June 15, 2011

Target Animal Safety Review Memorandum

Background

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

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® (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.

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*.[3]

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 Cats*[4] 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 3¼ cups of even the least calorie-dense maintenance formulas (i.e., the 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 ¾ 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.

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 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 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).

Table 1 Summary Statistics, Maximum Concentrations & Estimated Maximum Tolerable Limits of 15 Metals in 58 Dog & Cat Food Products Reported in Reference 1

Metal	Mean (Median)[a,b]	SD[c]	Maximum	MTL[d]
Antimony	98 (54)	176	1,097	40,000[e]
Arsenic	175 (155)	91	524	12,500[e]
Beryllium	15 (11)	17	84	>5,000[f]
Cadmium	88 (77)	52	306	10,000[f]
Cesium	17 (13)	12	61	NL[g]
Chromium	906 (641)	1,361	10,160	10,000[h,i]
Cobalt	351 (247)	342	1,788	2,500[h]
Lead	299 (150)	871	6,716	10,000[f]
Mercury	13 (6)	23	174	267[f,j]
Molybdenum	941 (866)	555	2,580	5,000[e]
Nickel	1,823 (1,468)	1,649	11,160	50,000[e,i]
Thallium	9 (8)	6	34	NL[k]
Thorium	24 (10)	33	160	NL[l]
Uranium	151 (25)	279	982	10,000[h]
Vanadium	412 (246)	517	2,705	1,000[h]

[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.

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

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 2¾ to 3⅓ 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]

> "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 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:

$$20 \ \mu g \ Hg/kg \ BW \div 0.075 \ kg \ of \ DM/kg \ BW = 267 \ \mu g \ Hg/kg \ DM$$

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:

$$5 \ \mu g \ Hg/kg \ BW \div 0.075 \ kg \ of \ DM/kg \ BW = 67 \ \mu g \ Hg/kg \ DM$$

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®, 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.

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."

> "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.

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.

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

References

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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	Product Type	Assumed DM (%)	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 Conc. (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

Appendix 1 continued

Sample ID	Product Type	Assumed DM (%)	Cesium Reported As-Is Conc. (µg/kg)	Cesium Calculated DM Conc. (µg/kg)	Chromium Reported As-Is Conc. (µg/kg)	Chromium Calculated DM Conc. (µg/kg)	Cobalt Reported As-Is Conc. (µg/kg)	Cobalt Calculated DM Conc. (µg/kg)	Lead Reported As-Is Conc. (µg/kg)	Lead Calculated DM Conc. (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

Appendix 1 continued

Sample ID	Product Type	Assumed DM (%)	Mercury Reported As-Is Conc. (µg/kg)	Mercury Calculated DM Conc. (µg/kg)	Molybdenum Reported As-Is Conc. (µg/kg)	Molybdenum Calculated DM Conc. (µg/kg)	Nickel Reported As-Is Conc. (µg/kg)	Nickle Calculated DM Conc. (µg/kg)	Thallium Reported As-Is Conc. (µg/kg)	Thallium Calculated DM Conc. (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

Appendix 1 continued

Sample ID	Product Type	Assumed DM (%)	Thorium Reported As-Is Conc. (µg/kg)	Thorium Calculated DM Conc. (µg/kg)	Uranium Reported As-Is Conc. (µg/kg)	Uranium Calculated DM Conc. (µg/kg)	Vanadium Reported As-Is Conc. (µg/kg)	Vanadium Calculated DM Conc. (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

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]	SD[b]	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.

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]	SD[b]	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.

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.