Sections in This Document

1. Purpose

The purpose of this document is to provide training guidance to analysts responsible for analysis of nutritional and toxic elements in food, feed, food ware, and other regulated products. This is general information to supplement on-the-job training, proficiency testing for beginning analysts, and formal classroom training (OTED courses LB 212, LB 307, and LB 404).

2. Scope

This document applies to all analysts involved in the analysis of samples for determination of nutritional and/or toxic elements in FDA samples.

3. Responsibility

It is the responsibility of laboratory management and quality assurance management to ensure that all analysts are properly trained and have the prerequisite skills necessary to conduct elemental analysis of FDA samples.

4. Background

Humans and animals are exposed daily to numerous elements, in varying forms and at different levels, through food (feed), water, and other FDA-regulated products (cosmetics).

Major essential elements include C, H, O, N, S, Ca, P, K, Na, Cl, and Mg. C, H, O, N, and S make up the bulk of the elemental constituents of plants and animals and are the major components of the organic substances in tissue. Fe, Zn, Cu, Co Mn, I, Mo, Cr, Se, F, (B for plants) have identified functions meeting the definition of essential elements in humans and animals (References 1, 2). Whether an element is essential has some bearing on an element's toxicity. Essential elements under homeostasis, (i.e. the level of absorption, body stores, and or excretion is under physiological control), tend to have a lower relative toxicity. However, many factors, such as the level of

exposure, the form of the element, the sensitivity of the host, and the physiological and nutritional status of the host, affect the toxicity of an element.

Nonessential and essential elements can be toxic. Nonessential elements where human toxicity has been reported include Pb, Cd, Hg, As, Al, Ba, Li, Pt, Te, Ti, Sb, Be, Ga, In, V, Ni, Sr, Sn, Ge, Ag, Au, Bi, Tl, and U. The essential elements, F, Co, Fe, Mo, Cu, Mg, Se, Cr, Mn, and Zn, are of practical toxicological significance. Se is the most toxic essential mineral elements. Presently, Pb, Cd, Hg (as methylmercury), and As (inorganic forms) are of the greatest concern and have the greatest program emphasis.

4.1. FDA Center for Food Safety and FDA Center for Veterinary Medicine

As part of its responsibilities for ensuring food safety, the FDA Center for Food Safety and Applied Nutrition (CFSAN) and FDA Center for Veterinary Medicine (CVM) routinely monitor the level and potential dietary uptake of toxic elements (contaminants) in food, feed and foodware. FDA Compliance Programs detail the sample collection and analysis for the determination of arsenic, lead, and cadmium in food, feed, and foodware, as well as methyl mercury, inorganic arsenic and selenium in food and feed.

4.2. Toxic Elements in Food, Feed and Foodware

Compliance Programs guide field and laboratory operations which cover toxic elements in targeted sampling. CPG 7304.019A (food) and CPG 7304.019B (foodware) are the applicable Compliance Programs for the toxic elements. See Reference 3.

4.2.1. Toxic Element in Food and Feed

See Compliance Program Guidance Manual 7304.019A Toxic Elements in Foods and 7371.003B Feed Contaminants Program - Elements. Lead and cadmium are identified as the toxic elements of concern in foods; particular emphasis is placed on foods consumed by children who are the most sensitive to adverse side effects.

There are few universal regulatory limits, i.e. tolerances, for toxic elements in foods; sample results that exceed normal concentrations are brought to the attention of CFSAN, who will conduct Health Hazard Evaluation of potential health hazards from the quantity of the toxic element found based upon food consumption of the product.

FDA has established Provisional Daily Total Tolerable Intakes (PDTTI) for lead for several at- risk groups (Reference 7). When the consumption of a contaminated food has exceeded a PDTTI, regulatory action *may be* taken on

an *ad hoc* basis. Food Chemical CODEX (FCC) lists many internationally recognized standards for lead in foods and food ingredients. While these are not regulatory tolerances, the FCC are often employed as lowest limits of actions for imported foods.

The prohibition of lead soldered cans and the removal of lead from gasoline have significantly reduced the lead exposure to the average consumer. The Total Diet Surveys indicate the average lead intake from food has decreased more than 95% since the 1970s. Nonetheless, FDA remains concerned about lead in regulated products, especially since more than half of our foods now come from outside the U.S., and a significant number of children in the U.S. remain exposed to excessive amounts of lead. Lead in the diet can be attributed to natural sources of lead in the soil, deposition of lead particles onto crops, pollution (lead gasoline usage), food processing and packaging techniques, spices, herbal supplements, ayurvedic medicine, and folk remedies. The use of lead-based solders in food cans is now prohibited (21CFR 189.240). Although the use of lead-based pigments in food wrappers is not prohibited, the United States and European Commission voluntarily stopped this practice. Candy food wrappers from other countries, particularly Mexico, have been found to contain percent levels of lead. Lead is found in folk remedies such as Azarcon, Greta, herbal medicines, and unapproved dyes in eye cosmetics (kajal, surma, kohl) from the Far and Middle Eastern countries (Reference 19). Spices, sourced from India, have recently been found to contain elevated levels of lead and chromium. Yellow lead chromate and red lead chromate appear to be contaminants added to enhance the color of the spice.

Cadmium is found in foods naturally and due to pollution. Cadmium is emitted into the atmosphere from smelters and waste incineration plants; the use of municipal sludge can dramatically increase cadmium levels in food. Recently cultivated agricultural areas derived from ancient seabeds are prone to producing elevated levels of cadmium in foods (e.g. spinach, lettuce). See Reference 17.

Arsenic and selenium both occur naturally in foods. Each can be present at toxicologically significant levels in groundwater and in soils.

Arsenic compounds are released to the atmosphere from natural and industrial sources. The major sources of arsenic emissions are the smelting of metals, burning of fossil fuels, and application of pesticides and herbicides. The arsenic compounds may accumulate in agricultural and horticultural soils and plants.

Arsenic in food is most often in alkylated forms. The alkylated forms of arsenic that arise in plants, shrimp (Reference 16), and some other animals have a relative low order of toxicity. Arsenate and arsenite are far more toxic and have proven to be carcinogenic in humans.

Selenium is the most toxic essential mineral element. Selenium often occurs as selenium analogues of sulfur-containing amino acids and metabolites in plants. While there have been numerous selenium intoxications reported for human and animals, these poisonings have been mainly due to errors in manufacturing dietary supplements and feed selenium supplements. Although human toxicity to selenium has been reported in China and other parts of the world where extreme selenium pollution exists, selenium deficiency appears to be the more significant public health concern.

Pigments used to decorate ceramicware, or glazes coating ceramicware may contain lead or cadmium. Traditional wares (e.g. Chinese classic enamel-on-porcelain wares, Mexican glazed folk terra cotta) have been found to contain excessive amounts of lead (Reference 3). Glazes that are improperly formulated, applied, or fired may permit unacceptable amounts of lead or cadmium to leach into food. The following colors in glaze or decorations are often indicative of ceramicware that may release cadmium: red, orange, yellow.

4.2.2. Lead and Cadmium in Foodware

See Compliance Program Guidance Manual 7303.019B Toxic Elements in Foodware.

The Food Additives provision of the FD&C Act does not permit a harmful level of a substance to migrate from the surface onto a food or beverage. Toxic Elements in Foodware (CPGM 7303.019B) focuses on lead and cadmium found in ceramicware and silver-plated hollowware used for eating, storing, holding and cooking foods.

The FDA and the State Administration of Entry/Exit Inspection and Quarantine of China (recently renamed the China National Certification and Accreditation Administration or CNCA) implemented a Memorandum of Understanding (MOU) pertaining to the safety of ceramic tableware produced in China and exported to the United States. The MOU specifies a certification system for ceramic tableware production facilities in China. This certification system is expected to provide FDA with reasonable assurance that ceramicware produced in these facilities and exported to the United States will not exceed FDA action levels for leachable lead and cadmium (Reference 20).

The CPGM focuses on the following areas: investigates the rate of compliance for Chinese Ceramicware from non-certified and certified factories, audits the effectiveness of the China certification program in improving the safety of ceramicware exported to the United States, and concentrates on sampling countries with prior violations, particularly small shipments entering from Mexico.

Monitoring of ceramicware is conducted in two steps. Screening tests for ceramicware are conducted in the field to identify items that are likely to contain leachable lead. Based on the results of the screening tests, official samples are collected and sent to the laboratory for further testing. There is no screening test for cadmium in ceramicware, or lead and cadmium in silver-plated hollowware. The investigator is directed to look for signs of improper glazing on the product, and/or collecting samples with those colors that may contain lead or cadmium.

In the absence of codified regulations or tolerances for ceramicware, FDA has established interim action guidelines for lead (CPG Sec 545.450) and cadmium (CPG Sec 545.400). See References 4 and 5. The surveillance of leachable lead and cadmium in ceramicware continues to be a program priority.

Past FDA regulatory efforts, an MOU with China, efforts by the commercial sector, and state regulations (e.g. California Proposition-65), have led to a vast improvement in the performance of daily-use tableware regarding the leachability of lead and cadmium. Most daily-use ceramicware pose relatively few regulatory problems for leachable levels of lead and cadmium. The traditional wares (especially from China) and folk terra cotta wares from Mexico and Central American countries continue to pose lead exposure risk, especially for children and the fetus. Many other elements are used in ceramicware bodies, their glazes, and decorations. Ba, Sb, Co, Cr, and others may leach from ceramicware. However, the regulatory significance of these elements has not been evaluated.

4.2.3. Mercury in Foods and Feed

See Compliance Policy Guide, Section 540.600, Fish, Shellfish, Crustaceans and other Aquatic Animals – Methyl Mercury (Reference 9).

Mercury, primarily as methyl mercury, was first identified as a regulatory issue in seafood in the 1970s. Mercury occurs naturally in the environment and is released from the Earth's crusts and oceans. Mercury is also released from

fossil fuels, such as coal, and burning industrial wastes. Fish absorb methyl mercury from water as it passes over their gills and through feeding aquatic organisms; methyl mercury binds tightly to proteins in fish tissue (Reference 21).

Studies of people exposed to high levels of mercury in highly contaminated fish were conducted in Minnamata, Japan. Over one hundred people died from eating fish (often daily over extended periods) from waters that were severely polluted with mercury from industrial discharge. Mercury poisoning occurred in unborn fetuses and children. An epidemic of mercury poisoning occurred with a wheat seed treated with alkyl mercury fungicide (Reference 21).

Presently, the FDA regulatory guideline for methyl mercury in seafood (CPG Sec 540.600) is one part per million (ppm) methyl-mercury expressed as Hg. FDA's action level of one ppm for methyl mercury in fish was established to limit the consumers methyl mercury exposure to levels ten times lower than the lowest levels associated with adverse effects. Seafood consumption recommendations are available based on established Hg surveillance environmental data.

4.3. Mercury in Cosmetics

The passage of the Food, Drug, and Cosmetic act in 1938 allowed for FDA regulation of cosmetic products, and additional legislation passed in 1977 required U.S. manufacturers to list ingredients on the labels of cosmetic products.

The use of mercury in some face cream products is intentional, as it provides skin bleaching properties and can reduce freckles, age spots, and brown spots by temporarily blocking the production of melanin. This temporary effect leads to continual use of the product. The presence of mercury at percent levels have been found in some of these products. This appears to be more common in imported products which are manufactured and sold in Asia, Mexico, and the Middle East, and can in some cases be imported into the U.S., purchased over the internet, or brought in personally from abroad for personal use.

Repeated use of products containing high levels of mercury can lead to chronic exposure through dermal contact. In addition, some of these products are known to contain volatile forms of mercury, and hence pose additional risk of exposure via inhalation. The use of mercury in cosmetics was banned by the EU in 1976 and by the FDA in 1990. FDA regulations allow for cosmetics meeting conditions of good manufacturing practices to have trace levels of mercury at levels of less than 1 ppm, with the exception of cosmetics used only in the area of the eyes where mercury is still allowed as a preservative at

levels no more than 65 ppm [21 CFR 700.13]. Mercury containing face cream products with claims such as “skin-bleaching” can be interpreted as an unapproved drug and/or an adulterated product.

4.4. Nutritional Elements in Foods, Feeds, and Dietary Supplements

Nutritional elements (secondary and minor nutrients) are determined in foods and feed to evaluate the levels of nutrients in foods, dietary supplements and feeds as compared to NLEA food labels, DSHEA dietary supplement labels, and feed labels. Infant formula, medical foods, dietary supplements, food, and feed are routinely tested for these nutrient types. Compliance Programs 7321.002 Medical Foods, 7321.005 NLEA Nutrient Sample Analysis, 7321.006 Infant Formula, 7321.008 DSHEA Dietary Supplement, Total Diet Study, and 7371.003B Feed Contaminants Program.

Total Diet Study (TDS), sometimes called the Market Basket Study, is an ongoing FDA program that determines levels of various pesticides, contaminants, and nutrients in foods for the purpose of estimated intakes of these substances in representing diets of selected age-sex groups in the United States Population. Elements analyzed include the following: arsenic, cadmium, calcium, copper, iron, lead, magnesium, manganese, mercury, nickel, phosphorous, potassium, selenium, sodium, and zinc (Reference 22).

4.5. Methods and Technology

This section is intended to expose the analyst to some of the more frequently used methods for determining toxic and nutritional metals in food, feed, and foodware. For more detailed information regarding methods on the determination of these and additional elements, standards, sample preparation, digestions, instrumentation, or data treatment consult the CFSAN website and the Elemental Analysis Manual (EAM) website.

4.5.1. Qualitative Identification of Lead in Ceramicware and Solder Alloys

Because the scope of the ceramicware program is limited to leachable lead and cadmium, and the use of lead is routine in ceramicware items, FDA investigators often employ qualitative tests to determine whether the item leaches (or contains) lead, and therefore warrants collection.

An equivalent, FDA validated test kit does not exist for cadmium. The presence of cadmium is usually “signaled” by the presence of rich yellow or red decorations on the food-bearing surface of the item. FDA developed the Quick Color Test (QCT) for Lead (References 10, 11, 12). The QCT test for lead, and similar forms of the test (e.g. the Rapid Abrasion Test (RAT),

Reference 13), have been commercialized (e.g. LeadCheck Swabs™, by Hybrivet, Reference 14). The tests determine if an item bears leachable lead or the item bears a leachable or non-leachable lead in the glaze or a decoration (Reference13). Some of these commercial test kits have also been validated for testing for the presence of lead in the solder of food cans, a prohibited practice (Reference 15). EAM 4.6 available here, and may be used to determine leachable lead from soldered cans (more information in §6.2.3).

The following documents, articles and methods are useful references: Compliance Program Guidance Manual 7304.019B Toxic Elements in Foodware (Domestic & Import); Gould et al. (1988). *Analytical Letters*, 2145-2154; Capar, S. G. (1998, August). Ceramic foodware lead screening using test kits. Laboratory Information Bulletin, LIB No. 4127, *14*, 1-8; Dolan, S.P. (1994). *Journal of AOAC International,* 719-722; Capar, S. G., Anderson, D.L., Hughes, D. D., Jacobs, R.M. (1996). Identification of lead solder on a metal can seam. Laboratory Information Bulletin, LIB No. 4041, *12*(12).

4.5.2. XRF analysis

X-ray fluorescence (XRF) is a rapid and usually non-destructive analytical technique for measuring the levels of elements in samples. Two core types of XRF are energy dispersive XRF (EDXRF) and wavelength dispersive XRF (WDXRF). The addition of the word “spectrometry” makes the acronyms XRFS, EDXRFS, and WDXRFS, respectively. Hardware and software options are very-well developed - highly capable and functional.

XRF can potentially measure all elements with Z≥11 (i.e., Al and heavier) but does not provide chemical form. It can be an add-on capability, such as in electron microscopy, but is usually stand-alone. XRF’s strongest application is in inorganic fields of study such as archaeology and minerology. For example, Perseverance (the rover in NASA’s Mars 2020 mission) will use XRF to study the composition of Mars’ surface. Although XRF is not widely used in food analysis, it can have application in the analysis of food safety.

XRF is a surface analysis technique where excitation causes x-rays to be emitted from atoms present in only the top few microns of sample surfaces. It is, therefore, best-suited for smooth and uniform surfaces. The x-ray energies/wavelengths indicate which elements are being detected and their intensities give quantitative information. WDXRFS is the more precise and has lower detection levels than EDXRFS, but WDXRFS systems are relatively large (and expensive), requiring significant floor space as opposed to EDXRFS systems, many of which are benchtop or even portable enough to use in a ‘point-and-shoot’ procedure. A typical application for the latter is to measure

lead in wall paint. Several FDA laboratories have hand-held EDXRFS systems that can be used for investigations such as looking for lead and cadmium in ceramicware surfaces.

4.5.3. Methods

A. Detection and Confirmation of Toxic Element Using the Innov-X-X-5000 Field Portable X- Ray Fluorescence Analyzer

B. Use of X-ray Fluorescence Spectrometry for Screening and/or Accurate Quantitation of Toxic Elements in Supplements, LIB #4461

C. Use of Field Portable XRF for Screening and Quantification of Mercury in Face Creams, LIB #4542

4.5.4. Leachable Lead and Cadmium from Ceramicware by ICP- AES

Inductively coupled plasma atomic emission spectrometry (ICP-AES, commonly atomic is interchanged with optical, and spectrometry interchanged with spectroscopy) is a rapid, multi-element technique. Samples, typically consisting of an aqueous acid liquid, either by prior dilution/dissolution with an acid solution (e.g leachate), or as the end product of an acid digestion (e.g. via microwave assisted decomposition, §6.2.4) are introduced to the ICP. During the free electron – analyte collision, analyte electrons absorb energy and are promoted to higher (excited) energy levels. Excited electrons drop back down to ground energy levels and excess energy is liberated as light. Each element has its own characteristic light spectrum. The AES uses an Echelle grating to separate wavelengths and light is quantified on a detector. Light intensity is measured and calibrated against known standards and the concentration in solution is calculated. Instrument software can correct for background light subtraction.

4.5.5. Method

A. EAM 4.6 Inductively Coupled Plasma-Atomic Emission Spectrometric Determination of Cadmium and Lead Extracted from Ceramic Foodware

4.5.6. Microwave Digestion

Homogenized food samples are added to an inert vessel with concentrated acid, the vessel is closed to prevent contamination and/or sample loss, and the food-acid mixture is heated by microwave radiation. Temperature is programmed and computer controlled; typically a linear rise in temperature over a set period of time to a predetermined temperature and then held at that elevated temperature (~200 °C) before cooling. The acid and heat combination

dissolve the food matrix so that the analyte of interest resides in solution. For a nitric acid digestion, carbohydrates typically digest around 140 °C , proteins around 160 °C and lipids around 180 °C. Hydrogen peroxide is usually added to provide an oxygen source so that dissolved carbon is liberated as CO_2, reducing unwanted matrix components from the test solution. Solutions are then diluted with water to reduce acid concentration for a suitable test solution.

4.5.7. Multi-Element, Simultaneous Sequential/Quantitative Analysis of Food and Feed by ICP-AES

As described, ICP-AES can be used for multiple elements and application to food matrices often requires microwave digestion.

4.5.7.1. Methods

A. EAM 4.4 https://www.fda.gov/media/95162/download

B. AOAC 2011.14 Calcium, Copper, Iron, Magnesium, Manganese, Potassium, Phosphorus, Sodium, and Zinc in Fortified Food Products. Microwave Digestion and Inductively Coupled Plasma-Optical Emission Spectrometry (Available in AOAC Methods Manual)

4.5.8. Multi-Element, Simultaneous Sequential/Quantitative Analysis of Foods and Feed by ICP-MS

When compared to ICP-AES, inductively coupled plasma mass spectrometry (ICP-MS) has lower detection limits, but higher operating costs. Samples are introduced to the ICP in the same way as ICP-AES. Ions at atmospheric pressure are entrained into a high vacuum mass spectrometer through a series of small, cone-shaped orifices downstream in the plasma. Once inside the mass spectrometer, ions are focused, separated according to their mass-to-charge ratio (*m/z*) and counted. Each element has a known set of stable isotopes, e.g. $^{75}As^{+}$ is measured at *m/z* 75. Test solution concentrations are typically determined using external calibration standards. Interferences are overcome by either kinetic energy discrimination using a helium filled collision cell, chemical resolution using ion-molecule reactions in a reaction cell, or by high resolution instrumentation. ICP-MS can also be combined with chromatographic separations where different molecular forms are temporally separated and then quantified individually, e.g. inorganic mercury separated from methyl-mercury.

4.5.8.1. Methods

A. EAM 4.7 Inductively Coupled Plasma-Mass Spectrometric Determination of Arsenic, Cadmium, Chromium, Lead, Mercury, and Other Elements in Food Using Microwave Assisted Digestion

B. EAM 4.8 High Pressure Liquid Chromatographic-Inductively Coupled Plasma-Mass Spectrometric Determination of Methylmercury and Total Mercury in Seafood

C. EAM 4.10 High Performance Liquid Chromatography-Inductively Coupled Plasma-Mass Spectrometric Determination of Four Arsenic Species in Fruit Juice

D. EAM 4.11 Arsenic Speciation in Rice and Rice Products Using High Performance Liquid Chromatography-Inductively Coupled Plasma-Mass Spectrometric Determination

E. EAM 4.12 Inductively Coupled Plasma - Mass Spectrometric Determination of 18 Elements in Bottled Water (draft available from CFSAN ORS)

F. EAM 4.13 Inductively Coupled Plasma - Mass Spectrometric Determination of Iodine in Food Using Tetramethyl Ammonium Hydroxide Extraction

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5. References

A. (1989). *Recommended dietary allowances* (10th ed.). Washington DC: National Academy Press.

B. (2001). *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.* Washington DC: National Academy Press.

C. U.S. Food and Drug Administration, Center for Food Safety and Applied Nutrition. (2001, May 25). Compliance program guidance manual, Compliance Program Guide:

D. 7304.019 - Toxic Elements in Food and Foodware, Imported and Domestic (FY 03 - 05). Washington DC: U.S. Government Printing Office.

E. U.S. Food and Drug Administration, Office of Enforcement. (Rev. 1995, December 12). Compliance policy guides, sec. 545.450 Pottery (Ceramics); Imported and Domestic Lead Contamination (CPG 7117.07), pp. 296-298.

F. U.S. Food and Drug Administration, Office of Enforcement. (Rev. 1995, December 12). Compliance policy guides, sec. 545.400 Pottery (Ceramics); Imported and Domestic Cadmium Contamination, pp. 294-296.

G. California Proposition-65, Lead, *California Code of Regulations*, Title 22, sec.12805 (b).

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I. Friberg, L., Piscator, M., and Nordberg, G. (Eds.). (1981). *Cadmium in the environment.*

J. Boca Raton, FL: CRC Press.

K. U.S. Food and Drug Administration, (current edition). Compliance policy guides, sec. 540.600 Fish, Shellfish, Crustaceans and Other Aquatic Animals - Fresh, Frozen or Processed - Methyl Mercury (CPG 7108.07), p. 288.

L. Gould, J. H., Capar, S. G., Jacobs, R. M., Plunkett, R. (1988). A quick color test to detect lead release from glazed ceramic and enameled metalware. *Anaytical Letters, 21*, 2145- 2154.

M. Dolan, S. P., Capar, S. G., Jacobs, R. M., Plunkett, R. J., Hawkins, G. S. (1994). Sensitivity of the quick color test for indicating lead release from ceramicware. *Journal of Association of Official Analytical Chemists, 77*, 454-457.

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P. *Journal of Association of Official Analytical Chemists International, 77*, 718-722.

Q. Capar, S. G. (1998, August). Ceramic foodware lead screening using test kits. Laboratory Information Bulletin, LIB No. 4127, *14*, 1-8.

R. Capar, S. G., Anderson, D.L., Hughes, D. D., Jacobs, R.M. (1996). Identification of lead solder on a metal can seam. Laboratory Information Bulletin, LIB No. 4041, *12*(12).

S. U.S. Food & Drug Administration, Center for Food Safety and Applied Nutrition. (1993, January). *Guidance Document for Arsenic in Shellfish.*

T. U.S. Food & Drug Administration, Center for Food Safety and Applied Nutrition. (1993, January). *Guidance Document for Cadmium in Shellfish.*

U. U.S. Food & Drug Administration, Center for Food Safety and Applied Nutrition. (1993, January). *Guidance Document for Lead in Shellfish.*

V. U.S. Food & Drug Administration, Center for Food Safety and Applied Nutrition. (2000, February/March). Ask the regulators, emerging international contaminant issues: development of Codex Alimentarius standards to address these issues. *Food Safety Magazine* (reprinted from February – March 2000 issue).

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X. (1994, September). Mercury in Fish: Cause for Concern? *FDA Consumer Magazine*

Y. (Rev. May 1995).

Z. U.S. Food & Drug Administration, Center for Food Safety and Applied Nutrition. (2001, April). *History of FDA's Total Diet Study*.

AA. Links to additional FDA references:

1. https://www.fda.gov/food/science-research-food/laboratory-methods-food
2. https://www.fda.gov/food/laboratory-methods-food/foods-program-compendium-analytical-laboratory-methods

6. Procedure

6.1. Regulatory

6.1.1 Regulatory Operations

6.2. Sample Preparation

6.2.1 Food Edible Portion

6.2.2 Food Homogenization

6.2.3 Digestion and Separation

6.2.4 Contamination Control

6.3. General Analytical Operations

6.3.1 Safety

6.3.2 Terminology

6.3.3 Uncertainty

6.3.4 Special Calculations

6.3.5 Reference Materials

6.3.6 Performance

6.3.7 Typical Element Concentrations

6.4. Analytical Methods

See Analytical Methods section of EAM.

7. Glossary/Definitions

A. See Glossary section of EAM.

8. Records

Refer to local Quality Management System requirements to determine the necessary records needed to meet accreditation and quality control expectations

9. Supporting Documents

Refer to local Quality Management System requirements to determine the necessary Supporting Document needed to meet accreditation and quality control expectations

10. Document History

Revision #	Status* (D, I, R)	Date	Author Name and Title	Approving Official Name and Title
1.2	R	09/01/2005	LMEB	LMEB
1.3	R	02/06/2012	LMEB	LMEB
1.4	R	02/14/2013	LMEB	LMEB
02	R	06/30/2020	LMEB	LMEB

* - D: Draft, I: Initial, R: Revision

11. Change History

Revision #	Change
1.2	Table of Contents – Titles changed for 6.1.4, 6.2.2, 6.3.1, deleted 6.3.3, Arsenic (total) and Selenium (total) in Food, 6.3.4 now 6.3.3 and 6.3.4 now 6.3.5 Added Section 6.6. Revised Section 6.1; method cited in 6.3.2 A.; method changed in Section 6.3.5 A.
1.3	Table of Contents – Titles changed for 6.2, 6.2.2, 6.2.4., & 6.6; deleted 6.3 6.2 – title changed; “novice” deleted from first sentence 6.2.2 – changed to Qualitative analysis by XRF & added Method 6.2.3 A. & C. – changed to GFAAS,GFAAS method & references 6.2.4 – changed to ICP-OES and changed method reference in A. 6.4 Appendix – changed to 6.2.3 & GFAAS; answers to questions 1., 2., & 6 changed to GFAAS Manual or EAM 4.2
1.4	Header – Division of Field Science changed to Office of Regulatory Science
02	• Removed references to technology no longer used by FDA in elemental analysis • Added technology and methods currently used by FDA in elemental analysis • Linked sections need by analysts for elemental analysis training the FDA Elemental Analysis Manual • Added applicable Compliance Program references • Added internal FDA references • Reformatted to the new LM format

12. Attachments

None