas requiring the largest quantity of food to meet energy requirements). A 50 lb. adult maintenance pet dog eating 5 cups of dry dog food per day is consuming 1.6 to 2.0 times their daily food requirement.

For the expected amount of wet food consumed per day, the authors have underestimated the amount needed to maintain a 50 lb. adult maintenance pet dog. As-fed, wet pet foods typically have a caloric density of about 1 kcal ME/g. Thus, at 375 grams of food, or 375 kcal ME per day, a 50 lb. adult maintenance dog is only receiving a little more than 1/3 (375/989=0.38 or 38%) of its daily energy requirement. The uncorrected disparity of differences in moisture in the expressed concentrations of elements in wet and dry products is the third critical mistake in the interpretation of the data. Thus, if one underfeeds a wet food, which when uncorrected for moisture is already less dense in mineral concentrations, and overfeeds a dry food, which is already more dense in mineral concentrations by virtue of its lower moisture content, it is not surprising that the daily exposures appear to be greater for the dry than the wet products.

Similar problems exist for the amounts of dry versus wet foods fed to the reference-size 10 lb. cat. The equation for energy requirements of pet cats in table 15-11, page 366, in the 2006 Nutrient Requirements of Dogs and Cats

4

indicates an average 10 lb. adult maintenance pet cat will typically require approximately 276 kcal ME per day [100\*((10/2.2)0.67)=276]. As-fed, dry cat foods that are not calorie-restricted products will generally contain somewhere between 360 and 425 kcal ME per cup. Energy requirements for an average 10 lb. pet cat will be met by just slightly more than 3⁄4 cup of even the least calorie-dense maintenance formulas (i.e., the formulas requiring the largest quantity of food to meet energy requirements). If a cup of dry cat food weighs 100 g, the weight of a 360 kcal/cup food meeting daily energy requirements would be 77 grams. This is in general agreement with 50 to 75 g amounts of dry foods typically needed to meet daily feline energy and nutrient requirements. A 10 lb. adult maintenance pet cat eating 1 cup of dry cat food per day is consuming at least 1.25 times their daily food requirement. For typical wet pet foods containing 1 kcal ME/g, a 10 lb. adult maintenance pet cat eating 175 g is consuming just under 2/3 of its daily energy requirement (175/276=0.63 or 63%). Although the relative range in the disparity between amounts of canned versus dry foods compared to daily energy requirements is less for the reference-size cat than the reference-size dog in the published studies, these systematic errors and their overall impact on the results and the authors’ conclusions are the same.

As indicated above, the third critical mistake is the authors’ failure to account, or correct, for the differences in moisture content of dry versus wet foods and the effect this has on the reported concentrations of elements or other nutrients in the foods. The exact dry matter (DM) content of each of the 58 products tested is likely to vary over a range of approximately 85 to 95% for dry foods and over a range of approximately 20 to 35% for wet (canned or pouched) foods. The authors had samples of specific products and it would have been possible to determine the specific moisture content of each product. Lacking equipment or willingness to expend the time and resources to measure moisture in each product sample, the authors could have used typical moisture or dry matter contents for dry versus wet pet foods to convert the measured quantities to a reasonable dry matter quantity for comparison.

Page 5 of 25 – 11024 Target Animal Safety Review

The authors repeatedly make comparisons between concentrations of metals in dry and canned products on an as-is or as-measured basis, concluding that the dry products have the greater concentrations of the measured metals and provide the greater exposures (Part I, pp. 53-54; Part II, pp. 50, 54). The conclusion of greater exposure is produced both from the uncorrected moisture content between dry versus wet products as well as the arbitrary overfeeding of dry and underfeeding of wet quantities of food. Such comparisons are scientifically meaningless without the concentrations being first corrected to an equal moisture basis and the product amounts established on the basis of some physiological standard such as amounts of dry matter providing daily caloric requirements or amounts of dry matter that can reasonably be expected to be consumed based on a percentage of the animal’s body weight.

A fourth substantive, if not critical, mistake is the authors’ failure to employ any appropriate statistical methods in summarizing, comparing or making inferences about the results.

The information on the initial pages of the journal does not make it clear whether manuscripts published in Spectroscopy® undergo scientific peer review. If one assumes that the information presented in the manuscripts did in fact undergo peer review prior to publication, then it is clear that neither the authors, nor the reviewers, nor the journal editor have sufficient expertise in animal nutrition, animal physiology, or mineral toxicology in domestic species to be aware of the mistakes and mischaracterizations contained in the approach involved with the manipulation of the raw data and the standards to which the calculated values were compared. A competent peer review would have pointed out these critical mistakes, and editors of a reputable scientific journal would not have allowed the manuscripts to be published without correcting these major mistakes as well as likely many of the other minor mistakes mentioned below.

***Minor Mistakes***

It is unclear from the description in the “Experimental” section of the first manuscript how many products of canned tuna, sardines, and chicken marketed for human consumption were analyzed to yield the reported concentrations for those products. Given that the authors reported the results for each pet food product, rather than summary statistics, it would appear that only one product of each of the foods marketed for human consumption was analyzed because there is only one result reported for each product type. To represent a result from a single product as representative of all products of that type is not scientifically justifiable or statistically sound. Just as with the samples of the various types of pet foods, there will also be variation in the metal content between different products of canned tuna, sardines, and chicken. Without an estimate and statistical analysis of the variability, it is not scientifically justifiable to conclude there are differences between the element content of pet food products and the fish and chicken products intended for people.

The authors repeatedly refer to the elements they measured as “toxic trace metals” both in the titles as well as throughout the manuscripts. Whether or not a metal is toxic is determined by multiple factors besides its name or elemental symbol. Toxicity not only depends on dose or exposure, which the articles have inappropriately estimated and compared to inappropriate standards, but also on such factors as solubility and valence of the element as well as the

Page 6 of 25 – 11024 Target Animal Safety Review

amounts of other metals, nutrients, and ingredients in the food. The articles provide no consideration of information on these other factors that influence element toxicity.

The authors also characterize the elements as being “contaminants,” apparently failing to consider that the presence of the elements in the diets could result from the elements being naturally occurring constituents of typical animal feed and pet food ingredients and not from a source of contamination at all. Three of the 15 elements (chromium in the +3 valence state, cobalt, and molybdenum) are known to be required nutrients for animals and 3 others (arsenic, nickel, and vanadium) are suspected of being required in the diets of animals, albeit in very miniscule amounts. A diet with no detectable level of a required element that is fed for long periods of time could be as detrimental to animal health when compared to a diet that contained toxic quantities of the element.

The authors do not report their empirical findings and consider their meaning in a comprehensively balanced and well reasoned discussion. Their apparent lack of knowledge about fundamentals in animal physiology and nutrition impact the manuscripts and lead to inappropriate characterizations, such as the discussion of essential nutrients as contaminants mentioned above. Other particularly telling examples are the authors’ incorrect characterization of specific ingredients in general, and carbohydrate sources in particular, as “fillers.” Filler is a subjective, derogatory characterization having no objective scientific definition from a nutritional perspective. Carbohydrates that are not fiber are digestible by dogs and cats, provide energy, and are not “fillers” or “diluents” in any nutritional sense. Some of the ingredients listed as fillers (i.e., corn gluten meal and soybean meal) are used for their protein contribution to the diet and animal, not their carbohydrate content.

The authors also raise the argument, long ago considered, evaluated, and answered, that butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) are possible human carcinogens but still used in pet foods in the United States. They fail to mention that BHA and BHT are generally recognized as safe for use as preservatives within specified limits in both food for people as well as food for other animals, and that cancer from consumption of BHA or BHT arises only in laboratory rodents that have a particular anatomical structure to their stomachs not found in people, dogs, cats, or most other domestic species of animals.

Finally, the authors also demonstrate a lack of understanding of the regulatory requirements for inclusion of ingredients in food, animal feed, and pet food, stating that ingredients “[...] may be generally recognized as safe (GRAS) for their intended use, but they must have approval as foods additives” (Part I, p. 48). Contrary to the author’s statement indicating that a GRAS substance must have approval as a food additive, the Federal Food, Drug, and Cosmetic Act exempts a substance that is GRAS for a particular use from the food additive approval requirements.

**Re-Evaluation of Reported Concentrations**

A re-evaluation was undertaken to determine whether any of the reported concentrations for any of the elements that appeared in “Analysis of Toxic Trace Metals in Pet Foods Using Cryogenic Grinding and Quantitation by ICP-MS, Part I”1 were likely to cause adverse health

Page 7 of 25 – 11024 Target Animal Safety Review

effects in dogs or cats that might consume the products for long periods of time as the sole source of food.

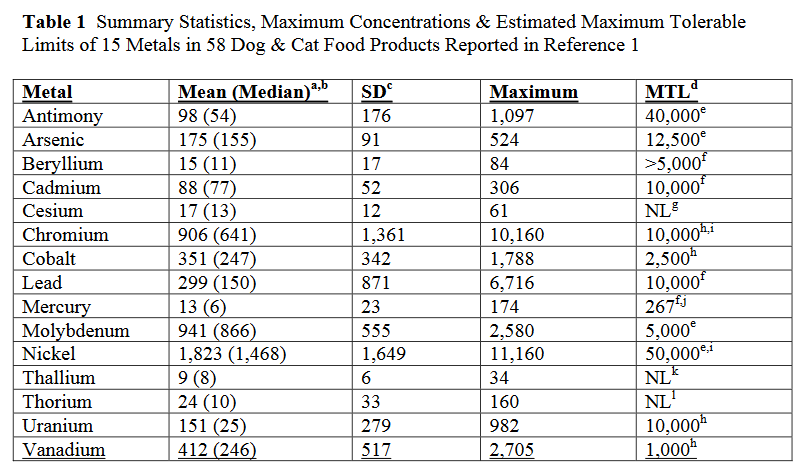
***Methods***

The as-is concentrations in micrograms (μg)/kg for the 15 elements in the 58 samples of dog and cat foods as reported in Tables IV, V, VI, and VII in “Analysis of Toxic Trace Metals in Pet Foods Using Cryogenic Grinding and Quantitation by ICP-MS, Part I” (reference 1) were accepted as being valid measurements. The reported concentrations were converted to μg/kg DM by assuming all dry products contained 88% dry matter and all wet (canned or pouched) products contained 25% dry matter. The metal concentrations on a DM basis were derived by dividing the reported concentrations by the decimal equivalent of the assumed DM percentage of the product. Comparisons were made between the largest DM concentration for each metal found in the pet foods and the lowest MTL listed or estimated for a mammalian species from information in Mineral Tolerance of Animals Second Revised Edition, 2005.3 No correction or additional safety factor was applied to a tolerance if dog- or cat-specific data were available for establishing the tolerance, or if the tolerance was set based on data obtained from a mammalian species known to be particularly sensitive to the specific metal. If a tolerance was based on data from monogastric laboratory animals or domestic swine and these species were not indicated to be particularly sensitive to the metal, the tolerance value was divided by 10 as a safety factor for cross-species extrapolation before comparing to the largest estimated DM concentration found in the pet foods. Additional information from other texts and public databases, where noted, was considered if no MTL for a specific metal was listed in Mineral Tolerance of Animals Second Revised Edition, 2005.

***Results and Conclusions***

Table 1 lists summary statistics, maximum concentrations, and the MTL set as described above, for the 15 metals measured in the 58 pet foods as reported in reference 1. Appendix 1 of this report lists, for each metal, the sample identifier, product type, the as-is concentration in μg/kg reported in reference 1, the assumed DM percentage, and the resulting DM concentration after conversion using the assumed DM percentage. Tables A2.1 to A2.6 in Appendix 2 of this report list summary statistics for each metal on a DM basis by product type (A2.1-A2.4) as well as summary statistics for all dog foods (A2.5) and for all cat foods (A2.6).

Page 8 of 25 – 11024 Target Animal Safety Review



a Number of samples (n) for Mercury = 49 as 9 samples had no reported result. n = 58 for all other metals.   
b All numbers in the table have units of μg/kg expressed on a dry matter basis.   
c SD=Standard Deviation. d MTL=Maximum Tolerable Limit. e MTL for species known to be more sensitive to the element than others. f MTL from studies using dogs or cats. g NL=Non Listed. The mean ± standard deviation for cesium levels in the 58 pet food samples on a dry matter

basis (17 ± 12 μg/kg) are similar to or slightly less than cesium concentrations reported in Chapter 10, Volume 2 of Trace Elements in Human and Animal Nutrition, indicating the concentrations in the pet foods are normal, naturally occurring background concentrations of cesium. h Estimated by reducing the lowest MTL from mammalian monogastric species by a factor of 10 for cross-

species extrapolation. i Soluble sources. j Non-reproducing cats. MTL for reproducing cats is 67 μg Hg/kg DM. k NL=Non Listed. Values for thallium content of foods reported in the Agency for Toxic Substances and

Disease Registry at http://www.atsdr.cdc.gov/ToxProfiles/TP.asp?id=309&tid=49 indicate the concentrations determined in the pet foods are normal, naturally occurring background concentrations of thallium. l NL=Non Listed. Values for thorium content of foods reported in the Agency for Toxic Substances and Disease Registry at http://www.atsdr.cdc.gov/toxprofiles/tp147-c5.pdf indicate the concentrations determined in the pet foods are normal, naturally occurring background concentrations of thorium.

Page 9 of 25 – 11024 Target Animal Safety Review

As shown in Table 1, none of the mean or median concentrations exceeded the listed MTL for any of the metals. Only chromium, mercury, and vanadium had measured concentrations in one to five products that exceeded a conservatively estimated MTL for these metals. These results occur because of the lack of dog- or cat-specific information, the need to extrapolate tolerances based on limited data from other species, the inability to accurately determine the solubility of the chromium sources necessitating worse-case assumptions be employed, and the lack of label information that potentially restricts the use of the product with the greatest concentration of mercury to non-reproducing animals. Even though one product had a chromium concentration, and five products had vanadium concentrations, above the estimated MTL in Table 1, it would not be possible from the information available in the scientific literature to demonstrate that the concentrations of chromium or vanadium would ordinarily render the products injurious to the health of dogs or cats. If the one cat food product with the greatest mercury content was labeled for feeding to all life stages of cats or to reproducing cats, it is possible the product would be considered adulterated if the reported mercury concentration was confirmed on an official sample using a validated analytical method. More explanation for how each MTL was determined and its relevance to the measured concentrations for the related metal and safety of the products is provided below.

Antimony (Sb)

The greatest concentration of antimony found in the 58 pet food samples analyzed was 1,097 μg Sb/kg DM. Lack of species-specific data prevented the MTSA Committee from setting a MTL for specific species of domestic animals. Rabbits are reported to be a species particularly sensitive to antimony, with rabbit-specific data suggesting that 3,000 μg Sb/kg body weight (BW)/day is an appropriate conservative limit.3 Assuming that rabbits eat 75 g DM/kg BW/day (7.5% of BW/day in DM) and the 3,000 μg Sb/kg BW dose in rabbits represents a no observed adverse effect level (NOAEL), then the calculated MTL would be 40,000 μg Sb/kg of DM which is the value listed in Table 1. The calculation to derive the value of 40,000 μg Sb/kg DM is:

3,000 μg Sb/kg BW ÷ 0.075 kg DM/kg BW = 40,000 μg Sb/kg DM

Because the greatest reported concentration of antimony was only 4.8% of the calculated MTL (1,907/40,000 = 0.0477 = 4.8%), no adverse effects due to antimony are expected from consumption of any of the 58 pet foods. In addition, 7.5% of BW/day in DM is an extremely large quantity of food for dogs or cats of any life stage to consume. Two percent of BW/day as DM intake is typical for maintenance adults with 4% of BW/day as DM intake being typical of females in peak lactation. The likely consequence of these considerations is that the calculated MTL is an underestimate of the true MTL for dogs and cats, i.e., the true MTL would be a larger value.

Arsenic (As)

The greatest concentration of arsenic found in the 58 pet food samples analyzed was 524 μg As/kg DM. Rats appear to be more sensitive to arsenic than other species with 12,500 μg As/kg DM being nontoxic but 50,000 μg/kg DM producing toxicity in rats. Based on the data from laboratory rats, the MTSA Committee set a general maximum tolerance for mammals of

Page 10 of 25 – 11024 Target Animal Safety Review

30,000 μg As/kg DM. The greatest reported concentration of arsenic was only 4.2% of the MTL for the sensitive mammalian species (524/12,500 = 0.0419 = 4.2%). Thus, no adverse effects due to arsenic are expected from consumption of these 58 pet foods.

Beryllium (Be)

The greatest concentration of beryllium in the 58 pet food samples analyzed was 84 μg Be/kg DM. The Mineral Tolerance of Animals Second Revised Edition, 2005 does not mention beryllium and contains no information concerning beryllium for any species. The EPA based the oral RfD for beryllium for people on a 1976 research report by Morgareidge, Cox and Gallo, that used dogs as the test animal.5 A summary of the research report by Morgareidge et al. can be found at http://www.epa.gov/iris/subst/0012.htm.

The study reported by Morgareidge et al. had 5 groups of 5 male and 5 female beagle dogs fed diets containing 0, 1,000, 5,000, 50,000, and 500,000 μg BE/kg diet. The 500,000 μg/kg group showed signs of obvious toxicity and was terminated after 33 weeks on study. The remaining 4 groups were fed their respective diets for 23⁄4 to 31⁄3 years. One dog in the 50,000 μg/kg group died after 70 weeks on study and had less severe, but similar, gastrointestinal lesions to those observed in the 500,000 μg Be/kg diet group. None of the remaining 9 dogs in the 50,000 μg Be/kg diet group or any other group had any gross or microscopic abnormalities at the end of the study. The EPA concluded that the NOAEL for dogs was greater than 5,000 μg Be/kg diet and used dose-response modeling for estimating a NOAEL as a starting point for setting the oral RfD for people. Using 5,000 μg Be/kg as the MTL, the greatest reported concentration of beryllium was only 1.7% of the MTL (84/5,000 = 0.0168 = 1.7%). Thus, no adverse effects due to beryllium are expected from consumption of these 58 pet foods.

Cadmium (Cd)

The greatest concentration of cadmium in the 58 pet food samples analyzed was 306 μg Cd/kg DM. The MTL for mammalian species in Mineral Tolerance of Animals Second Revised Edition, 2005 was 10,000 μg Cd/kg DM. Dogs have consumed diets containing 10,000 μg Cd/kg DM (as cadmium chloride) for 8-9 years with no adverse effects (Mineral Tolerance of Animals, Second Revised Edition, 2005, Chapter 9, pages 79-96). The greatest reported concentration of cadmium was only 3.1% of the MTL (306/10,000 = 0.0306 = 3.1%). Thus, no adverse effects due to cadmium are expected from consumption of these 58 pet foods.

Cesium (Cs)

The greatest concentration of cesium in the 58 pet food samples analyzed was 61 μg Cs/kg DM. The Mineral Tolerance of Animals Second Revised Edition, 2005 does not mention cesium and contains no information concerning cesium for any species.

*The following statements come from page 434 of Trace Elements in Human and Animal Nutrition, Fifth Edition, Volume 2.6*

Page 11 of 25 – 11024 Target Animal Safety Review

“The cesium content of foodstuffs and feeds has not been examined extensively. Some isolated values have appeared, including 0.1-0.3 μg/g [100 to 300 μg/kg] dry fruit kernels, 0.06-0.07 μg/g [60 to 70 μg/kg] dry maple syrup, 0.1-0.3 μg/g [100 to 300 μg/kg or ppb] dry nuts, except Brazil nuts, which contained 1.3 μg/g [1,300 μg/kg], 9 nanograms (ng)/g [9 μg/kg] fresh orange juice, and 12.1 ng/g [12.1 μg/kg] fresh banana pulp. Duke found 3-11 ng cesium per gram dry weight [3-11 μg/kg], and Oakes et al. found <1-3.3 ng/g fresh weight [<1-3.3 μg/kg], in a limited variety of examined fruits and vegetables.”

Because the mean ± standard deviation for cesium concentrations in the 58 pet food samples on a dry matter basis (17 ± 12 μg/kg) are similar to or slightly less than the values reported in Trace Elements in Human and Animal Nutrition, Fifth Edition, Volume 2, it suggests that the cesium values reported by Atkins et al. represent normal, naturally occurring, background concentrations of this element. Furthermore, without data demonstrating the amounts of cesium contained in the products are harmful to dogs or cats, FDA could not prove any of the products were unsafe and therefore, adulterated.

Chromium (Cr)

The greatest concentration of chromium in the 58 pet food samples analyzed was 10,160 μg Cr/kg DM. The MTL for mammalian species in Mineral Tolerance of Animals Second Revised Edition, 2005 was 100,000 μg Cr/kg DM from soluble sources such as chromium chloride. However, none of the species with an MTL were identified as being particularly sensitive to chromium, and no data from dogs or cats are available for demonstrating equivalency to rodents or swine, or for setting a dog- or cat-specific tolerance. Therefore, a safety factor of 10 was applied to the general mammalian tolerance for soluble sources of chromium for cross-species extrapolation resulting in the value of 10,000 μg Cr/kg DM listed in Table 1. One wet dog food product was estimated to contain 10,160 μg Cr/kg DM, 160 μg/kg DM greater than the conservatively estimated tolerance due to the combined assumptions for dry matter content and solubility of chromium sources in the product. These assumptions are not trivial because a 1% increase in product DM would cause the estimated concentration to be less than the conservatively estimated tolerance, and any decrease in solubility would also affect the chromium availability relative to the tolerance. Furthermore, without data demonstrating 10,160 μg Cr/kg DM to be harmful to dogs, FDA could not prove a dog food containing 10,160 μg Cr/kg DM was adulterated.

Cobalt (Co)

The greatest concentration of cobalt in the 58 pet food samples analyzed was 1,788 μg Co/kg DM. The MTL for mammalian species in Mineral Tolerance of Animals Second Revised Edition, 2005 was 25,000 μg Co/kg DM. However, none of the species with an MTL were identified as being particularly sensitive to cobalt, and no data from dogs or cats are available for demonstrating equivalency to rodents or swine, or for setting a dog- or cat-specific tolerance. Therefore, a safety factor of 10 was applied to the general mammalian tolerance for cross-species extrapolation resulting in the value of 2,500 μg Co/kg DM listed in Table 1. The

Page 12 of 25 – 11024 Target Animal Safety Review

greatest reported concentration of cobalt was 72% of the conservatively estimated MTL (1,788/2,500 = 0.7152 = 72%). Thus, no adverse effects due to cobalt are expected from consumption of these 58 pet foods.

Lead (Pb)

The greatest concentration of lead in the 58 pet food samples analyzed was 6,716 μg Pb/kg DM. The MTL for mammalian species in Mineral Tolerance of Animals Second Revised Edition, 2005 was 10,000 μg Pb/kg DM. The MTSA Committee noted that dogs have been shown to tolerate diets containing 10,000 μg Pb/kg DM from highly available sources (lead acetate) without changes in hematopoetic (bone marrow & blood cells) or kidney function, the organs most impacted by adverse effects from lead. The greatest reported concentration of lead was 67.2% of the MTL (6,716/10,000 = 0.6716 = 67.2%). Thus, no adverse effects due to lead are expected from consumption of these 58 pet foods.

Mercury (Hg)

The greatest concentration of mercury in the 58 pet food samples analyzed was 174 μg Hg/kg DM. The next greatest concentration in any of the samples analyzed was 62 μg Hg/kg DM. Both products were cat foods. Cats are known to be more sensitive to methylmercury (organic mercury) than most other animal species and organic forms of mercury are generally more toxic than inorganic mercury compounds. Therefore, an MTL of 267 μg Hg/kg DM for organic mercury in non-reproducing cats was calculated based on data provided on page 254 in Mineral Tolerance of Animals Second Revised Edition, 2005 indicating a NOAEL for methylmercury of 20 μg Hg/kg BW in cats and assuming a DM consumption of 75 g DM/kg BW (7.5% of BW/day in DM). The calculation to derive the value of 267 μg Hg/kg DM is:

20 μg Hg/kg BW ÷ 0.075 kg of DM/kg BW = 267 μg Hg/kg DM

For cats involved in reproduction, information on page 255 in Mineral Tolerance of Animals Second Revised Edition, 2005 indicates 5 μg Hg/kg BW has been shown to be safe which converts to a DM concentration of 67 μg Hg/kg DM assuming a DM consumption of 75 g DM/kg BW (7.5% of BW/day in DM). The calculation to derive the value of 67 μg Hg/kg DM is:

5 μg Hg/kg BW ÷ 0.075 kg of DM/kg BW = 67 μg Hg/kg DM

All products analyzed contained less than the non-reproducing cat-specific tolerance of 267 μg Hg/kg DM, and all but one of the products contained less than the reproducing cat-specific tolerance of 67 μg Hg/kg DM. It is not clear if the product containing 174 μg Hg/kg DM was intended to be fed to reproducing cats or not. The greatest reported concentration of mercury was only 65.2% of the calculated non-reproductive MTL (174/267 = 0.6518 = 65.2%), but was more than twice the MTL for cat reproduction (174/67 = 2.597 = 260%). The one product containing 174 μg Hg/kg DM, identified as sample C-44, might pose a health risk if fed to queens or toms engaged in reproduction. It would be prudent for SPEX CertiPrep

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, to notify the manufacturer or guarantor listed on the product’s label of the result so that the responsible party(ies) could determine if any corrective action is needed.

Page 13 of 25 – 11024 Target Animal Safety Review

It is likely that the mercury content in the sampled products is in both inorganic as well as organic forms of mercury. In addition, 7.5% of BW/day in DM intake is an extremely large quantity of food for dogs or cats of any life stage to consume, with the likely consequence being both non-reproductive and reproductive calculated MTL’s are an underestimate of the true MTL for cats and dogs, i.e., the true MTL is a larger value.

Molybdenum (Mo)

The greatest concentration of molybdenum in the 58 pet food samples analyzed was 2,580 μg Mo/kg DM. The MTSA Committee set a MTL of 5,000 μg Mo/kg DM for sensitive species. The greatest reported concentration of molybdenum was 52% of the MTL for species sensitive to molybdenum (2,580/5,000 = 0.516 = 52%). Thus, no adverse effects due to molybdenum are expected from consumption of these 58 pet foods.

Nickel (Ni)

The greatest concentration of nickel in the 58 pet food samples analyzed was 11,160 μg Ni/kg DM. The MTSA Committee set a MTL of 50,000 μg Ni/kg DM from soluble sources for sensitive species. The greatest reported concentration of nickel was 22.3% of the MTL for species sensitive to nickel (11,160/50,000 = 0.2232 = 22.3%). Thus, no adverse effects due to nickel are expected from consumption of these 58 pet foods. The MTSA Committee noted that dogs have been shown to tolerate diets containing 1,000,000 μg Ni/kg DM (as nickel sulfate) for 2 years without signs of adverse effects.

Thallium (Tl)

The greatest concentration of thallium in the 58 pet food samples analyzed was 34 μg Tl/kg DM. The Mineral Tolerance of Animals Second Revised Edition, 2005 does not mention thallium and contains no information concerning thallium for any species.

The following statements about thallium concentrations in food come from section 5.1 Overview (page 49) and from section 5.4.4 Other Environmental Media (page 56) in the Toxicological Profile for Thallium (Agency for Toxic Substances & Disease Registry [ATSDR], July 1992) and can be found at http://www.atsdr.cdc.gov/ToxProfiles/TP.asp?id=309&tid=49

“Major releases of thallium to the environment are from processes such as coal- burning and smelting, in which thallium is a trace contaminant of the raw materials, rather than from facilities producing or using thallium compounds. Humans may be exposed to thallium by ingestion, inhalation, or dermal absorption. However, the general population is exposed most frequently by ingestion of thallium-containing foods, especially home-grown fruits and green vegetables.”

Page 14 of 25 – 11024 Target Animal Safety Review

“Trace amounts of thallium are found in most foods, but few foods, except vegetables grown in thallium-polluted soil, are likely to have significant thallium concentrations [...].”7,8

“Data on thallium content of specific foods grown and consumed in the United States were not located. However, a recent study of the thallium content of food in the United Kingdom reports levels of thallium in meat, fish, fats, and green vegetables [...].”

9

Because thallium had the least mean concentration (8.9 μg Tl/kg DM), the least median concentration (7.5 μg Tl/kg DM) and the least maximum concentration (34 μg Tl/kg DM) of the 15 elements measured in the 58 pet foods, and because these amounts are consistent with the statement from the ATSDR Toxicological Profile that trace amounts of thallium are found in most foods, this suggests that the amounts of thallium reported in reference 1 by Atkins et al. likely represent normal, naturally occurring, background concentrations for thallium in food. Furthermore, without data demonstrating the amounts of thallium contained in the products are harmful to dogs or cats, FDA could not prove any of the products were unsafe and therefore adulterated.

Thorium (Th)

The greatest concentration of thorium in the 58 pet food samples analyzed was 160 μg Th/kg DM. The Mineral Tolerance of Animals, Second Revised Edition, 2005 does not mention thorium and contains no information concerning thorium for any species.

The following statements about thorium concentrations in food come from section 5.4.4 Other Media (page 77) in the Toxicological Profile for Thorium (Agency for Toxic Substances & Disease Registry [ATSDR], October 1990) and can be found at http://www.atsdr.cdc.gov/ToxProfiles/tp147.pdf.

“Because the concentrations of thorium in foods are very low, very few data exist [...]. Vegetables grown in an area of high natural activity in Brazil had the following concentrations of thorium (μg/g in dry sample)[...]: brown beans, 0.011; potato, 0.0019; zucchini, 0.011; corn, 0.0022; carrot, 0.0074; and sweet potato, 0.0027.”10

The above reported thorium concentrations in brown beans, potato, zucchini, corn, carrot, and sweet potato would be equivalent to 11, 1.9, 11, 2.2, 7.4, and 2.7 μg/kg, respectively. The median thorium concentration of 9.7 μg Th/kg DM in the 58 pet food samples is slightly above, but reasonably similar to, the median concentration of 5.1 μg Th/kg (2.7 + 7.4)/2 = 5.1 μg Th/kg) in the six samples reported in the ATSDR Toxicological Profile. This suggests that the amounts of thorium reported in reference 1 by Atkins et al. likely represent normal, naturally occurring, background concentrations for thorium in food. Furthermore, without data demonstrating the amounts of thorium contained in the products are harmful to dogs or cats, FDA could not prove any of the products were unsafe and therefore adulterated.

Page 15 of 25 – 11024 Target Animal Safety Review

Uranium (U)

The greatest concentration of uranium in the 58 pet food samples analyzed was 982 μg U/kg DM. The MTL for mammalian species in Mineral Tolerance of Animals was 100,000 μg U/kg DM. However, none of the species with an MTL were identified as being particularly sensitive to uranium, and no data from dogs or cats are available for demonstrating equivalency to rodents or swine, or for setting a dog- or cat-specific tolerance. Therefore, a safety factor of 10 was applied to the general mammalian tolerance for cross-species extrapolation, resulting in the value of 10,000 μg U/kg DM listed in Table 1. The greatest reported concentration of uranium was 9.8% of the conservatively estimated MTL (982/10,000 = 0.0982 = 9.8%). Thus, no adverse effects due to uranium are expected from consumption of these 58 pet foods.

Vanadium (V)

The greatest concentration of vanadium in the 58 pet food samples analyzed was 2,705 μg V/kg DM. The lowest MTL for mammalian species in Mineral Tolerance of Animals Second Revised Edition, 2005 was 10,000 μg V/kg DM for horses and swine. However, none of the species with an MTL were identified as being particularly sensitive to vanadium, and no data from dogs or cats are available for demonstrating equivalency to horses or swine, or for setting a dog- or cat-specific tolerance. Therefore, a safety factor of 10 was applied to the lowest mammalian tolerance for cross-species extrapolation, resulting in the value of 1,000 μg V/kg DM listed in Table 1. Five products had vanadium concentrations, from 1,172 to 2,705 μg V/kg DM, that were greater than the conservatively estimated MTL in Table 1.

Even though the estimated DM concentrations of vanadium in 5 products are greater than the conservatively estimated MTL, FDA would not be able to prove a pet food containing more than 1,000 μg V/kg DM was adulterated without data demonstrating that such concentrations were definitely harmful to dogs or cats. From studies investigating vanadium toxicity in laboratory rodents, signs of chronic toxicity are not generally observed unless amounts of vanadium comparable to more than 20,000 μg V/kg DM at an assumed consumption of 7.5% of BW/day in DM intake are administered. As previously indicated, 7.5% of BW/day in DM intake is an extremely large quantity of food for dogs or cats of any life stage to consume. Thus, a value of 1,000 μg V/kg DM as a MTL is likely to be overly conservative relative to what limited data are currently available regarding vanadium toxicity in mammals.

Page 16 of 25 – 11024 Target Animal Safety Review

*Summary of Conclusions*

The reported concentrations when interpreted within the context of the information available in the scientific literature regarding mineral toxicities in domestic animals show no indication for concern for long term safety of any of the products based on any of the measured quantities for antimony, arsenic, beryllium, cadmium, cesium, cobalt, lead, molybdenum, nickel, thallium, thorium, and uranium, or for mercury in non-reproducing dogs and cats. Only one cat food if intended for reproducing cats would exceed the maximum tolerance established by the NRC MTSA Committee for mercury in reproducing cats.

Our concerns for product safety are negligible based on the reported concentrations for the amount of chromium and vanadium. Any potential safety concern may arise only from insufficient data in the target species to demonstrate a species-specific tolerance and results from a theoretical tolerance being extrapolated from other species.

The reported concentrations do not demonstrate that any of the metals were directly added to, or were contaminants in, any of the products, as opposed to being constituents of acceptable ingredients used to make the products. Based on the information in the scientific literature, with the possible exception dependent on the intended use, of the one cat food product containing 174 μg Hg/kg DM, FDA could not show that any of the measured concentrations for any metal in any of the dog or cat foods sampled would cause any of the products to be adulterated due to any of the metals being present in amounts that definitely render the product injurious to health.

Attachments:

References Appendices 1 and 2

Page 17 of 25 – 11024 Target Animal Safety Review

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Page 18 of 25 – 11024 Target Animal Safety Review

Appendix 1 Calculated Dry Matter Concentrations from Reported As-Is Concentrations of 15 Metals Measured in 58 Pet Foods Identified by Sample ID in Reference 1

Sample ID

Antimony Reported As-Is Conc. (μg/kg)

Antimony Calculated DM Conc. (μg/kg)

Arsenic Reported As-Is Conc. (μg/kg)

Arsenic Calculated DM Conc. (μg/kg)

Beryllium Reported As-Is Conc. (μg/kg)

Beryllium Calculated DM Conc. (μg/kg)

Cadmium Reported As-Is Conc. (μg/kg)

Cadmium Calculated DM Product

Assumed

Conc. Type

DM (%)

(μg/kg) D-1 Dry 88 55.6 63 212 241 16.6 19 70.2 80 D-2 Dry 88 47.3 54 184 209 45.2 51 130 148 D-3 Dry 88 68 77 162 184 5.6 6 70.4 80 D-4 Dry 88 61.3 70 140 159 6.74 8 62.1 71 D-5 Dry 88 73.4 83 145 165 2.4 3 48.7 55 D-9 Dry 88 81.1 92 83 94 13.7 16 58 66 D-10 Dry 88 522 593 64 73 2.44 3 69.5 79 D-11 Dry 88 80.7 92 248 282 74.3 84 117 133 D-12 Dry 88 965 1097 134 152 2.45 3 65.7 75 D-15 Dry 88 292 332 209 238 52.4 60 47.7 54 D-18 Dry 88 81.9 93 30.4 35 2.35 3 18 20 D-19 Dry 88 50 57 238 270 14.9 17 50.3 57 D-20 Dry 88 66.3 75 43.2 49 2.36 3 18.9 21 D-21 Dry 88 58 66 129 147 36.7 42 56.5 64 D-41 Dry 88 54.7 62 80.2 91 2.33 3 82.5 94 D-42 Dry 88 57.6 65 69.7 79 6.48 7 82.3 94 D-56 Dry 88 122 139 94.7 108 2.37 3 50.3 57 D-57 Dry 88 48.7 55 206 234 57.2 65 108 123 D-17 Wet 25 4.07 16 23 92 2.51 10 10.1 40 D-22 Wet 25 2.25 9 20 80 3 12 21.7 87 D-23 Wet 25 18.1 72 70.7 283 7.59 30 16.9 68 D-24 Wet 25 3.21 13 90.6 362 2.85 11 26.1 104 D-26 Wet 25 2.1 8 31.5 126 2.8 11 8.36 33 D-28 Wet 25 6.46 26 43.9 176 2.93 12 26.9 108 D-31 Wet 25 8.05 32 32.7 131 2.97 12 17.7 71 D-32 Wet 25 15 60 36.7 147 2.78 11 16.5 66 D-33 Wet 25 3.03 12 38.3 153 2.42 10 28 112 D-39 Wet 25 7.84 31 45.2 181 3.62 14 25.2 101 D-53 Wet 25 1.68 7 25.1 100 2.87 11 36.5 146 D-54 Wet 25 1.84 7 21.4 86 3.27 13 10 40 D-55 Wet 25 11.6 46 50.9 204 2.86 11 35.9 144 C-6 Dry 88 72.8 83 161 183 4.25 5 42.5 48 C-7 Dry 88 32.3 37 135 153 2.42 3 53.9 61 C-8 Dry 88 370 420 118 134 2.39 3 27.6 31 C-13 Dry 88 430 489 275 313 4.03 5 45.8 52 C-14 Dry 88 188 214 111 126 9.27 11 31.9 36 C-16 Dry 88 58 66 150 170 6.32 7 58.7 67 C-40 Dry 88 32 36 108 123 8.82 10 31 35 C-43 Dry 88 143 163 293 333 2.83 3 48.1 55 C-46 Dry 88 124 141 74.2 84 2.05 2 41.3 47 C-47 Dry 88 25.5 29 120 136 2.31 3 32 36 C-48 Dry 88 51 58 226 257 5.66 6 69.9 79 C-49 Dry 88 37.8 43 137 156 2.42 3 37.5 43 C-50 Dry 88 75.8 86 120 136 2.48 3 43.9 50 C-25 Wet 25 3.85 15 32.1 128 5.64 23 38.4 154 C-27 Wet 25 4.25 17 95 380 9.6 38 20.2 81 C-29 Wet 25 3.06 12 49.4 198 2.82 11 15.9 64 C-30 Wet 25 2.15 9 73.6 294 3.03 12 20.2 81 C-34 Wet 25 8.43 34 12.5 50 2.73 11 38.7 155 C-35 Wet 25 4.22 17 54.7 219 2.85 11 31.2 125 C-36 Wet 25 13.2 53 24.1 96 3.67 15 28.1 112 C-37 Wet 25 3.24 13 53.4 214 2.72 11 37.7 151 C-38 Wet 25 1.95 8 51.7 207 2.76 11 21.2 85 C-44 Wet 25 11.9 48 48.6 194 3.62 14 38.5 154 C-45 Wet 25 6.86 27 131 524 7.35 29 23 92 C-51 Wet 25 8.94 36 49.2 197 2.57 10 60.7 243 C-52 Wet 25 3.89 16 35.2 141 14.9 60 35.7 143 C-58 Wet 25 2.23 9 24.5 98 2.67 11 76.6 306

Page 19 of 25 – 11024 Target Animal Safety Review

Appendix 1 continued

Sample ID

Cesium

Cesium

Chromium

Chromium

Cobalt

Cobalt

Lead

Lead Reported

Calculated

Reported

Calculated

Reported

Calculated

Reported

Calculated As-Is

DM

As-Is

DM

As-Is

DM

As-Is

DM Product

Conc.

Conc.

Conc.

Conc.

Conc.

Conc.

Conc.

Conc. Type

(μg/kg)

(μg/kg)

(μg/kg)

(μg/kg)

(μg/kg)

(μg/kg)

(μg/kg)

(μg/kg) D-1 Dry 88 14 16 455 517 217 247 131 149 D-2 Dry 88 20.6 23 1710 1943 247 281 70 80 D-3 Dry 88 15.9 18 927 1053 189 215 144 164 D-4 Dry 88 14.1 16 939 1067 144 164 134 152 D-5 Dry 88 8.98 10 677 769 838 952 289 328 D-9 Dry 88 13.9 16 421 478 134 152 75.2 85 D-10 Dry 88 13 15 646 734 157 178 120 136 D-11 Dry 88 27.9 32 1490 1693 237 269 121 138 D-12 Dry 88 9.22 10 645 733 160 182 175 199 D-15 Dry 88 11 13 1080 1227 200 227 174 198 D-18 Dry 88 7.18 8 171 194 34.8 40 132 150 D-19 Dry 88 16 18 664 755 879 999 281 319 D-20 Dry 88 7.01 8 547 622 201 228 72.7 83 D-21 Dry 88 13.6 15 1080 1227 227 258 79.6 90 D-41 Dry 88 16.7 19 541 615 648 736 245 278 D-42 Dry 88 18 20 695 790 275 313 933 1060 D-56 Dry 88 10 11 492 559 131 149 136 155 D-57 Dry 88 24.7 28 1490 1693 772 877 232 264 D-17 Wet 25 1.57 6 75.9 304 62.6 250 19.2 77 D-22 Wet 25 6.71 27 101 404 77 308 54.9 220 D-23 Wet 25 13.6 54 2540 10160 66.7 267 51.3 205 D-24 Wet 25 1.31 5 93.8 375 447 1788 17.8 71 D-26 Wet 25 1.27 5 59 236 76 304 37.3 149 D-28 Wet 25 3.55 14 165 660 107 428 65 260 D-31 Wet 25 2.85 11 186 744 35.7 143 38 152 D-32 Wet 25 1.08 4 265 1060 41.5 166 42.4 170 D-33 Wet 25 2.84 11 19.6 78 43.7 175 23.5 94 D-39 Wet 25 2.92 12 302 1208 80.3 321 51.3 205 D-53 Wet 25 3.62 14 145 580 54 216 16 64 D-54 Wet 25 3.62 14 32.7 131 57.6 230 24.2 97 D-55 Wet 25 2.54 10 212 848 58.3 233 32.8 131 C-6 Dry 88 11.6 13 618 702 124 141 407 463 C-7 Dry 88 5.92 7 516 586 372 423 74.6 85 C-8 Dry 88 5.61 6 427 485 114 130 121 138 C-13 Dry 88 9.2 10 661 751 109 124 119 135 C-14 Dry 88 6.49 7 1220 1386 279 317 5910 6716 C-16 Dry 88 6.88 8 736 836 132 150 215 244 C-40 Dry 88 8.3 9 338 384 196 223 117 133 C-43 Dry 88 14.5 16 548 623 916 1041 188 214 C-46 Dry 88 11.4 13 331 376 157 178 109 124 C-47 Dry 88 12.6 14 580 659 249 283 156 177 C-48 Dry 88 11.1 13 450 511 282 320 201 228 C-49 Dry 88 7.52 9 620 705 154 175 151 172 C-50 Dry 88 9.13 10 703 799 712 809 212 241 C-25 Wet 25 4.19 17 130 520 39.2 157 19.7 79 C-27 Wet 25 2.68 11 470 1880 413 1652 29.2 117 C-29 Wet 25 1.7 7 84.6 338 48.7 195 29.8 119 C-30 Wet 25 1.68 7 58.1 232 65.3 261 32 128 C-34 Wet 25 4.77 19 28.5 114 55.8 223 44.1 176 C-35 Wet 25 8.72 35 27.4 110 83.7 335 171 684 C-36 Wet 25 3.74 15 335 1340 67 268 55.1 220 C-37 Wet 25 13.9 56 14.5 58 43.2 173 22.3 89 C-38 Wet 25 3.32 13 47.1 188 64.9 260 29.5 118 C-44 Wet 25 15.2 61 45.8 183 68.1 272 16.2 65 C-45 Wet 25 5.29 21 80.6 322 54.2 217 22.7 91 C-51 Wet 25 5.92 24 789 3156 63.3 253 23.2 93 C-52 Wet 25 2.95 12 425 1700 52 208 30.5 122 C-58 Wet 25 9.55 38 32.3 129 61.8 247 62.4 250

Assumed DM (%)

Page 20 of 25 – 11024 Target Animal Safety Review

Appendix 1 continued

Sampl e ID

Mercury

Mercury

Molybdenu

Molybdenu

Nickel

Nickle

Thalliu

Thallium Reporte

Calculate

m Reported

m

Reporte

Calculate

m

Calculate d As-Is

d DM

As-Is Conc.

Calculated

d As-Is

d DM

Reporte

d DM Produc

Conc.

Conc.

(μg/kg)

DM

Conc.

Conc.

d As-Is

Conc. t Type

(μg/kg)

(μg/kg)

Conc.

(μg/kg)

(μg/kg)

Conc.

(μg/kg) (μg/kg)

(μg/kg) D-1 Dry 88 6.68 8 894 1016 967 1099 3.93 4 D-2 Dry 88 15.5 18 933 1060 1200 1364 8.31 9 D-3 Dry 88 1.79 2 634 720 1020 1159 7.33 8 D-4 Dry 88 5.4 6 707 803 640 727 8.55 10 D-5 Dry 88 6.74 8 582 661 744 845 4.46 5 D-9 Dry 88 17.6 20 807 917 514 584 5.7 6 D-10 Dry 88 26.8 30 960 1091 2780 3159 5.62 6 D-11 Dry 88 5.28 6 1770 2011 925 1051 10.4 12 D-12 Dry 88 2.74 3 778 884 1010 1148 2.59 3 D-15 Dry 88 - - 556 632 649 738 7.19 8 D-18 Dry 88 1.79 2 327 372 145 165 3.86 4 D-19 Dry 88 2.65 3 595 676 1440 1636 5.85 7 D-20 Dry 88 3.48 4 407 463 1240 1409 3.6 4 D-21 Dry 88 1.78 2 893 1015 2480 2818 3.42 4 D-41 Dry 88 - - 1100 1250 2340 2659 3.23 4 D-42 Dry 88 - - 997 1133 1370 1557 2.13 2 D-56 Dry 88 - - 520 591 1120 1273 10.5 12 D-57 Dry 88 19 22 1790 2034 2040 2318 8.96 10 D-17 Wet 25 2.88 12 88.6 354 48.4 194 1.74 7 D-22 Wet 25 0.971 4 587 2348 745 2980 1.36 5 D-23 Wet 25 4.17 17 457 1828 824 3296 5.89 24 D-24 Wet 25 0.994 4 130 520 1270 5080 2.77 11 D-26 Wet 25 2.1 8 94.6 378 675 2700 2.6 10 D-28 Wet 25 - - 122 488 1000 4000 2.93 12 D-31 Wet 25 - - 176 704 337 1348 2.11 8 D-32 Wet 25 2.1 8 212 848 114 456 3.86 15 D-33 Wet 25 2.67 11 192 768 483 1932 3.43 14 D-39 Wet 25 - - 278 1112 410 1640 2.96 12 D-53 Wet 25 1.91 8 244 976 415 1660 2.51 10 D-54 Wet 25 0.835 3 268 1072 207 828 2.11 8 D-55 Wet 25 1.6 6 348 1392 281 1124 7.48 30 C-6 Dry 88 19.3 22 540 614 718 816 1.69 2 C-7 Dry 88 10.6 12 2270 2580 1060 1205 2.89 3 C-8 Dry 88 12.4 14 583 663 669 760 4.31 5 C-13 Dry 88 54.6 62 617 701 574 652 2.2 3 C-14 Dry 88 4.43 5 778 884 919 1044 1.79 2 C-16 Dry 88 1.7 2 340 386 566 643 6.1 7 C-40 Dry 88 7.93 9 1240 1409 3190 3625 3.3 4 C-43 Dry 88 0.98 1 905 1028 1450 1648 3.42 4 C-46 Dry 88 - - 804 914 2230 2534 2.96 3 C-47 Dry 88 - - 1077 1224 2240 2545 3.02 3 C-48 Dry 88 5.28 6 1740 1977 1520 1727 4.07 5 C-49 Dry 88 5.33 6 1130 1284 3040 3455 3.29 4 C-50 Dry 88 0.887 1 555 631 1250 1420 5.37 6 C-25 Wet 25 2.3 9 123 492 2790 11160 2.01 8 C-27 Wet 25 5.52 22 128 512 972 3888 2.19 9 C-29 Wet 25 4.2 17 59.5 238 379 1516 2.94 12 C-30 Wet 25 2.03 8 152 608 305 1220 2.23 9 C-34 Wet 25 1.05 4 281 1124 511 2044 8.62 34 C-35 Wet 25 1.09 4 30.7 123 514 2056 4.24 17 C-36 Wet 25 4.15 17 437 1748 266 1064 3.86 15 C-37 Wet 25 13.4 54 43.6 174 986 3944 4.58 18 C-38 Wet 25 1.01 4 195 780 232 928 2.49 10 C-44 Wet 25 43.6 174 20.9 84 809 3236 1.7 7 C-45 Wet 25 1.01 4 314 1256 350 1400 1.25 5 C-51 Wet 25 5.13 21 437 1748 384 1536 2.82 11 C-52 Wet 25 4.76 19 276 1104 385 1540 1.3 5 C-58 Wet 25 10.6 42 48.8 195 256 1024 4.31 17

Assume d DM (%)

Page 21 of 25 – 11024 Target Animal Safety Review

Appendix 1 continued

Sample ID

Thorium

Thorium

Uranium

Uranium

Vanadium

Vanadium Reported

Calculated

Reported

Calculated

Reported

Calculated As-Is

DM

As-Is

DM

As-Is

DM Product

Conc.

Conc.

Conc.

Conc.

Conc.

Conc. Type

(μg/kg)

(μg/kg)

(μg/kg)

(μg/kg)

(μg/kg)

(μg/kg) D-1 Dry 88 12.7 14 119 135 556 632 D-2 Dry 88 45.2 51 762 866 1690 1920 D-3 Dry 88 30 34 22.1 25 633 719 D-4 Dry 88 26.1 30 28.4 32 583 663 D-5 Dry 88 86.9 99 43.3 49 324 368 D-9 Dry 88 31.3 36 650 739 714 811 D-10 Dry 88 16.2 18 94.5 107 229 260 D-11 Dry 88 71.3 81 864 982 2380 2705 D-12 Dry 88 10.2 12 11.3 13 213 242 D-15 Dry 88 54.3 62 421 478 1100 1250 D-18 Dry 88 3.73 4 14.9 17 60.6 69 D-19 Dry 88 18.8 21 36.2 41 339 385 D-20 Dry 88 3.54 4 13.5 15 77.9 89 D-21 Dry 88 24.8 28 350 398 856 973 D-41 Dry 88 41.7 47 22.3 25 285 324 D-42 Dry 88 27.1 31 19 22 210 239 D-56 Dry 88 10.9 12 34.3 39 129 147 D-57 Dry 88 67.2 76 689 783 1960 2227 D-17 Wet 25 0.502 2 0.784 3 62.2 249 D-22 Wet 25 5.49 22 3.56 14 71.5 286 D-23 Wet 25 26 104 180 720 293 1172 D-24 Wet 25 0.95 4 5.34 21 46.6 186 D-26 Wet 25 1.28 5 0.874 3 72.9 292 D-28 Wet 25 6.71 27 19.1 76 88 352 D-31 Wet 25 0.235 1 0.805 3 33.4 134 D-32 Wet 25 0.741 3 0.868 3 33.2 133 D-33 Wet 25 0.585 2 13.6 54 8.82 35 D-39 Wet 25 1.21 5 6.5 26 39.2 157 D-53 Wet 25 0.694 3 4.1 16 20.9 84 D-54 Wet 25 1.23 5 2.69 11 12 48 D-55 Wet 25 0.634 3 3.34 13 23.5 94

C-6 Dry 88 8.2 9 16.4 19 205 233 C-7 Dry 88 7.96 9 15.5 18 132 150 C-8 Dry 88 4.47 5 6.92 8 197 224 C-13 Dry 88 5.41 6 13.4 15 172 195 C-14 Dry 88 19.3 22 226 257 391 444 C-16 Dry 88 9.34 11 11.4 13 351 399 C-40 Dry 88 7.47 8 61.2 70 183 208 C-43 Dry 88 7.79 9 25.7 29 221 251 C-46 Dry 88 6.57 7 15.4 18 145 165 C-47 Dry 88 11.6 13 34.4 39 268 305 C-48 Dry 88 10.1 11 22 25 277 315 C-49 Dry 88 7.15 8 18.1 21 111 126 C-50 Dry 88 12.4 14 27.7 31 180 205 C-25 Wet 25 1.15 5 3.14 13 82.3 329 C-27 Wet 25 40.1 160 241 964 156 624 C-29 Wet 25 1.29 5 1.35 5 48.4 194 C-30 Wet 25 1.52 6 4.76 19 58 232 C-34 Wet 25 0.62 2 3.91 16 21.9 88 C-35 Wet 25 0.452 2 2.7 11 7.52 30 C-36 Wet 25 0.287 1 5.51 22 21.2 85 C-37 Wet 25 0.988 4 18.1 72 22.1 88 C-38 Wet 25 2.53 10 34.4 138 36.5 146 C-44 Wet 25 0.509 2 8.37 33 106 424 C-45 Wet 25 0.45 2 5.68 23 20.8 83 C-51 Wet 25 5.25 21 52.2 209 86.5 346 C-52 Wet 25 33 132 233 932 109 436 C-58 Wet 25 8.69 35 7.33 29 82.3 329

Assumed DM (%)

Page 22 of 25 – 11024 Target Animal Safety Review

Appendix 2 Summary Statistics for DM Metal Content by Product Type of the 15 Metals Measured and Reported in Reference 1 Table A2.1 Summary Statistics for DM Metal Content of Dry Dog Food Products Reported in Reference 1 Metal Mean (Median)

**a**

**SD**

**b**

Minimum Maximum Antimony 176 (76) 266 54 1,097 Arsenic 156 (156) 77 35 282 Beryllium 30 (8) 26 3 84 Cadmium 76 (73) 34 20 148 Cesium 17 (16) 6 8 32 Chromium 926 (762) 473 194 1,943 Cobalt 359 (238) 303 40 999 Lead 224 (153) 223 80 1,060 Mercury 10 (6) 9 2 30 Molybdenum 963 (901) 454 372 2,034 Nickel 1,428 (1,216) 817 165 3,159 Thallium 7 (6) 3 2 12 Thorium 37 (30) 28 4 99 Uranium 265 (45) 346 15 982 Vanadium 779 (509) 773 69 2,705 a Number of samples (n) for Mercury = 14 as 4 samples had no reported result. n = 18 for all other metals. b All numbers in the table have units of μg/kg expressed on a dry matter basis. c SD=Standard Deviation.

Table A2.2 Summary Statistics for DM Metal Content of Wet Dog Food Products Reported in Reference 1 Metal Mean (Median)a SDb Minimum Maximum Antimony 26 (16) 22 7 72 Arsenic 163 (147) 82 80 362 Beryllium 13 (11) 5 10 30 Cadmium 86 (87) 37 33 146 Cesium 15 (11) 13 4 54 Chromium 1,291 (580) 2,687 78 10,160 Cobalt 372 (250) 432 143 1,788 Lead 146 (149) 64 64 260 Mercury 8 (8) 4 3 17 Molybdenum 984 (912) 587 354 2,348 Nickel 2,095 (1,660) 1,442 194 5,080 Thallium 13 (11) 7 5 30 Thorium 14 (4) 28 1 104 Uranium 74 (14) 195 3 720 Vanadium 248 (157) 295 35 1,172

a Number of samples (n) for Mercury = 10 as 3 samples had no reported result. n = 13 for all other metals. b All numbers in the table have units of μg/kg expressed on a dry matter basis. c SD=Standard Deviation.

Page 23 of 25 – 11024 Target Animal Safety Review

**Appendix 2 continued**

Table A2.3 Summary Statistics for DM Metal Content of Dry Cat Food Products Reported in Reference 1 Metal Mean (Median)

**a**

**SD**

**b**

Minimum Maximum Antimony 143 (83) 149 29 489 Arsenic 177 (153) 76 84 333 Beryllium 5 (3) 3 2 11 Cadmium 49 (48) 14 31 79 Cesium 11 (10) 3 6 16 Chromium 677 (659) 259 376 1,386 Cobalt 332 (223) 282 124 1,041 Lead 698 (177) 1,811 85 6,716 Mercury 13 (6) 18 1 62 Molybdenum 1,100 (971) 613 386 2,580 Nickel 1,698 (1,420) 1,034 643 3,625 Thallium 4 (4) 2 2 7 Thorium 10 (9) 4 5 22 Uranium 43 (21) 66 8 257 Vanadium 248 (224) 95 126 444 a Number of samples (n) for Mercury = 11 as 2 samples had no reported result. n = 13 for all other metals. b All numbers in the table have units of μg/kg expressed on a dry matter basis. c SD=Standard Deviation.

Table A2.4 Summary Statistics for DM Metal Content of Wet Cat Food Products Reported in Reference 1 Metal Mean (Median)a SDb Minimum Maximum Antimony 22 (16) 15 8 53 Arsenic 210 (197) 123 50 524 Beryllium 19 (12) 14 10 60 Cadmium 139 (134) 67 64 306 Cesium 24 (18) 17 7 61 Chromium 734 (277) 932 58 3,156 Cobalt 337 (250) 381 173 1,652 Lead 168 (119) 158 65 684 Mercury 29 (17) 45 4 174 Molybdenum 728 (608) 581 84 1,748 Nickel 2,611 (1,538) 2,663 928 11,160 Thallium 13 (11) 8 5 34 Thorium 28 (5) 51 1 160 Uranium 178 (26) 331 5 964 Vanadium 245 (213) 175 30 624

a Number of samples (n) = 14 for all metals. b All numbers in the table have units of μg/kg expressed on a dry matter basis. c SD=Standard Deviation.

Page 24 of 25 – 11024 Target Animal Safety Review

**Appendix 2 continued**

Table A2.5 Summary Statistics for DM Metal Content of All Dog Food Products Reported in Reference 1 Metal Mean (Median)

**a**

**SD**

**b**

Minimum Maximum Antimony 113 (62) 214 7 1,097 Arsenic 159 (152) 78 35 362 Beryllium 18 (11) 21 3 84 Cadmium 80 (75) 35 20 148 Cesium 16 (14) 10 4 54 Chromium 1,079 (734) 1,746 78 10,160 Cobalt 364 (247) 356 40 1,788 Lead 191 (152) 177 64 1,060 Mercury 9 (7) 7 2 30 Molybdenum 972 (884) 505 354 2,348 Nickel 1,708 (1,364) 1,150 165 5,080 Thallium 9 (8) 6 2 30 Thorium 27 (18) 30 1 104 Uranium 185 (26) 304 3 982 Vanadium 556 (286) 667 35 2,705

a Number of samples (n) for Mercury = 24 as 7 samples had no reported result. n = 31 for all other metals. b All numbers in the table have units of μg/kg expressed on a dry matter basis. c SD=Standard Deviation.

Table A2.6 Summary Statistics for DM Metal Content of All Cat Food Products Reported in Reference 1 Metal Mean (Median)

**a**

**SD**

**b**

Minimum Maximum Antimony 81 (36) 119 8 489 Arsenic 194 (170) 103 50 524 Beryllium 12 (11) 13 2 60 Cadmium 96 (79) 66 31 306 Cesium 17 (13) 14 6 61 Chromium 707 (520) 683 58 3,156 Cobalt 335 (247) 331 124 1,652 Lead 423 (135) 1,264 65 6,716 Mercury 22 (9) 36 1 174 Molybdenum 907 (780) 615 84 2,580 Nickel 2,172 (1,536) 2,063 643 11,160 Thallium 8 (6) 7 2 34 Thorium 19 (8) 38 1 160 Uranium 113 (23) 248 5 964 Vanadium 246 (224) 139 30 624 a Number of samples (n) for Mercury = 25 as 2 samples had no reported result. n = 27 for all other metals. b All numbers in the table have units of μg/kg expressed on a dry matter basis. c SD=Standard Deviation.