Contents

12.1 Introduction

FDA’s Winchester Engineering and Analytical Center specializes in radioactivity analyses. There are several programs in this regard; “Radionuclides in Foods,” “the Total Diet Study,” and “Radiopharmaceutical Analyses.”

FDA has monitored radionuclides in the food supply for over thirty years. The Public’s concern about health risks due to radionuclide contamination has increased as a result of the nuclear accidents at Three Mile Island (March, 1979) and Chernobyl (April, 1986). The radionuclides in foods program provides long term monitoring of the food supply to establish baselines and show long-range trends with regard to tritium, gamma-ray emitters, and Strontium 90 (Sr-90). This program is overseen by FDA’s Center for Food Safety and Nutrition (CFSAN). The activities herein are coordinated with the radionuclide monitoring efforts of the US EPA and US Department of Agriculture.

The Total Diet Study (TDS) was initiated in the early 1960s to monitor possible contamination of foods by radionuclides resulting from atmospheric nuclear tests. Though atmospheric nuclear tests are now rare and are banned by many countries, other potential sources of radionuclide contamination exist. The foods tested in this program represent the general US food supply and American diet.

Radiopharmaceuticals are an extension of the Pharmaceutical Program. USP as well as NDA/ANDA methodology is utilized to indicate conformance to specifications.

12.2 Radiation Safety

A. Objective

To familiarize the trainee with the safety issues inherent within the radionuclide section's activities. All new hires are given basic radiation safety training covering the following topics: radiation exposure to man, sources of radiation, biological effects of radiation, radiation protection guides, and safety.

The Basic Radiation Safety Course, a more comprehensive study than the new-hire course, covers the topics found in Section 12.2.B

B. Assignment

The Basic Radiation Safety Course, offered to scientists and investigators, includes the following:

1. *Radiation Exposure to Man*
   Identification of natural and man-made sources of radiation and their contribution to background radiation levels are discussed.

2. *Review of atomic structure and radioactivity*
   The basic structure of the atom, atomic nomenclature, units of nuclear mass and energy, the definition of an element and isotope are discussed. The types of radioactive emissions (including alpha particles, beta particles, gamma rays) are defined.

3. *Interaction of radiation with matter*
   Charged particles interactions (ionization, excitation and *bremsstrahlung*), photon interactions with atoms are discussed.

4. *Units of Radioactivity and Radiation*
   Radioactive decay, the rate of radioactive decay (half-life), and units used to measure decay rate are defined.

5. *Correlation of Units of Activity, Exposure, and Biological Effects*
   Units of measure for radioactivity, exposure, dose, and dose rate are defined. Problem solving exercises demonstrate the calculation of exposure rate resulting from an external source of radioactive material. The biological effects (somatic and genetic effects, acute and chronic effects, and threshold and non-threshold effects) are discussed.

6. *Basic Principles of Radiation Detection Instruments, Personnel Monitoring and Radiation Survey Instruments*
   Instruments that measure the presence of radiation include personnel monitoring instruments, survey instruments, and laboratory instruments. The instrument's theory of operation and its applications are discussed. See Section 12.3 for "Laboratory Instruments for Radioactivity Measurement."

7. *Radiation Protection Guides and Dose Limits*
   Radiation protection guides, the "as low as reasonably achievable" (ALARA) principle, and dose limits are discussed. The Nuclear Regulatory Commission, Agreement States, and the Environmental Protection Agency are the principal guide limit authorities.

8. *Principles of Radiation Protection*
   The basic principles of protecting personnel from ionizing radiation will depend upon the type and energy of radiation, and intensity and location of the source. External radiation hazards are controlled through time, distance, and shielding. Contamination control (containment and cleanliness) prevents internal radiation exposure. The purpose of surveys is discussed.

9. *Regulatory Issues:*
   Management of Radioactive Wastes
   The regulations pertaining to the management of radioactive waste are provided by NRC in Title 10, Part 20 (Energy) of the Code of Federal Regulations (CFR).
   Transportation of Radioactive Materials
   The regulations pertaining to the transportation of radioactive materials are provided by NRC in Title 10, Part 20, and also Title 49 (Transportation) of the CFR.
   Receiving of Radioactive Packages
   A model procedure is found in the U. S. Nuclear Regulatory Commission's Regulatory Guide10.8, Appendix L.

C. Questions

1. Define the term “atom.” Explain what the “A” & “Z” numbers of an isotope represent.

2. Discuss the characteristics of alpha-particle decay, beta-particle decay, gamma-ray and x-ray emission. Which types of radiation have an electrical charge? Discuss the difference between x-ray and gamma ray emission.

3. Define “ionization.”

4. Describe the three ways in which photons interact with atoms.

5. What is the difference between genetic and somatic effects of ionizing radiation?

6. Define the threshold theory and the linear non-threshold theory.

7. Describe the principal types of personal dosimetry; discuss the use of control badges.

8. Define the three methods used for minimizing radiation exposure.

9. Define “survey.”

D. References

1. U.S. Food and Drug Administration. (2003). *RH1002 FDA Basic radiation safety course, Basic radiation safety resource manual*. Jefferson, AK.

2. U.S. Food and Drug Administration, Winchester Engineering and Analytical Center. (1995). *Radiation safety manual*. Winchester, MA.

3. Friedlander, G., Kennedy, J., Macias, E., Miller, J. (1981). *Nuclear and radiochemistry* (3rd ed.). New York: John Wiley & Sons.

12.3 Laboratory Radiation Detection Instrumentation

A. Objective

To familiarize the trainee with the radionuclide laboratory equipment.

B. Assignment

The trainer will discuss the location, care, and calibration procedures for equipment found in the radionuclide laboratory. The training exercises include calibration of the instruments defined below.

Typical equipment (including single channel and multichannel analyzers) found in the radionuclide laboratory includes the following:

1. gas-flow proportional counter,
2. low background beta counter (Tennelec),
3. liquid scintillation counter,
4. alpha spectrophotometer,
5. gamma spectrophotometer,
6. ionization chamber,
7. solid state silicon surface barrier detector,
8. high purity germanium detector,
9. sodium iodide (Tl) detector, and
10. x-ray detector.

C. Questions

1. Describe the theory of operation and its application in the laboratory for the following: a proportional counter, a scintillation counter, and a solid state detector coupled to a multichannel analyzer.

2. What is the formula for gamma-ray resolution?

D. References

1. U.S. Food and Drug Administration. (2003). *RH1002 FDA Basic radiation safety course, Basic radiation safety resource manual*. Jefferson, AK.

2. U.S. Food and Drug Administration, Winchester Engineering and Analytical Center. (1995). *Radiation safety manual*. Winchester, MA.

3. Friedlander, G., Kennedy, J., Macias, E., Miller, J. (1981). *Nuclear and radiochemistry* (3rd ed.). New York: John Wiley & Sons.

4. Dean, J. *Analytical chemistry handbook* (1st ed.). New York: McGraw-Hill, Inc.

12.4. Radionuclides in Foods Program

A. Objective

The trainer will provide the various methodologies, reading and reference materials pertinent to radioactivity testing, and on the job training for the radionuclide analyses found in the food program.

B. Assignment

Reserved training food samples (e.g. dried mushrooms, jam, leafy vegetables) are analyzed for gamma emitting radionuclides, Strontium 90, and tritium. More difficult food matrixes (e.g. high fat) and analyses (e.g. plutonium) are introduced as training progresses.

The radionuclide in foods program includes the following analyses:

1. gamma emitting radionuclides,
2. strontium 90,
3. tritium,
4. plutonium, and
5. radium 226 / radium 228.

C. Questions

1. What is the purpose for using the 400 mL fill line in analysis of gamma emitting radionuclides?

2. What is the formula for converting K-40 picoCuries per kilogram (pCi/kg) to natural K grams per kilogram (gm/kg)?

3. Describe the separation methods utilized for Sr-89/90 in the Market Basket Analysis of Strontium 90 method.

4. Describe the sample preparation for the analysis of tritium by liquid scintillation analysis.

5. What purpose does sodium nitrite serve in the plutonium method?

D. Methodology References

1. International Atomic Energy Agency. (1989). Technical Report Series Publication 295.

2. Cunningham, W. C., Anderson, D. L., and Baratta, E. J. (1994). Radionuclides in domestic and imported foods in the United States, 1987-1992. *Journal of AOAC International*, 77(6)**,** 1422-1427.

3. Capar, S. G., and Cunningham, W. C. (2000). Element and radionuclide concentrations in food: FDA total diet study, 1991 – 1996. *Journal of AOAC International, 83*(1) 157-177.

4. Horowitz, W. (Ed.). (current ed.). *AOAC official methods of analysis* (Chap. 13, Radioactivity). Gaithersburg, MD: AOAC International.

5. U.S. Department of Energy. (1979). *Environmental measurements laboratory: procedures manual* (HASL-300, Rev. 1992). New York: U.S. Department of Commerce.

6. U.S. Environmental Protection Agency. (1979). *Radiochemical analytical procedures for analysis of environmental samples*, EMSL-LV-0539 – 17. Las Vegas, NV: U.S. Government Printing Office.

7. American Public Health Association. *Standard examination for the examination of water and wastewater* (20th ed., Pt. 7000, Radioactivity). Washington, DC: American Public Health Association.

8. Baratta, E. J. and Reavey, T. C. (1969, November.-December). Rapid determination of strontium90 in tissue, food, biota, and other environmental media by tributyl phosphate. *Journal of Agricultural and Food Chemistry, 17*(6), 1337-1339.

9. Apidianakis, J.C. (2000). *Determination of strontium-90 in foods* (WEAC SOP RN-2, FDA Total Diet Study).

10. Douglas, G. S. (Ed.). (1967). *Radioassay procedures for environmental samples* (Public Health Service Publication No. 999-RH-27, Ashing Procedures). Washington DC: U.S. Government Printing Office.

11. Mango, P. J., Bratta, E., Ferri, E. (1964). *Northeast Radiological Health Laboratory, analysis of environmental samples, chemical and radiochemical procedures* (NERHL-64-1). Winchester, MA: U.S. Government Printing Office.

12. Troianello, E.J. (1978, October 18). Dehydration of food samples for assay of tritium in free water. *Laboratory Information Bulletin*, No. 1913.

13. Lumsden, E., Baratta, E. (1977, January 31). Isotopic determination of Pu in food ash. *Laboratory Information Bulletin*, No. 2015.

12.5 Radiopharmaceutical Program

A. Objectives

The trainer will provide reading and reference materials pertinent to pharmaceutical and radiopharmaceutical testing, methodology, and on the job training for radiopharmaceutical analyses.

B. Assignment

The trainee will read the ORA Laboratory Manual, Volume IV, Section 3: Drug Analysis.

The USP/NDA methods for radiopharmaceuticals include conventional pharmaceutical analyses and may include the following procedures for measuring radioactivity:

1. assay for radioactivity,
2. radiochemical purity,
3. radionuclidic purity, and
4. radionuclide identification.

The trainee will analyze the simpler technetium cold kits. Samples reserved from previous radiopharmaceutical surveillance studies may serve as training samples (e.g. technetium 99m medronate kit, technetium 99m gluceptate kit). More difficult radiopharmaceuticals, (e.g. Cyanocobalamin Co-57 cobalt tablets, Sodium Chromate Cr-51 solution for injection) will be introduced as the trainee progresses.

C. Questions

1. Define radiochemical purity and radionuclidic purity.

2. Define the term "cold kit." What precautions are to be taken when preparing a cold kit with Tc-99m? What happens when air is inadvertently introduced into the cold

kit?

3. Discuss the theory of operation and use of Tc-99m/Mo-99 generator.

D. References

1. *United States pharmacopoeia and national formulary* (current ed.).
2. *ORA Laboratory Manual*, Volume IV, Section 3: Drug Analysis.

12.6 Quality Assurance and Quality Control

A. Objective

Instrument certification includes a National Institutes of Technology (NIST) Radionuclide Program contract. The contract ships approximately twenty blind radioactive samples to the laboratory. The samples are analyzed, as a minimum, on the ionization chambers.

Proficiency testing for the market basket program includes NIST, NIST traceable, and International Atomic Energy Agency (IAEA) standards. Minimum proficiency testing for the market basket program includes one gamma emitting radionuclide other than K-40, K-40, and Sr-90.

Assignment

The trainee will work with an experienced analyst and receive instruction through reading materials and on the job training. Beginner exercises include a minimum of one gamma-emitting radionuclide standard for the calibration of the ionization chambers and/or High Purity Germanium Detectors, and a strontium performance evaluation sample.

Questions

1. Name additional instrumentation used in the NIST instrument certification program.
2. Define acceptable results for the Market Basket Program proficiency studies. Define the procedure if the Market Basket proficiency study fails

12.7 Answer Key

12.2 Radiation Safety

1. **Define the term "atom."** An atom is the smallest component of an element having the properties of that element. An atom consists of a central nucleus, comprised of positively charged protons and uncharged neutrons, surrounded by negatively charged electrons. The number of protons in the nucleus of the atom determines the identity of the element. The atomic mass number, **A**, is equal to the sum of the number of protons, **Z**, plus the number of neutrons, N, in the nucleus.

2. **Discuss the characteristics of alpha-particle decay, beta-particle decay, and gamma-ray and x-ray emission. Which types of radiation have an electrical charge? Discuss the difference between x-ray and gamma-ray emission.** Alpha-particle decay is characterized by the emission of a highly energetic helium nucleus, or alpha particle, from the nucleus of a radioactive isotope, resulting in the transformation of the isotope to one whose nucleus contains two fewer protons and two fewer neutrons. Beta-particle decay is characterized by the ejection of an ordinary electron from the nucleus of a radioactive isotope, resulting in the transformation of a neutron into a proton in the nucleus. Positron decay, sometimes called beta-plus decay, is characterized by the ejection of a positively charged electron from the nucleus, resulting in the transformation of a proton into a neutron in the nucleus. Gamma rays and x-rays are electromagnetic radiation emitted by atoms following radioactive transformation. Alpha and beta particles and positrons carry charge; gamma and x-rays are uncharged. X-rays and gamma rays are electromagnetic radiation; x-rays originate in the extra nuclear structure of atoms and gamma rays originate in the nuclei of atoms.

3. **Define "ionization."** Ionization is the process of removing an atomic electron from the electric field of the nucleus, resulting in an ion pair consisting of the remaining positively charged atom and the negatively charged electron.

4. **Describe the three ways in which photons interact with atoms.** Photons interact with matter primarily via the following mechanisms: photoelectric effect, Compton Effect, and pair production. In the photoelectric effect, a photon interacts with an atomic electron, resulting in the emission of an electron having energy equal to that of the incident photon minus the binding energy of the electron. The incident photon disappears. In the Compton Effect, a photon collides with an electron resulting in a scattered photon and a scattered electron. The scattered photon has less energy than that of the incident photon, and the difference between the incident and scattered energy of the photon is transferred to the scattered electron. In pair production, a photon of energy greater than 1.02 MeV spontaneously disappears as it passes near a nucleus, resulting in the production of an electron and a positron (an electron-positron pair).

5. **What is the difference between genetic and somatic effects of ionizing radiation?** Genetic effects are those that occur in the descendants of a parent whose DNA molecules are modified due to exposure to ionizing radiation. Somatic effects are those which occur in the exposed individual. Genetic effects may affect subsequent unexposed generations; somatic effects are limited to the exposed individual.

6. **Define the threshold theory and the linear non-threshold theory.** The threshold theory of dose response is used to describe radiation effects that occur only after a minimum, or threshold, dose has been received. The magnitude of the effect increases with the dose received, and there is a clear causal relationship between radiation exposure and the observed effect. The linear non-threshold theory is used to describe the frequency of occurrence of a defined radiation effect as a function of dose received by an exposed population. The plot of frequency of response vs. dose is linear and passes through the origin of the plot.

7. **Describe three types of personal dosimeters worn by individuals for personnel monitoring; discuss the use of control badges.** Personal dosimeters are devices worn by individuals to measure radiation exposure. Three types of personal dosimeters are: pocket meters, film badges, and thermoluminescent dosimeter (TLD) badges. Pocket meters are generally based on an air wall ionization chamber and can either be of the "direct reading" type, where the dose may be read from a scale or other indicator on the device, or the "indirect reading" type, where an instrument is needed to read the dose. Film badges consist of one or more small sheets of photographic film enclosed in a light-tight container that may be affixed to clothing. The exposed film is developed to obtain the radiation dose. TLD badges contain thermoluminescent crystals that absorb and store energy when exposed to radiation, and emit light when heated. The light output is proportional to the radiation dose. The dose is read by heating the TLD crystal in a device equipped to detect the emitted light. Control badge readings are used to correct personal dosimeter readings to more accurately reflect the exposure received by individuals working with radiation. Control badges are generally maintained in an area remote from radiation areas but under similar environmental conditions as those where personal dosimeters are worn.

8. **Define the three methods used for minimizing radiation exposure.** Radiation exposure may be limited by minimizing the time or duration of exposure, by maximizing the distance between the radiation source and the exposed individual, and by maximizing the shielding between the source and the exposed individual.

9. **Define "survey."** A survey is an evaluation of radiological conditions to determine the presence of surface or airborne contamination, unknown sources, or dose rate in the area.

12.3 WEAC Laboratory Radiation Detection Instrumentation

1. **Describe the theory of operation and its application in the laboratory for the following: a proportional counter, a scintillation counter, and a solid state detector coupled to a multichannel analyzer.** A proportional counter consists of a gas-filled chamber containing two electrodes across which an electrical potential is applied. Under the influence of the electric field, ions generated by radiation in the gas are collected, producing an output signal proportional to the energy deposited in the counter by the radiation. Therefore particle identification and energy measurement are possible for any charged particle. A scintillation counter consists of a medium that produces light when ionizing radiation passes through it, and a detector, usually a photomultiplier tube, which amplifies the light and produces an output signal. The scintillator may be solid, liquid, or gas. Photons, neutrons, and charged particles may be detected using scintillation counters. A solid state detector consists of a semiconductor crystal across which a bias voltage is applied. Charges generated in the crystal by radiation are collected and produce a voltage pulse proportional to the energy deposited in the crystal. The pulse-height distribution or spectrum may displayed using a multichannel analyzer (MCA) and consists of a plot of counts versus energy.

2. **What is the formula for gamma-ray resolution?**
   The formula for gamma-ray resolution is:

$$percentage\ resolution = \frac{\Delta E}{E} \times 100$$

   where ΔE = full width at half maximum (FWHM) of the photopeak in energy units, and E = energy of the photopeak.

12.4 Radionuclides in Foods Program

1. **What is the purpose for using the 400-mL fill line in the analysis of gamma-emitting radionuclides?** The 400-mL fill line is the level to which a plastic sample container is filled in order to maintain a constant geometry for all samples counted on the detector. The detector is also calibrated using a radioactive source in an identical plastic container filled to the 400-mL line.

2. **What is the formula for converting K-40 in becquerels per kilogram (Bq/kg) to natural K in grams per kilogram (g/kg)?**
   Each gram of natural potassium (K) contains 31.3 becquerels of K-40; the formula to calculate the amount of potassium based on K-40 is as follows:

$$natural\ potassium\left(\frac{g}{kg}\right) = K\text{–}40\left(\frac{Bq}{kg}\right) \div 31.3\left(\frac{Bq\ K\text{–}40}{g\ K}\right).$$

3. **Describe the separation methods utilized for Sr-90 in the Market Basket Strontium 90 method.** In this method the activity of Y-90, the decay product of Sr-90 present in radioactive secular equilibrium with Sr-90 in the sample, is measured. A known quantity of food homogenate is dried and charred at high temperature, and the ash is dissolved in nitric acid. The acid solution is shaken in a separatory funnel with tributylphosphate and strontium and yttrium carrier solutions. Y-90 is differentially dissolved (or separated from Sr-90) in the organic phase. After a series of procedures, Y-90 as oxalate is deposited onto a paper filter, and assayed using a beta particle counter. The Y-90 activity is then used to calculate the Sr-90 activity in the original food sample.

4. **Describe the sample preparation for the analysis of tritium by liquid scintillation analysis.** A weighed, edible portion of sample is transferred to a special glass distillation tube. An identical tube, used as a water trap, is joined to this tube and to a vacuum pump via an adapter. The sample tube is sealed and mildly heated, and the water trap is evacuated using the pump, and chilled. The two tubes are then joined together via the adapter and water vapor from the sample is gradually collected in the cold trap. The collected water is then mixed with liquid scintillator solution (sometimes referred to as a "cocktail") which produces visible light when ionizing radiation (emitted by tritium) passes through it. The light pulses are detected and counted in the liquid scintillation counter.

5. **What purpose does sodium nitrite serve in the plutonium method?** The addition of sodium nitrite ensures that all of the plutonium is in the Pu^{+4} state. The plutonium is adsorbed onto the anion exchange column in the nitrate form.

12.5 Radiopharmaceutical Program

1. **Define radiochemical purity and radionuclidic purity.** Radiochemical purity is the degree to which a radioactive compound is free of chemical contaminants. Radionuclidic purity is the degree to which a radioactive substance is free of radionuclides other than those declared.

2. **Define the term "cold kit." What precautions are to be taken when preparing a cold kit with Tc-99m? What happens when air is inadvertently introduced into the cold kit?** A "cold kit" is a compound or complex that is combined, or reconstituted, with Tc-99m resulting in a radioactive pharmaceutical. The compound is usually contained in a septum-sealed vial into which sodium pertechnetate solution may be injected by syringe. The vial may also be under vacuum or contain an inert gas. Procedures for reconstituting the kit are specified in the labeling. Precautions to prevent the accidental introduction of air while

adding the pertechnetate solution may be neededd. Air inadvertently introduced into the vial may react with reducing agents or other chemicals in the vial resulting in the production of radiochemical impurities in the drug.

3. **Discuss the theory of operation and use of a Tc-99m/Mo-99 generator.** A Tc-99m/Mo-99 generator contains Mo-99 fixed on an alumina column. Tc-99m, the decay product of Mo-99, is removed, or eluted, from the generator by passing a saline solution through the column, resulting in a sodium pertechnetate solution. The pertechnetate solution may be used to reconstitute cold kits.

12.6 Quality Assurance/Quality Control

1. **Name additional instrumentation certified in the NIST instrument certification program.** Instruments certified using NIST-traceable standards include two Capintec ion chambers, four solid state detectors and computerized spectrometer, the Tennelec beta counter, and the Packard liquid scintillation counter.

2. **Define acceptable results for the Market Basket Program proficiency studies. Define the procedure if the Market Basket proficiency study fails.** (See local laboratory standard operating procedures for the proficiency sample program.)